

# Comparison of Surgical Outcomes in Chronic Otitis Media (Mucosal) following Type 1 Tympanoplasty with and without Cortical Mastoidectomy

Sanjeev Mohanty<sup>1</sup>, Devipriya V<sup>2</sup>, Sreenivas C<sup>2</sup>, Vinay Raj T<sup>2</sup>

## ABSTRACT

**Introduction:** Chronic suppurative otitis media is one of the most common cause of reversible conductive hearing loss in the world especially in developing countries because of poor socio-economic status, poor nutrition, poor hygiene and lack of health education. It affects both sexes and all age groups. Successful outcome of tympanoplasty depends on various factors. This study was conducted to compare surgical outcome in tubotympanic disease following Type 1 tympanoplasty with and without cortical mastoidectomy.

**Material and methods:** A prospective comparative study, comprising of 50 patients with chronic otitis media mucosal type who were randomly divided into two equal groups with 25 patients undergoing type 1 tympanoplasty and 25 patients undergoing type 1 tympanoplasty with cortical mastoidectomy.

**Results:** In our study, there was no significant difference in the graft uptake rate or the hearing improvement in both these groups.

**Conclusion:** Cortical Mastoidectomy is recommended in patients of Chronic Otitis media (Mucosal) with subtotal perforations. The graft uptake rate is similar in both the groups of patients with central perforation (involving one or two quadrants). In successful graft take up, results of hearing improvement and graft mobility are similar with or without mastoidectomy. Possibility of finding mastoid antral pathology is more in patients having Chronic otitis media (mucosal) with sub total perforation as observed in this study.

**Keywords:** Cortical mastoidectomy, Tympanoplasty with mastoidectomy, Tympanoplasty

Chronic otitis media – Mucosal type

## MATERIAL AND METHODS

For this study 50 patients having Chronic otitis media with central perforation were selected, based on the following inclusion and exclusion criteria. Ethical clearance was obtained from the institutional ethical board and informed consent was obtained from the patients before the start of the study.

All patients with dry and quiescent ears were included in the study. Chronic otitis media squamous type, traumatic perforations, previous ear surgeries and patients having sensorineural hearing loss were all excluded.

The 50 patients were randomly divided into two equal groups with 25 patients under going type 1 tympanoplasty and 25 patients undergoing type 1 tympanoplasty with cortical mastoidectomy

After a proper selection and evaluation, the patients underwent the standardized procedure of type 1 tympanoplasty with or without cortical mastoidectomy

Per operatively the middle ear and mastoid cavity were inspected for the disease process such as; polypoidal mucosa, granulation tissue, fibrous tissue, glue and the peroperative findings were recorded. The disease was cleared from the middle ear and the mastoid antrum and a type 1 Tympanoplasty with or without cortical mastoidectomy was done for the subjects according to their group.

All the cases were taken up under general anesthesia and the post aural approach was used. Temporalis fascia graft placed by underlay technique for the repair of the tympanic membrane in all the patients.

Post operatively all the patients were discharged on the 2<sup>nd</sup> post-operative day. Patients were started on systemic antibiotics, analgesics and antihistamines for duration of one week. Post operatively all the patients were followed up for a total of 6 months with regular intervals at 1<sup>st</sup>, 3<sup>rd</sup> and 6<sup>th</sup> month.

Post operatively all the study patients were assessed for the status of the graft, mobility of the graft and the hearing improvement. Pure tone audiogram was done for all the patients at the end of 6 months to assess the level of hearing improvement.

<sup>1</sup>Professor, <sup>2</sup>Assistant Professor, Sri Ramachandra University, Chennai, India

**Corresponding author:** Dr Sanjeev Mohanty, Professor and HOD, Department of ENT, Head and Neck Surgery, Sri Ramachandra University, Chennai – 600116, India

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## STATISTICAL ANALYSIS

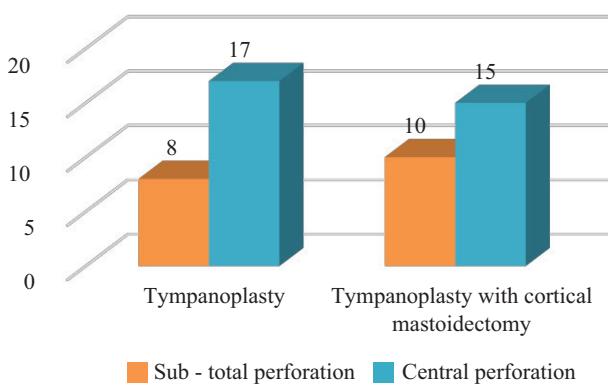
SPSS version 21 was used for the statistical analysis. Student t test and Pearson's chi-squared test were applied to compare the symptoms in both the groups. Categorical variables were analyzed using descriptive statistics.

## RESULTS

The type of perforation was classified as central and sub total perforation. In the tympanoplasty group 17 out of the 25 had central perforation and 8 out of 25 had sub total perforation (figure-1). In the cortical mastoidectomy group, 15 out of the 25 patients had central perforation and 10 out of 25 patients had sub total perforation. The P value calculated was 0.77 which was statistically insignificant.

P Value for the graft uptake was calculated in each group, using the Pearson's chi-squared test with yate's continuity correction, was found to be 0.74 which was not significant as shown in table-1. The percentage of mobility of the graft (post-operatively) in Group A was 48% and in Group B was 28%. Students independent 't' test was used to calculate significance of mean values of the pure tone hearing levels between the 2 groups as shown in table-2.

The pre op mean and standard deviation of pure tone average in tympanoplasty group was higher than the mean pre op value in the cortical mastoidectomy group. However there was no significant difference in mean P value, which was 0.60 and was



**Figure-1:** Type of perforation

insignificant. The mean post op pure tone average value and standard deviation in the 2 groups were  $30.4 \pm 5.8$  and  $29.6 \pm 8.7$ . The p value calculated was 0.60 and 0.71 pre and post operatively and was statistically insignificant.

Table-3 shows the comparison of the pre operative mean and the standard deviation of pure tone average values within each group

Student paired T Test was used to calculate the P value and was found to be  $< 0.001$  which was statistically found to be significant which meant there was significant improvement in the post operative hearing levels in the 2 groups

## DISCUSSION

Chronic suppurative otitis media owing to poor socio economic status and poor environmental conditions account for morbidity in about 5 % of the total population. ENT surgeons by performing a corrective surgery for chronic otitis media can change the lifestyles of the patient profoundly. The medical line of management only can lessen the severity of the symptoms.

The age and sex of the patients in both the groups were comparable and bore no statistical significance. Pearson's chi-squared test was applied to compare the symptoms in both the groups and were found to be comparable i.e. were statistically insignificant.

The type of perforation was classified into central and subtotal. 8 (32%) of the patients in the tympanoplasty group and 10 (40%) in the cortical mastoidectomy group had subtotal perforation. The presence of polypoidal tissue in the middle ear was compared between both the groups and the P value calculated was 0.05 and was found to be statistically significant. Presence of myringosclerosis was statistically insignificant when compared between both the groups.

The pre operative hearing levels were divided into 20-30db and 30-45 db hearing loss categories on the basis of pre operative pure tone audiogram. In tympanoplasty group 6 patients had pure tone average within the 20-30 db and 19 patients in 30-45 db level. In the mastoidectomy group there were 16 patients with pure tone average between 20-30 db and 9 patients within 30-45 db.

In tympanoplasty group 10 patients per operatively had polypoidal mucosa in the middle ear, 7 had adhesion in the

Group	Graft taken up	Graft rejected	Mobility
Tympanoplasty	20 (80%)	5 (20%)	12 (48%)
Tympanoplasty with cortical mastoidectomy	18 (72%)	7 (28%)	7 (28%)

**Table-1:** Graft rejection rate

Group	Tympanoplasty	Tympanoplasty with cortical mastoidectomy	P – Value
	Mean +/- standard deviation	Mean +/- standard deviation	
Pre op	$34.3 \pm 5.8$	$33.3 \pm 7.0$	0.60
Post op	$30.4 \pm 5.8$	$29.6 \pm 8.7$	0.71
Change	$3.9 \pm 3.4$	$3.8 \pm 4.7$	0.88

**Table-2:** Pure tone average of both groups

Group	Pre op Mean +/- std	Post op Mean +/- std	Change Mean +/- std	P Value
Tympanoplasty	$34.3 \pm 5.8$	$30.4 \pm 5.8$	$3.9 \pm 3.4$	$<0.001$
Tympanoplasty with cortical mastoidectomy	$33.3 \pm 7.0$	$29.6 \pm 8.7$	$3.8 \pm 4.7$	$<0.001$

**Table-3:** Pure tone average of both groups

region of the oval window, round window and in the ossicular chain thus reducing the overall mobility of the chain (figure-2). In the cortical mastoidectomy group 16 patients had polypoidal tissue per operatively in the middle ear, 12 patients had antral disease blocking the patency of the aditus ad antrum, 5 patients had adhesions and 3 patients had glue in the antrum.

The percentage of graft uptake in tympanoplasty group at first follow up was 68 % and in the mastoidectomy group was 72 %. Of the 5 patients who had graft failure in the tympanoplasty group, 4 of them had polypoidal tissue in the middle ear with subtotal perforations and one patient had central perforation with normal middle ear mucosa. Of the 7 patients who had graft failure in the mastoidectomy group, 4 of the patients had subtotal perforation and 3 of them had central perforation. Out of them, 6 of these patients had antral disease and polypoidal tissue in the middle ear (figure-3).

Pearson's chi-squared with Yate's continuity correction was used to calculate the p value, which was 0.74 and statistically significant. The graft failure in the tympanoplasty group can be attributed to the presence of the polypoidal tissue and the subtotal perforation in which the presence of the antral disease was more likely.

A post-operative hearing improvement of 10 db after 6 months was considered to be a significant improvement in hearing levels. In our study 6 patients from the tympanoplasty group and 8 patients from the mastoidectomy group showed more than 10 db improvement.

The mean post op pure tone average value and standard deviation in the 2 groups was  $30.4 \pm 5.8$  and  $29.6 \pm 8.7$ . The P value calculated was 0.60 and 0.71, pre and post operatively and were statistically insignificant. Hence the hearing improvement in both the groups post operatively is similar irrespective of the procedure done.

In a study conducted by Mutoh t et al comparing the results efficacy of mastoidectomy in methicillin resistant staph aureus and methicillin susceptible staph aureus infected otitis media, mastoidectomy had significantly better results concerning post operative complications in discharging ears with MRSA infected chronic otitis media.<sup>4</sup>

In a separate study by Rickers J, Petersen CG comparing the long term follow up evaluation of mastoidectomy in children with non cholesteatoma chronic otitis media they concluded that mastoidectomy in these patients should be kept as a last resort when intensive conservative treatment and myringoplasty.<sup>5</sup>

In another similar study Balyan FR et al compared the graft success rate and the final functional hearing outcome and found tympanoplasty without mastoidectomy as preferable treatment modality in non cholesteatoma ears ( $p > 0.05$ ).<sup>6</sup> Vijayendra et al advocated the opening of the antrum to prevent the graft failure in 2-3 % of patients.<sup>7</sup>

In their retrospective analysis of 251 cases of non cholesteatoma cases of chronic otitis media by Y. Mishiro et al who underwent tympanoplasty with and without mastoidectomy, graft success rates were 90.5 % in group A and 93.3% in group B. The rates of the post-operative air bone gap within 20db were 81.6% in Group A and 90.4% in Group B, without a statistically significant difference.<sup>8</sup>

Glasscock had reported a 96% success rate with underlay technique. 86% graft uptake by underlay technique was found

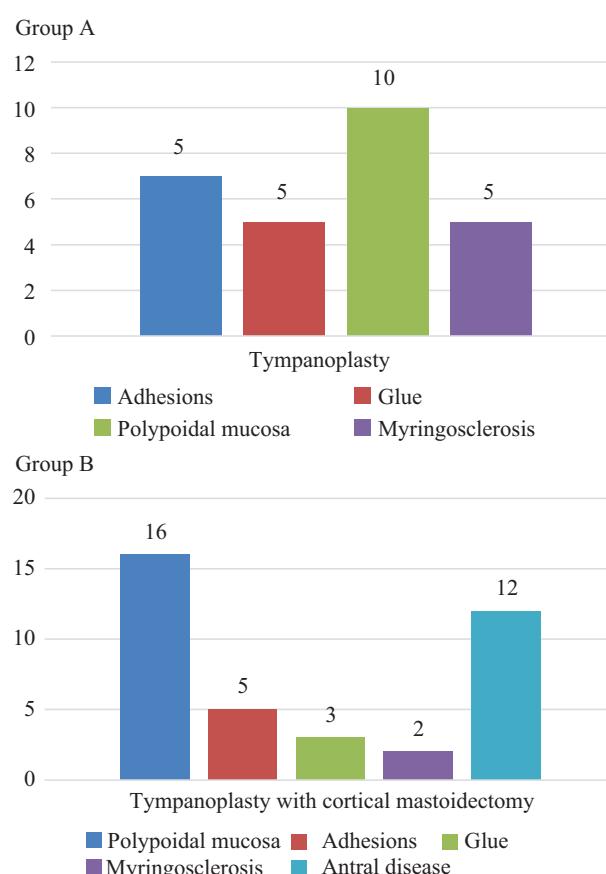


Figure-2: Per operative findings

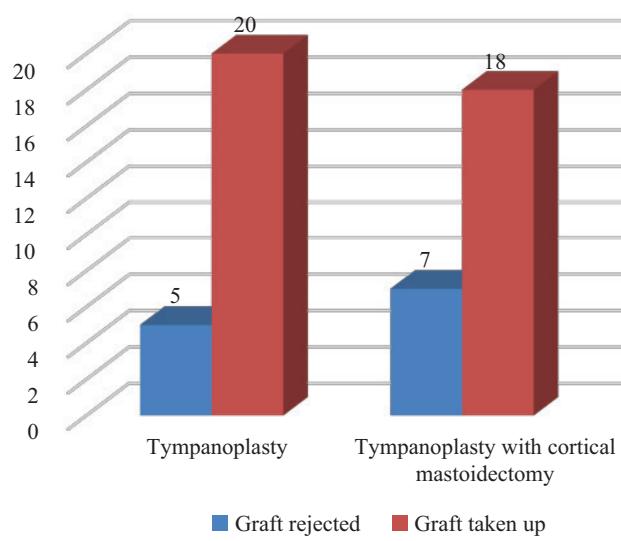


Figure-3: Graft take up

by Rizer.<sup>10</sup> Smyth and Patterson in their report of 153 patients showed it to be 78 % with a longer follow up.<sup>11</sup> In our study graft take up rate in patients who underwent only tympanoplasty was 80% and those with tympanomastoidectomy was 72%.

## CONCLUSION

Cortical Mastoidectomy is recommended in patients of Chronic Otitis media (Mucosal) with subtotal perforations. The graft uptake rate is similar in both the groups in patients with central perforation involving one or two quadrants.

In successful graft take up, results of hearing improvement and graft mobility are similar with or without mastoidectomy.

Possibility of finding mastoid antral pathology is more in patients having Chronic otitis media (mucosal) with sub total perforation as observed in this study.

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# Ultrasonographic Study of Fetal Anomalies in Hydromnios Complicating Pregnancy

P. Ananthalakshmi<sup>1</sup>, P. Sarweswar Reddy<sup>2</sup>

## ABSTRACT

**Introduction:** Polyhydromnios has been recognized as a clinical landmark of congenital malformations and impending severe perinatal compromise. So the present study aims to ascertain the incidence of various etiological factors, maternal complications and associated foetal anomalies in cases of polyhydromnios.

**Material and Methods:** The present prospective study conducted for a period of 1 year on fifty pregnant women with polyhydromnios which was clinically suspected. All cases of overdistended uterus were taken for study. The study was conducted over a period of 1 year.

**Results:** The present study comprised of fifty cases of polyhydromnios confirmed by ultrasound and looked for congenital malformations. Most of these patients belonged to low socioeconomic status about 70%. Most of these cases were in age group of 20-30 years. Coming to parity most of these cases were multiparous women, among them grandmulti were about 8%. Teenage pregnancies were about 22%. Among the 50 cases studies most of these were mild variety, severe variety was 8% of cases. Toxaemia of pregnancy was observed in 22%.

Rh isoimmunisation was found in 2% of cases. Anaemia is the most common associated medical condition seen in all grades of hydromnios, (which was seen in 64% of cases). Multiple pregnancy was observed in 8% of cases. Twin pregnancy was 6%, out of which Monozygotic twins were 4%, Dizygotic twins were 2%, Triplets were 2%. In this study the overall incidence of congenital malformation was 20%. Most commonly seen congenital anomalies were open neural tube defects.

**Conclusion:** This study ascertained the incidence of various etiological factors, maternal complications and associated foetal anomalies of polyhydromnios. The technical innovations in the medical field should be utilised properly.

**Keywords:** Ultrasonography, Polyhydromnios, congenital malformation.

## INTRODUCTION

Prenatal diagnosis of volume of amniotic fluid when done by physical examination alone may be difficult and is frequently inaccurate. Amniotic fluid and its distribution throughout the uterine cavity is readily identified by ultrasound examination. This objective method of evaluation may be used to evaluate amniotic fluid volume and its adequacy. Semi quantitative estimation of amniotic fluid volume by an ultrasound method is a component of fetal bio-physical profile scrutiny.<sup>1</sup>

Hydromnios is associated with maternal diseases and fetal conditions which may require active intervention, planning and management. Apart from inherent problems of hydromnios such as unstable lie, malpresentation, premature rupture of membranes, cord prolapse, uterine inertia, accidental haemorrhage, post partum haemorrhage and retained placenta, the overall incidence of congenital anomalies in hydromnios is also high, ranging from 15-20% reported by several authors

throughout the world.<sup>3</sup> Perinatal death rate is 80-90% in those cases where the hydromnios is associated with congenital anomalies of fetus indicating poor prognosis. Ultrasound is playing an important role in the antenatal diagnosis and management of the congenital anomalies in utero.

Early detection of defects of fetus by ultrasound allows decision to be made regarding continuation of pregnancy, termination of pregnancy, or in utero treatment, mode of delivery, place of delivery, post-partum management of problems like P.P.H, retained placenta and counseling of the parents regarding management of the problem, prognosis and risk of recurrence and at the same time we can give genetic counseling to the couple. An additional important application is the detection of deformation secondary to uterine constraining. If the fetus is in an unusual lie, a careful ultrasound examination should be done also to determine if deformation related to abnormal positioning are present. At the same time we can also know the fetal wellbeing and maturity of the fetus.

The present study aimed to ascertain the incidence of various etiological factors, maternal complications and associated foetal anomalies in cases of polyhydromnios

## MATERIAL AND METHODS

The present prospective study was conducted on fifty pregnant women with polyhydromnios which were clinically suspected and confirmed by USG. All cases of over distended uterus (clinically suspected hydromnios were scanned, those cases confirmed by ultrasound) were taken for study. The study was conducted over a period of 1 year from July 2013 to June 2014 in Government maternity hospital, Hyderabad. Ethical clearance was obtained from the Hospital Ethical Committee and informed consent was taken from the patients before the start of the study. Ultrasound that was used in this study was real time ultrasound scanner using linear array transducer with the patient in supine position.

The cases were taken after clinical examination. The criteria for diagnosing hydromnios was single amniotic fluid pocket vertical diameter 8 cm and more than 8 cm at any period of gestation on ultrasound examination. The cases were graded into mild, moderate and severe according to the definitions proposed by Hill and associates from Mayo's clinic depending upon the

<sup>1</sup>Assistant Professor, Government Maternity Hospital, Petlaburj, Hyderabad, <sup>2</sup>Associate Professor, Kurnool Medical College, Kurnool, India

**Corresponding author:** Dr. Ananthalakshmi, Assistant Professor, Government Maternity Hospital, Petlaburj, Hyderabad, India

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size of the amniotic pocket measured in four quadrants with electronic calipers of the ultrasound system. Mild hydromnios is 25-29 cms, Moderate hydromnios is 30-34 cms, Severe hydromnios is 35- or more. These patients that were taken under study were followed until delivery to estimate the complications during delivery and to know fetal outcome.

## STATISTICAL ANALYSIS

Microsoft office 2007 was used for the making tables. Descriptive statistics like mean and percentages were used to infer data.

## RESULTS

Table-1 shows the grading of hydromnios based on age distribution, Socio-Economic status, parity, amniotic fluid pocket vertical diameter, various religions, history of consanguinity. In the present study majority of women are between the age of 20-25 years of about 46% and next commonly seen age group was being 26-30 years. Between age group 20-30 the number of cases observed were 72%. It was observed that majority of these patients belonged to class 3 and class 4 i.e. of about 94%. In this study regarding gravidity of these patients high incidence of hydromnios was seen in primi gravida (30%) and in 2<sup>nd</sup> gravida about 28%, in 3<sup>rd</sup> gravida about 22%, in 4<sup>th</sup> gravida about 12% and in grand multi about 8%. In present study incidence of hydromnios of mild variety is being 62% and severe variety is only 8%. In all cases of severe hydromnios association of congenital anomalies of fetus was seen. In this study, majority of the patients belonged to Hindu religion (70%), next were muslims (28%), least commonly observed in Christian patients (2%). History of consanguineous marriage was present in about 16 cases of which about 9 cases were 1<sup>o</sup> relative (56.2%) and 7 were 2<sup>o</sup> relatives (43.8%).

Table-2 shows grading of hydromnios in relation to gestational age, in relation to polyhydromnios, in relation to number of fetuses, based on maternal condition. In the present study, the various gestational periods at random was taken and most of the women were between 33-36 weeks (32%), between 28-32 weeks (14%). In the present study most of the cases were idiopathic ie, about 60% of cases, congenital anomalies were found in about 20% of cases, 8% were multiple pregnancies, 10% diabetic and 2% erythroblastosis foetalis. Most of the cases in this study hydromnios was seen with singleton pregnancies i.e. about 92%. Among multiple pregnancies twins were seen in 6% and triplets 2%, among twins monozygotic twins were 4% and dizygotic twins were 2%. In the present study about 64% of the patients had anaemia. The others maternal condition observed in this study were diabetes 10%, Rh isoimmunisation 2% and urinary tract infection in 2% of the cases.

Out of 10 cases of congenital anomalies 4 cases (40%) were anencephaly. 3 cases (30%) of anencephaly are associated with meningo myelocele. Out of 10 cases, 4 cases are hydrocephalus, 30% associated with meningocele, cleft lip, cleft palate and one case with absent ears. The anomalies that were not detected on ultrasound examination but detected at the time of birth were absence of ears and meningocele (Table-3). In the present study among 50 cases of polyhydromnios studied, total number of congenital anomalies were 10, out of which 1 case was not detected by ultrasound. It was missed, making the ultrasonic

Age Group (in years)	Number of cases	Percentage
15- 19	11	22%
20-25	23	46%
26-30	13	26%
31-35	01	2%
36-40	02	4%
Socio-Economic Status		
Class-1	03	6%
Class-2	--	--
Class-3	17	34%
Class-4	30	60%
Parity		
Primi	15	30%
2 <sup>nd</sup> gravid	14	28%
3 <sup>rd</sup> gravid	11	22%
4 <sup>th</sup> gravid	06	12%
Grand Multi	04	08%
Liquor		
Mild (25-29 cms)	31	62%
Moderate (30-34 cms)	10	20%
Severe (35 and above)	4	8%
Religion		
Hindus	35	70%
Muslims	14	28%
Christians	01	02%
History of consanguineous marriage		
Absent	34	68%
Present	16	32%
In 1 <sup>st</sup> degree relatives	09	56.2%
In 2 <sup>nd</sup> degree relatives	07	43.8%

Table-1: Demographic data

Gestational Age (weeks)	Number of cases	Percentage
0-28	07	14%
28-32	07	14%
33-36	16	32%
37-40	20	40%
Cause		
Unknown Causes (Idiopathic)	--	60%
Congenital malformation of foetus	--	20%
gestational diabetes	--	8%
Erythroblastosis Foetalis	--	10%
Acute Hydromnios	--	02%
Gestations		
Single ton pregnancies	46	92%
Twins	03	08%
Monozygotic twins	02	04%
Dizygotic twins	01	02%
Triplets	01	02%
Maternal condition		
Anaemia	--	64%
Toxemia of pregnancy	--	22%
Diabetes	--	10%
Rh isoimmunisation	--	02%
UTI	--	02%

Table-2: Grading of hydromnios

accuracy in detecting congenital anomalies of the fetus was being 90%.

Structural Anomaly	Detected by U.S.G	Found at birth	Not detected by U.S.G
Anencephaly	7	--	--
Meningomyelocele	3	1	1
Hydrocephalus	4	--	--
Encephalocele foetal ascites	1	--	--
Clift lip, cleft plate	1	--	--
Ears Absent	--	1	1
Polydactyly	--	--	--
Trachio Oesophageal fistula	--	--	--
Posterior urethral valves	--	--	--
Hydronephrosis congenital talipes, equinovarus	--	--	--
Total	16	2	2
Studies	Detected	Not detected	Accuracy
50	10	1	90%

**Table-3:** Structural anomalies

Mode of delivery	Number of cases	Percentage
Abdominal L.S.C.S	11	22%
Vaginal	39	78%
Aided	7	18%
Un-aided	32	82%
Complications		
Premature rupture of membranes	4	8%
Abruption placenta	2	4%
Hypotonic uterine inertia	2	4%
Atonic post partum haemorrhage	6	12%
Adherent placenta	36	72%
Intra Uterus deaths		
Preterm foetus <37 weeks	30	60%
Mature foetus ≥37 weeks	20	40%
Birth Weight (Kgs)		
1-1.5	10	20%
1.5-2.0	13	26%
2.0-2.5	15	30%
2.5-3.0	08	16%
3.0-3.5	02	04%
3.5-4.0	02	04%
Cause of deaths		
Congenital Anomalies	90	18%
Incompatible with life prematurity	05	10%
Birth trauma	02	04%
Intra uterine growth retardation	01	02%

**Table-4:** Mode of delivery

Table-4 shows mode of delivery in 50 cases of polyhydromnios, complications during delivery, term and preterm labour, intra uterus death, birth weight of foetuses, various causes of prenatal deaths. Regarding the mode of delivery in these cases 11 cases were delivered by lower segment cesarean section, 39 cases were by vaginal delivery, out of which 7 cases (18%) were by forceps deliveries and vacuum extractions and rest of them 32 cases (82%) were normal vaginal deliveries. In the present study it was observed as intra uterine death in 6% of cases and preterm fetuses in 60% of cases and mature fetuses in 40% cases. Among them 31 were male fetuses 29 were female fetuses. The birth weight of fetuses in the present study were as follows: Between 1-1.5 kg 20%, between 1.5-2.0 kg 26%, between 2-2.5 kg 30% (higher incidence) between 2.5-3 kg 16%, but 3-3.5 kg 4% and between 3.5-4 kg also 4%. In majority of the cases the perinatal

death was found to be due to prematurity (34%). In the rest of the cases the death were due to congenital anomalies incompatible with life (20%), birth trauma (6%) and dysmaturity 2%.

## DISCUSSION

The present prospective study comprised of fifty cases of polyhydromnios that were taken from the obstetrics department of government maternity hospital petlaburj hyderabad and which were confirmed by ultrasound only were taken for the study. All these 50 cases were screened for congenital malformation of the fetus and the results were given in detail. Out of 50 cases studies 46% were in the age group of 20-25 years. 26% between 26-30 years 22% below 19 years, 2% between 31-35 years and 4% in 36-40 years age group. According to the religion hindus were 70%, muslims 28 % and Christians 2%. Majority of the patients in this study belonged to low socio economic status 60% and rest are middle class (34%) and higher class (6%). Regarding the gravidity 70% were multigravidae, 30% were primigravidae and 8% of grand multis. These cases of hydromnios were graded by detection of vertical diameters of amniotic fluid pockets by ultrasonogram. It was observed that mild hydromnios (25-29 cms) in 20% of cases and severe hydromnios (35 cm and above) in 8% of cases was present. Most of these patients were from rural areas (Table-1). The present study was correlated with the study of Hill and his colleagues from mayo's clinic.<sup>4</sup> According to Carlson DE<sup>5</sup> the criteria for diagnosing hydramnios was amniotic fluid pocket size 8cm or more at any period of gestation. Regarding the various ethological factors found in hydromnios in the present study no cause was found in 60% of cases and in 40 % of cases the following were probable causes. Congenital malformation 20% diabetes 10% multiple gestation 8% and Rh isoimmunisation in 2% of the cases. Maternal conditions associated with hydromnios in the present study were anaemia 64%, toxæmia of pregnancy 22% other maternal conditions that were associated with polyhydromnios was 2% of cases with Rh isoimmunisation and others 2% with urinary tract infection. In the present study singleton pregnancies was found in 92% of cases and twin pregnancies in 6% and triplets in 2% (Table-2). Out of 3 cases of twin pregnancies 2 were monzygotic twins and 1 dizygotic twins. So hydromnios seems to be more common in monozygotic twins. Hydromnios was found in these cases at about 30-32 weeks of gestation and these cases were managed by bedrest and haematinics. Among 4 cases of multiple gestation, 2 cases of twins had uneventful

vaginal deliveries at 37 to 38 weeks of gestation. The weight of these babies were between 1.8kg to 2.3kg and they were healthy. There was no perinatal mortality observed in these cases. One case had preterm labour at 35 weeks of gestation and both babies were alive with birth weight 1.5kg and 1.2kg. another case of triplets was undiagnosed and was misdiagnosed as twins three babies were alive at birth agar 2-4 and birth weight 1kg, 1.2kg, and 1kg.<sup>2</sup> This case had preterm labour at 33 weeks gestation and three babies died of prematurity. The amniotic fluid pocket vertical diameter in Hill study<sup>7</sup> was mild 80% moderate 17% severe 5%. Beverly Hashimoto and colleagues<sup>8</sup> in their study of ultrasound evaluation of polyhydromnios – twin gestation was identified in 25% of cases; but in present study the incidence was some what low ie, 8%. According to the incidence of congenital malformation in twin pregnancy itwas found to be 6-7% but in the present study there was no congenital anomaly detected in multiple gestation. they also stated that polyhydromnios associated with monozygotic twins, the incidence of congenital anomalies of the fetus was high. As such these patients must be closely scrutinized to exclude congenital anomalies of fetus. Another study of Stoll CG et al<sup>9</sup> shows that the frequency of congenital malformation was nearly twice in multiple pregnancies, when compared to singleton pregnancies. In this study the association of diabetes with polyhydromnios is being 25-50%. Among the 5 cases, 2 cases were clinically established insulin dependent diabetes mellitus. One patient's blood sugar was under control. One patient was on insulin therapy throughout the pregnancy. She had a bad obstetric history. (4<sup>th</sup> gravida with previous 3 pregnancy losses.) Patient had intrauterine growth restriction. Pregnancy was terminated at 38 weeks of gestation by elective L.S.C.S in view of B.O.H and I.U.G.R. an alive female child with dysmaturity weighting 2.5 kg was delivered and the baby is alive and well. Other cases of diabetes were under control with diet alone. Patients had uneventful deliveries at term, babies were mature, alive and weighing about 2-2.5kg each. The gross structural fetal anomalies detected in this study were 20%, most common anomalies that were observed in polyhydromnios were being open neural tube defects. Out of 10 cases of congenital anomalies that were detected, 6 cases were anencephaly out of which 2 cases were associated with menigomyelocele, 3 cases were hydrocephalus, out of which 1 case had absent of ears and eyes along with hydrocephalus. Remaining one case with hydropsfetalis (Table-3).

All anencephalus cases were accurately diagnosed by ultrasonogram (100%). In all these, the pregnancies were terminated soon after diagnosis. All were female fetuses. Over all accuracy rate of ultrasonography to detect structural abnormalities of the fetus in this study was 90% whereas Hotta M<sup>10</sup> reported the incidence as 75%. In the present study 3 cases of hydrocephalus were observed. All were diagnosed antenatally by ultrasonogram out of these 3 cases 2 cases presented as cephalic and one presented as breech. In cases of cephalic presentations CSF tapping was done and delivered subsequently. 1 patient had atonic P.P.H which was managed by the routine measures. 2 case of mild hydrocephalus detected in the present study were associated with menigomyelocele which was not detected ultrasonographically. One case of hydrocephalus thatwas detected in the present study, ears and eyes were absent with cleft lip and palate. One case of fetal

ascites was detected in this study. Out of 50 cases, 78% had vaginal delivery and the rest of 22% had caesarean section. Indication for caesarean section in these cases was mostly obstetric cause. Among 50 cases, 36% had preterm vaginal deliveries and rest of 64% had term deliveries. The gross perinatal mortality encountered in this study was 34%. The various causes for perinatal mortality was being congenital malformations incompatible with life in 1 case, Birth trauma in 2 cases; prematurity in 5 cases; dysmaturity in 1 case (Table-4).

## CONCLUSION

This study ascertained the incidence of various etiological factors, maternal complications and fetal anomaliesassociated with polyhydromnios. The technical innovations in the medical field should be utilised properly. At least all the Government maternity Hospitals should be provided with high resolution ultrasound units and trained technical personnel so that routine ultra sonography will be offered to all the antenatal patients.

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# Closure of Relapsed Spaces with Composite Lingual Buttons – Two Case Reports

Rasool Karim Nizaro Siyo<sup>1</sup>, Binu Purushothaman<sup>2</sup>, Sameer Cherote<sup>3</sup>, Rahul. C. S<sup>3</sup>

## ABSTRACT

**Introduction:** It is interesting to note that patients who have strictly followed retention protocols and those who have violated the same have met with relapse in varying degrees. The reasons can also be varied like, periodontal ligament traction, continued abnormal growth pattern after orthodontic therapy, lack of adequate stabilization of teeth by surrounding bones in new position etc. The correction of relapsed malocclusions can be done with simple procedures like composite lingual buttons.

**Case report:** Two patients one female aged 27 years and one male 29 years came to department of orthodontics with complaint of anterior spacing after treatment with fixed appliance therapy and chief complaint of open bite and spacing between upper and lower anteriors respectively. Both patients were treated with composite lingual buttons and satisfactory results were obtained.

**Conclusion:** In this era of peak advancement in orthodontic technology with lasers, self-ligating brackets, lingual braces, CAD/CAM technology, nanotechnology and robotics orthodontists should be aware of or should not ignore such simple, economical and effective techniques to tackle certain situations and ward off few disappointed patients to retain and uphold our faith in the society.

**Keywords:** Composite lingual button, relapse, Orthodontics, invisible

## INTRODUCTION

It is interesting to note that patients who have strictly followed retention protocols and those who have violated the same have met with relapse in varying degrees.<sup>1</sup> The reasons can also be varied like

1. Periodontal ligament traction
2. Continued abnormal growth pattern after orthodontic therapy.
3. Lack of adequate stabilization of teeth by surrounding bones in new position.
4. Muscular imbalance at the end of orthodontic therapy.
5. Cause of malocclusion un-eliminated at the end of treatment.
6. Third molar eruption after the orthodontic treatment leading to late anterior crowding.

A simple technique to close relapse of anterior spacing in pre-treated cases can be done with composite lingual button as follows. Patient having anterior spacing with adequate incisal clearance is considered ideal case.

## Procedure

- a. **Fabrication of composite lingual button<sup>2</sup>:** After appropriate case selection 6 elastic separators are placed on a mixing pad. A cut is made on each separator with scalpel to facilitate easy removal after curing it on teeth. Each separator is filled with flowable composite and cured for

ten seconds (Figure-1).

- b. **Teeth preparation:** Palatal / lingual surfaces of selected anteriors are properly prophylaxed, and then etched with 37% phosphoric acid for 10-15 seconds and dried properly. Bonding agent is then applied and cured. A thin amount of flowable composite is applied on the prepared teeth surface. After completing these procedures the cured composite buttons are placed with gentle pressure to remove excess composite and cured for 10 seconds on each side. The separator can be removed at this stage (Figure-2). The pre-cut made on the separator facilitates easy removal. The space occupied by the separator forms the groove for E-chain engagement (Figure-3). The same procedure is repeated in the lower arch if the case demands. Patient to be reviewed after 1 week. Change of E-chain can be considered if necessary.

In the subsequent visits after correction, replace the E chain with ligature wire in figure of eight mode around composite button to form a permanent lingual retainer. Either prefabricated invisalign buttons or bondable metal buttons can be used as alternatives to composite.

Cases with mild to moderate anterior spacing can also be managed by the same method. Cases without adequate incisal clearance can be done by increasing the occlusal clearance with composite on the functional cusps.

## CASE REPORT

### Case 1

A female patient aged 27 years came to KMCT dental college with complaint of anterior spacing after treatment with fixed appliance therapy (Figure-4). She was very much reluctant to wear braces or removable appliance again. The option of closure of anterior spaces with composite lingual buttons was offered and complied by the patient. Since spacing was largely confined to, 11, 12, 21 and 22 lingual composite buttons were placed only on them.

At 2nd week almost half of the space was closed. Composite lingual buttons was given on lingual side of all lower anteriors. The elastomeric chain was replaced for upper anteriors and newly engaged for lower anteriors. During 3rd week only negligible space was remaining, which was closed by the 4th

<sup>1</sup>Professor, <sup>2</sup>Professor and Head, <sup>3</sup>Postgraduate Student, Department of Orthodontics, K.M.C.T Dental College, Calicut, Kerala, India

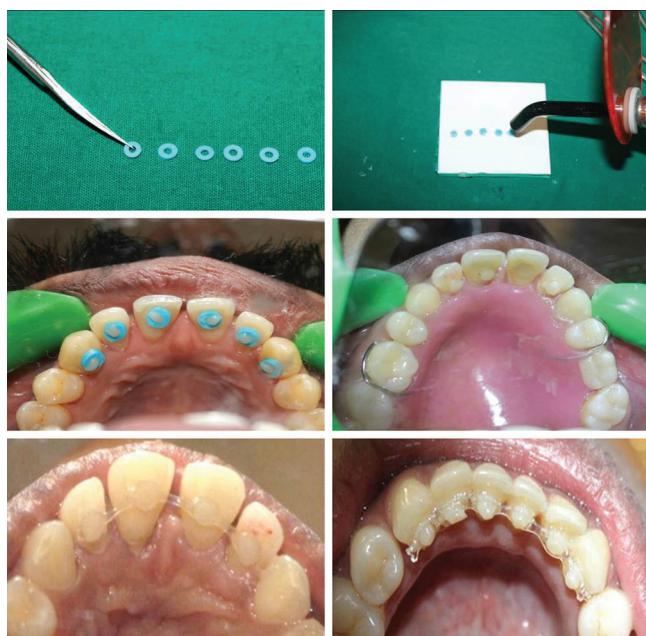
**Corresponding author:** Dr.Sameer Cherote, Postgraduate Student, Department of Orthodontics, K.M.C.T Dental College, Calicut, Kerala, Pin: 673572, India

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week (Figure-5). Permanent lingual retainer was placed with coaxial wire in figure of eight mode around composite button.

### Case 2

A male patient aged 29 years came to KMCT dental college with a chief complaint of open bite and spacing between upper and lower anteriors (fig 6, 7). He had a history of fixed orthodontic treatment. He was not ready for retreatment with braces due to restraints of time and money. Composite lingual button with elastomeric chain was planned. All six teeth in the upper and lower anteriors were bonded with composite lingual button as explained. Elastomeric chain was engaged and changed in subsequent weekly appointments (fig 7). By the end of 4 weeks all anterior spaces were closed (fig 8). Fixed retention with coaxial wire was placed after treatment. Removable or fixed tongue guard was planned later for open bite correction. Open bite can also be corrected by modifying the same lingual button by sharpening the it so as to inflict trauma to tongue, thereby patient himself will keep away from tongue thrusting habit and thereby elimination of etiology open bite.<sup>4</sup>



**Figure-1:** Cutting the separators and curing after filling composite;  
**Figure-2:** Intra-oral view after bonding and removal of separators;  
**Figure-3:** Placement of E-chain

### DISCUSSION

The clinician should expect some loss of the dental alignment obtained during orthodontic therapy in the long term in cases in which the orthodontic retainer has been removed by the orthodontist or lost by the patient.<sup>1</sup> The most effective way to retreat anterior crowding or spacing after retention requires the use of brackets and archwires. However, patients are often reluctant to wear braces again for retreatment. Several alternatives have been proposed for tooth realignment, which may involve the use of an active removable appliance, retention with lingual spurs or the use of nickel-titanium archwires as retention devices.<sup>2</sup> A simple technique to close relapse of anterior spacing in pre-treated cases can be done with this composite lingual button technique. This innovative and low cost procedure can effectively close the relapse of anterior spacing in 1 to 2 months.<sup>1</sup> Either prefabricated invisible buttons or bondable metal buttons can be used as alternatives to composite lingual buttons. Furthermore this composite lingual button can be sharpened so as to inflict trauma which can be used for openbite



**Figure-6:** Pre-treatment extraoral; **Figure-7:** Pre-treatment intraoral



**Figure-4:** Pre-treatment condition; **Figure-5:** After space closure



**Figure-8:** Comparison between pre-treatment and post-treatment conditions

correction secondary to tongue thrusting.

## CONCLUSION

In this era of peak advancement in orthodontic technology with lasers, self-ligating brackets, lingual braces, CADCAM technology, nanotechnology and robotics orthodontists should be aware of or should not ignore such simple, economical and effective techniques to tackle certain situations and ward off few disappointed patients to retain and uphold our faith in the society.

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# Comparison of Glottis View and Hemodynamic Response by using Macintosh and MacCoy Laryngoscopes for Endotracheal Intubation in General Anaesthesia for Elective Surgery

Lipika Baliarsing<sup>1</sup>, Mangesh Gore<sup>2</sup>, Prashant Akulwar<sup>3</sup>

## ABSTRACT

**Introduction:** The aim of laryngoscopy is to obtain good visualization of the vocal cords to facilitate smooth endotracheal intubation. To reduce hemodynamic response to Intubation, laryngoscope blades of different shapes have been designed and studied. We tried to evaluate efficacy of MacCoy laryngoscope blade (straight) versus conventional Mcintosh (curved) blade in providing good glottic view and reducing hemodynamic response during endotracheal intubation.

**Material and methods:** 200 American Society of Anaesthesia grade I and II patients requiring general anaesthesia were randomly divided in two groups; Group I (macintosh blade) and group II (MacCoy blade). Laryngoscopy was done by the attending anaesthesiologist by either of the blade to intubate the trachea. The Cormac-lehane grade was obtained from anaesthesia charts maintained by anaesthesiologist at the end of the procedure. Haemodynamic parameters were also recorded at periodic intervals during the procedure.

**Results:** When Cormack-lehane(C & L) grading was compared between two groups we found that in group I; Grade I was 36%, Grade II was 38% and Grade III was 13%. In group 2, 82% patients had C and L grading I, 18% C & L grade II and zero C&L grade III. Rise in mean arterial blood pressure following intubation was more in Macintosh group as compared to the MacCoy group which was found to be statistically significant.

**Conclusion:** MacCoy blade provides better visualization of larynx and intubating conditions with minimal Hemodynamic response to laryngoscopy and intubation as compared to Macintosh blade.

**Keywords:** Cormac-Lehane grade, Hemodynamic stability, MacCoy blade, Macintosh Blade,

## INTRODUCTION

Laryngoscopy forms an important part of General Anesthesia and endotracheal intubation. Laryngoscopes are used to view the larynx and adjacent structures for inserting endotracheal tube into the trachea. The aim of laryngoscopy is to obtain good visualization of the vocal cords to facilitate smooth endotracheal intubation.

Direct laryngoscopic view is best seen in sniffing in the morning air position which improves glottis view.<sup>1</sup> To reduce hemodynamic response to Intubation, laryngoscope blades of different shapes have been designed and studied. Many factors have shown to influence laryngoscopic view of vocal cords. These include forward displacement of mandible, prominent or absent teeth, backward displacement of the tongue. The proof of this can be easily obtained by the existence of many different types of laryngoscope blades.<sup>2,3</sup>

Furthermore, laryngoscopy and endotracheal intubation trigger major stress responses; one due to sympathetic stimulation releasing catecholamines that leads to tachycardia and

hypertension which increases the myocardial oxygen demand and the other due to vagal stimulation leading to parasympathetic activation that manifests as bradycardia and hypotension. Both of these may be catastrophic in patients with known history of ischemic heart disease.<sup>4,5</sup>

This prospective observational study was designed to evaluate the efficacy of MacCoy laryngoscope blade (straight) versus Macintosh (curved) blade in providing good glottic view and reducing hemodynamic response during endotracheal intubation.

This study was undertaken with the aim to compare the laryngoscopic view and hemodynamic responses using MacCoy blade versus Macintosh blade for intubation

## MATERIAL AND METHODS

After obtaining approval from institutional ethics committee and obtaining valid written informed consent from individual patients, 200 ASA grade I and II patients requiring general anaesthesia were randomly divided in two groups; Group I (macintosh blade) and group II (MacCoy Blade). Patients in Both the groups were given identical premedication and were induced the same way.

**Sample size:** Sample size was calculated with help of difference in mean method and sample size is found to be 100 per group at 80% power and 95% confidence interval. Accordingly we had total of 200 patients which were later got divided randomly in two groups.

After induction, laryngoscopy was done by the attending anaesthesiologist by either of the blade to intubate the trachea. Heart Rate, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Blood Pressure (MBP) were recorded in each patient at various time intervals viz. baseline (i.e before coming to operating room), pre-induction ,post- induction ,pre-intubation, at 1 and 3 minutes after intubation. The Cormac-lehane grade was obtained from anaesthesia charts maintained by anaesthesiologist at the end of the procedure.

## STATISTICAL ANALYSIS

After data entry – data analysis was done with the help of SPSS

<sup>1</sup>Professor, <sup>2</sup>Assistant Professor, <sup>3</sup>Ex-Resident, Department of Anaesthesiology, Topiwala National Medical College and B.Y.L. Nair Charitable Hospital, Mumbai-08, Maharashtra, India

**Corresponding author:** Dr. Mangesh Suresh Gore, 11,Bima Chhaya CHS, M.P. Road, Mulund (EAST), Mumbai-400081, India

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version 21 using parametric and non-parametric test. Quantitative data such as heart rate, blood pressure (both systolic & diastolic) and Mean arterial pressure were analyzed with help of mean, SD and median. Comparison among study group was done with the help of paired and unpaired t test. Qualitative data such as Cormac Lehane grading for glottis view among study group was assessed by chi square test. 'P' value  $< 0.05$  taken as significant.

## RESULTS

When data was analysed, no statistically significant difference pertaining to age, sex, MPC grade and ASA grade amongst two study groups was found. When Cormack-Lehane (C & L) grading was compared between two groups it was found that in group I (Macintosh blade) Grade I was 36%, Grade II was 38% and Grade III was 13% (Table-1).

In group 2 (MacCoy), 82% patients had C and L grading I, 18% C & L grade II and zero C&L grade III (Table-1).

Visualization of larynx was better in patients with MacCoy blade as compared to that of Macintosh blade which was found to be statistically significant between the two groups. There was no statistically significant variation noted in heart rate during base line and pre induction periods in both the groups.

Rise in heart rate following intubation was more in Macintosh group as compared to the MacCoy group which was found to be statistically significant. There was no statistically significant variation noted in mean arterial blood pressure during base line and pre and post induction periods in both the groups.

Rise in mean arterial blood pressure following intubation was more in Macintosh group as compared to the MacCoy group which was found to be statistically significant ( $P < 0.05$ ) (Table-2).

## DISCUSSION

Laryngoscopy forms an important part of general anaesthesia

and endotracheal intubation. To ease the process of intubation, laryngoscope blades of different shapes have been designed and studied.

Thus, use of different types of laryngoscope blades can help in decreasing haemodynamic response and at the same time facilitate good laryngoscopic view for smooth endotracheal intubation.

In this prospective observational study we evaluated the laryngoscopic view, and haemodynamic response using Macintosh blade and was compared with that obtained using MacCoy blade. The laryngeal view was compared using Cormack and Lehane grading. In Group II (MacCoy blade), 82% patients had Grade I view and 18% patients had Grade II view. In Group I (Macintosh blade), 36% patients had Grade I view, 38% had Grade II view and 26% had Grade III view.

This shows that the visualization of larynx was better with MacCoy blade as compared to Macintosh blade which was found to be statistically significant as shown in the study by Sakai T et al. They compared the grade of laryngeal visualization with the MacCoy, Macintosh and the Miller blade in 117 patients for elective surgery under general anesthesia requiring tracheal intubation. They found that the grades of laryngeal visualization with McCoy blade were significantly better than those with Macintosh blades.<sup>6</sup>

Harioka et al, studied 219 patients and concluded that without external laryngeal pressure, the MacCoy blade provided a better laryngoscopic view than that obtained by the Macintosh laryngoscope ( $p < 0.05$ ).<sup>7</sup> Beilin b, yardeni iz et al, in their study found that the McCoy blade significantly improves laryngoscopic view<sup>8</sup>.

MacCoy EP, Mirakhur RK. et al compared the stress response to laryngoscopy, using the Macintosh and MacCoy blade. The cardiovascular changes and catecholamine concentrations were compared in 20 patients before and after laryngoscopy with

Cormack Lehane Grade		Type of laryngoscope blade		Total
		MacCoy	Macintosh	
Grade 1	Count	82	36	118
	Percent	82.0%	36.0%	59.0%
Grade 2	Count	18	38	56
	Percent	18.0%	38.0%	28.0%
Grade 3	Count	0	26	26
	Percent	0.0%	26.0%	13.0%
Total	Count	100	100	200
	Percent	100.0%	100.0%	100.0%
Chi-Square test	Value	df	P Value	Association is Significant
Pearson Chi-Square	51.075	2	0.231	

Table-1: Cormack Lehane grading

MAP (mmHg)	MacCoy			Macintosh			P Value
	Mean	SD	% Change	Mean	SD	% Change	
BL	94.24	8.65		92.31	6.64		0.079
Pre induction	94.24	7.58	0.00%	94.53	7.05	2.40%	0.480
Post induction	89.76	7.03	4.75%	90.54	7.06	1.92%	0.433
After intubation	84.11	6.80	3.05%	104.11	7.93	12.78%	0.221
After 1 min	94.90	6.36	0.71%	99.03	8.01	7.28%	0.351
After 3min	81.63	7.26	-0.65%	86.74	8.82	6.96%	0.386
Note: P Value calculated by Unpaired T test.							

Table-2: Comparison of mean arterial pressure

either the Macintosh or the MacCoy laryngoscope blades. There was significant increase in both heart rate (33%) and arterial blood pressure (27%) after laryngoscopy using the Macintosh blade ( $P < 0.05$ ). Use of the MacCoy blade did not result in any significant change in either heart rate or arterial blood pressure. It was concluded that the stress response to laryngoscopy is less marked with the use of MacCoy blade and it is probably due to a reduction in the force necessary to obtain a clear view of the larynx.<sup>9</sup>

Nishiyama T, et al. 1998 compared the stress response during laryngoscopy using three different laryngoscopes, Macintosh, Miller, or MacCoy. Blood pressure, heart rate (in 58 patients) and plasma concentration of catecholamine (in 29 patients) were measured before, during and after laryngoscopy without tracheal intubation. The results suggest that the stress response during laryngoscopy without intubation is the highest with the Miller blade and the least with the MacCoy blade.<sup>10</sup>

The results in our study shows that the MacCoy laryngoscope blade improves the visualization of the larynx and significantly attenuates haemodynamic parameters during laryngoscopy and intubation as compared to that with Macintosh laryngoscope blade.

It can be utilized as an additional tool along with pharmacological interventions for obtunding stress response to laryngoscopy and endotracheal intubation. This shows that Haemodynamic response to laryngoscopy was less with MacCoy blade as compared to that with Macintosh blade which was found to be statistically significant ( $P < 0.05$ ) as shown in the study by MacCoy EP, et al and also this shows that the visualization of larynx was better with MacCoy blade as compared to Macintosh blade which was found to be statistically significant,  $P < 0.05$ , as shown in the study by Sakai T et al.<sup>6</sup>

## CONCLUSION

Thus, our study shows that MacCoy blade provides better visualization of larynx and intubating conditions with minimal hemodynamic response to intubation as compared to Macintosh blade. MacCoy blade which is a modification of the Macintosh blade with its tip levering significantly, Improves the visualization of the larynx. MacCoy blade provides better visualization of larynx and intubating conditions with minimal Hemodynamic response to laryngoscopy and intubation as compared to Macintosh blade.

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# A Randomized Control Trial Comparing Propofol with Midazolam and Fentanyl Combination for Sedation in Gastrointestinal Endoscopies

Urvi H. Desai<sup>1</sup>, Deepa Shriyan<sup>2</sup>, Dipankar Dasgupta<sup>3</sup>

## ABSTRACT

**Introduction:** Propofol can be easily titrated and has a rapid recovery profile, thus has revolutionised sedation practices in gastrointestinal (GI) endoscopy. The objective of this study was to compare efficacy and safety of propofol with midazolam and fentanyl combination for GI endoscopy sedation.

**Material and methods:** Sixty patients scheduled for gastrointestinal endoscopy were recruited for this study. Patients were randomly allocated into either Group P (propofol alone) or Group MF (combination of midazolam and fentanyl). The parameters used to measure the efficacy were, time of onset of sedation, depth of sedation (Ramsays sedation scale), amnesia and early recovery of sedation (Modified Aldrete Score). Safety was evaluated using cardiovascular and respiratory parameters. Adverse events like hypoxia, hypotension, bradycardia were recorded. PSPP software was used for statistical analysis.

**Results:** It was observed that P group patients were more deeply sedated with a mean RSS of 5.1 compared to 3.07 of the MF group. Full recovery (Aldrete score 10) at ten minutes after the end of the procedure was seen in 73.33% of the patients of the propofol group compared to 50% of the MF group which was insignificant. Propofol group had significant haemodynamic changes (hypotension) as compared to MF group. Respiratory complications were seen in both the groups but they were few and not significant.

**Conclusion:** We conclude that both the groups are of same merit and safe.

**Keywords:** Endoscopist satisfaction, conscious sedation, propofol

combination for sedation in gastrointestinal endoscopies. The parameters used to measure the efficacy was time of onset of sedation, depth of sedation, amnesia and recovery. Safety were evaluated using cardiovascular parameters (heart rate, blood pressure) and respiratory parameters (respiratory rate, oxygen saturation).

## MATERIAL AND METHODS

This study was conducted at Jaslok Hospital and Research centre, Mumbai over a six month period, after departmental review board approval. Informed and valid consent were obtained from the patients. A prospective randomised controlled trial on sixty patients undergoing gastrointestinal endoscopies was carried out, to study efficacy and safety of propofol versus midazolam and fentanyl combination for procedural sedation.

A sample size estimate was calculated from mean values of Ramsays sedation scale of MF and P groups using the formula from ausvet.com.au. Taking variance of standard deviation as 1.22 and maintaining 95% confidence limit and 80% power of study, minimum sample size calculated was 10. We included all 60 patients of ASA I-III undergoing elective gastrointestinal (GI) endoscopies lasting up to one hour.

The endoscopic procedures included were oesophagogastroduodenoscopy (OGDscopy), endoscopic ultrasound (EUS), endoscopic retrograde cholangiopancreatography (ERCP) and colonoscopy. Patients excluded from the study were children under 18 years, pregnant patients, patients with active GI bleeding, mechanically ventilated patients, allergic to egg or soya beans and those with difficult airway.

A thorough pre-anaesthetic evaluation was carried out in all the patients. Patients were randomised using block of 5 method. 60 patients were divided in two groups of 30 each. Group (MF) received midazolam and fentanyl and Group (P) received propofol 1%. Preliminary data collected were age, sex, weight, ASA status, heart rate, respiratory rate, systolic and diastolic blood pressure and oxygen saturation. After confirming consent and starvation status, intravenous access was obtained. Monitoring included pulse oximetry, electrocardiogram

<sup>1</sup>Assistant Professor, Department of Anaesthesia, LTMMC and GH, Sion, <sup>2</sup>Assistant Professor, Department of Anaesthesia, BYL Nair Hospital, Mumbai Central, <sup>3</sup>Director, Department of Anaesthesia, Jaslok Hospital and Research Centre, Mumbai, India

**Corresponding author:** Dr. Urvi H Desai, A-402, Building 1, Plot C-2, N G Royal Park, Kanjurmarg (E), Mumbai - 42, India

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(ECG), non invasive arterial blood pressure measurement and graphic analysis of respiratory rate. All patients were given supplemental oxygen through nasal cannula at 4 litre /minute. Group MF received injection fentanyl 2 $\mu$ g/kg IV, followed by midazolam 0.05mg/kg slow. When the patient demonstrated signs of sedation like dysarthria, nystagmus or ptosis, sedation was stopped. If the patient achieved the required sedation plane while injecting the drug, the total dose was not given. After one minute of injecting the total calculated dose if the patient did not show any signs of sedation then, an additional dose of 0.5mg of midazolam and 50 $\mu$ g of fentanyl were given. For maintenance, group MF received incremental doses of 0.5mg midazolam and 50 $\mu$ g fentanyl every fifteen to twenty minutes. In group P the patients received intravenous injection of propofol 1mg/kg slowly. After 30 seconds of injecting the total calculated dose, if the patient did not show signs of sedation then, additional increments of 10-20 mg were given. Patients were maintained on 10-20 mg bolus top-ups every five to ten minutes. The time interval between the injection of sedative and the start of endoscopy was recorded as the onset time of sedation. During the procedure the patients were maintained at Ramsays sedation scale (RSS) of 3 or 4. In addition oral and oropharyngeal cavities were topically anaesthetised using three puffs of 10 % lignocaine spray (one puff= 10 mg) in upper GI scopy. In colonoscopy, 2% lignocaine jelly was used in the perianal area prior to insertion.

Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), oxygen saturation ( $SpO_2$ ) and respiratory rate (RR) were measured every five minutes till the end of procedure. Episodes of bradycardia HR< 50 min and hypotension (decrease in SBP< 20mmHg from the base line), were recorded as adverse events. Hypotension was considered as moderate when the decrease in SBP was between 20 and 50 mmHg and severe when it was > 50 mmHg from baseline. Respiratory depression ( $SpO_2$  <95 %), airway obstruction and apnoea (no respiratory activity > 15 seconds) were also noted as adverse respiratory events. These were corrected before proceeding further with endoscopy. At the end of the procedure after the scope was removed, the level of sedation was recorded by using the Ramsays Sedation scale. The interval between the removal of the scope till the patients opened their eyes was recorded as awakening time. The modified alredre scoring system was used to assess the recovery of patients every five minutes thereafter for half hour. Score of 10 was the best score. Patients were assessed for amnesia of intra operative events by subjective questionnaire. Patients were assessed for nausea vomiting and post procedural pain. The endoscopists were given the visual analogue scale to rate the overall satisfaction with sedation and technical ease.

## STATISTICAL ANALYSIS

Qualitative data that included gender, weight, ASA grade

was assessed by Chi square test and by Fisher's Exact test. Quantitative data was represented by using mean  $\pm$  SD and analyses between the groups were done by using unpaired t-test and Chi square test. Statistical software, PSPP was used for statistical analysis.

## RESULTS

Sixty patients were studied in our trial. The demographic data is summarised in Table-1. Patients in the MF group received mean dose of 2.48mg and 129  $\mu$ g of midazolam and fentanyl for induction and Group P achieved sedation with the mean induction dose of 63.3 mg. Group P had mean onset time of action of 44 seconds compared to MF group, in which it was 85.33 seconds which was statistically significant. Total mean dose for maintenance required in Group MF was fentanyl 173 $\mu$ g and midazolam 3.25 mg. In group P total mean maintenance dose was 180.83 mg (6 mg/kg/hr). It was observed that at the end of procedure patients in the P group were more deeply sedated with a mean RSS of 5.1 compared to 3.07 of the MF group. This difference was statistically significant. The time to awaken the patients in the P group was significantly more, which was 2.47 min compared to 0.07 min in the MF group. Recovery was assessed using the Modified Aldrete System at the end of the procedure. At 10 min after the end of the procedure 73.33% of the patients in the propofol group were fully recovered with a score of 10 compared to 50% of the MF group which was statistically insignificant (P 0.11). At the end of 30 minutes all the patients in both the groups had recovered except one patient in the P group and two patients in the MF group. Recovery time of both groups was almost same (11.5 +/- 8 min in the MF group vs 10.3 +/- 5 min in the P group) which was not significant (Table-2).

We observed 46.6% of patients in the P group had hypotension which was statistically significant. 4 patients had severe hypotension and 10 patients had moderate hypotension. In the midazolam group only three patients had moderate hypotension. No patients had bradycardia <50 /min or ECG changes. Mean fall in systolic blood pressure in the MF group was 14.54 mmHg which is clinically not significant. Mean decrease in the SBP in the P group was 33.27mmHg which was significant clinically. Mean percentage decrease in the in SBP from the baseline was significantly more in the P group. It was 11.3% in the MF group compared to 23.26% in the P group. There was no significant difference in the mean percentage decrease in the diastolic blood pressures as well as heart rate between the groups. The incidence of airway obstruction was more in group P. Respiratory depression was seen in five patients in group MF compared to two in the P group. Two patients in both groups had apnea transiently. In the MF group the mean lowest saturation and respiratory rate were less from the baseline. This was statistically significant. In the P group also there is significant difference between baseline respiratory rate and its mean lowest.

	<b>MF (Mean<math>\pm</math> SD)</b>	<b>P (Mean )</b>	<b>P value</b>
Age (Yrs )	50.93 $\pm$ 16.68	52.7 $\pm$ 17.06	0.687
Weight (kg)	61.27 $\pm$ 9.9	63.37 $\pm$ 13.36	0.492
Duration of procedure (min)	23.67 $\pm$ 12.52	20.17 $\pm$ 13.68	0.305

\* P < 0.05 significant, MF - Midazolam Fentanyl, P- Propofol

**Table-1:** Demographic characteristics. The results are given as mean or median (SD).

No such difference is seen with saturation in the P group. The mean percentage decreases in saturation were equivalent in both the groups and insignificant. The mean decrease in the respiratory rate (RR) in the MF group was significantly more compared to the P group (20% versus 10.9%) (Table-3).

Endoscopists satisfaction was graded using the visual analogue scale (VAS). Mean VAS in the MF group was 80.67% compared to 77.5% in the P group (Table-2). The difference was insignificant. Patient tolerance was assessed by a subjective questionnaire in terms of amnesia, post operative pain, nausea and vomiting. 43% of patients in the MF group could recall the procedure done, either partially or completely compared to 6.7% of the patients in the P group. This was statistically significant ( $P = 0.001$ ). Thus 93.3 % of patients of P group had amnesia. Only one patient of MF group had pain post procedure and two patients of the P group had nausea and one vomited. During scope insertion, some patients showed resistance in the form of coughing, gagging and hiccups in both groups, however the difference is insignificant.

## DISCUSSION

Anaesthetic management in gastro intestinal endoscopies is confined to either topical anaesthesia or its combination with sedation. Propofol is a short-acting anaesthetic agent that has a favourable pharmacokinetic profile in comparison to the benzodiazepines and opioids with regard to rapid induction of sedation, faster recovery, and equivalent levels of amnesia. Midazolam is a benzodiazepine depressant of the central nervous system that is commonly used in synergy with opioid fentanyl for conscious sedation during GI endoscopy. This combination has some limitations like a delay of onset of action, lingering sedative effects that delay discharge, and prolonged recovery, and morbidity as a result of respiratory depression. Therefore optimal propofol administration methods for gastrointestinal procedures needs to be studied further.

Propofol follows a rapid redistribution pattern after injection, hence top up interval for the propofol group was more frequent in our study than the MF group. As a result to maintain the level of sedation and prevent the patient from waking up during the procedure, closed titration of propofol was required. In a study done by Christopher N, quality of sedation, operating conditions, and recovery profiles were similar in intermittent bolus

injections, conventional syringe infusion and target controlled infusion.<sup>4</sup> Sedation level was assessed at scope removal. It was not assessed during the procedure so as to prevent and minimise interruptions. In MF group synergistic effect of the two drugs helped in maintaining the patients at a moderate level of sedation. In our study the propofol group patients were deeply sedated. Propofol does not have analgesic properties, it has a narrow therapeutic window and absence of a reversal agent can lead to over sedation.<sup>5</sup> Deep sedation can increase the cardiovascular complications like hypotension and bradycardia and also depresses airway reflexes resulting in gastric aspiration. Airway patency can also be compromised and ventilation may need to be assisted. In our study patients receiving propofol were more deeply sedated, however there was no incidence of aspiration. Therefore to reduce complications balanced propofol sedation was proposed as a method that would provide safe and effective sedation by combining a low dose of propofol with opioid analgesic and or benzodiazepine.<sup>6,7</sup>

Amnesia for the total procedure is important because it improves patient tolerance and acceptance for any repeat endoscopy. More number of patients in the propofol group (93.3%) had amnesia as compared to MF group (56.7%) which was significant ( $P=0.001$ ). This could be because of deeper plane of sedation in the P group. Our study is contrary to the study of K.W Patterson et al. who showed that 68 % of midazolam group were amnesic compared to 14 % of the propofol group.<sup>8</sup> In his study only single bolus technique was used with both drugs. The induction dose of midazolam was much higher (0.08mg/kg) compared to our study.

In the combination group, last top up of drug was given 10 to 15 min prior to the completion of the procedure. However in the propofol group last top up was given few minutes prior. It was thus observed that more number of patients had full recovery immediately after awakening in the combination group as compared to propofol group. At the end of 30 minutes most of the patients in both groups had completely recovered. On an average recovery time in both groups was almost same with majority of patients in the propofol group recovering in the first 10 minutes.

This could be due to the rapid clearance and rapid redistribution of propofol. In 2002 Sipe et al compared the use of propofol versus midazolam plus meperidine in 80 patients undergoing

	<b>MF (Mean ± SD)</b>	<b>P (Mean ± SD)</b>	<b>P value</b>
Onset of sedation (s)	85.33 ± 41.89	44 ± 24.37	<0.001*
Ramsays Sedation Scale	3.07 ± 1.05	5.1 ± 1.49	<0.001*
Awakening (Min)	0.07 ± 0.22	2.47 ± 2.28	<0.001*
Recovery Time (min)	11.5 ± 8	10.3 ± 5	0.48
Endoscopist Satisfaction (VAS %)	80.67 ± 10.73	77.5 ± 11.95	0.28

\*P<0.05 is significant MF- Midazolam Fentanyl, P - Propofol, VAS - Visual analogue scale

**Table-2:** Comparison of efficacy between the two groups. The results are given as mean or median (SD).

	<b>MF (Mean )</b>	<b>MF (SD)</b>	<b>P (Mean )</b>	<b>P (SD)</b>	<b>P value</b>
SBP % decease over baseline	11.03	8.52	23.26	13.06	<0.001*
HR % decrease over baseline	7.65	8.45	6.37	6.42	0.51
RR % decrease over baseline	20.03	18.47	10.95	15.45	0.043*
Saturation % decrease over baseline	1.37	3.22	1.83	5.62	0.69

\*P<0.05 is significant, MF- Midazolam Fentanyl, P- Propofol; SBP - Systolic blood pressure, HR- Heart rate, RR- Respiratory rate

**Table-3:** Comparison of safety parameters. The results are given as mean or median (SD).

colonoscopy. Mean time to sedation was significantly faster with propofol, the depth of sedation was greater and also these patients recovered faster.<sup>9</sup> By 30 minutes all patient had achieved full recovery in the propofol group compared to 65% in the midazolam group. Mean dose of midazolam was 4.7 mg with mean duration of 12.2 min compared to our study where the mean total dose was 3.25mg with mean total duration of 23.6 minutes. Therefore in our study recovery of patients in the MF group at the end of 30 min is much higher (93.3%).

T.W. Weherman et al<sup>10</sup> studied patients for ERCP who received either midazolam pentazocine combination or propofol for sedation. Full recovery was achieved after 19 +/- 8 min in the propofol group compared to 29 +/- 8 min in the midazolam group. This is contrary to our study in which the mean recovery time was much shorter in both the groups (10.3 +/- 5 min in P vs 11.5 +/- 8 in the MF group). This could be because the total doses of propofol (388 +/- 212 mg) and midazolam (7.8 +/- 3.1 mg) used were much higher compared to our study.

Vargo et al<sup>11</sup> did a similar study in 2002 in 75 patients undergoing advanced upper GIscopy. He compared sedation between propofol and midazolam meperidine groups. Recovery time was much shorter in propofol group (18.6 min vs 70.5 min). At the end of 15 min 76 % in propofol group achieved full recovery compared to 8% in the midazolam meperidine group. In our study also at 10 min 73.3% of patients in the Propofol group had full recovery compared to 50 % in the MF group. Fentanyl is shorter acting drug than pethidine. Total dose of midazolam used in Vargo study (9.2mg) was much higher. Hence the recovery of patients in the midazolam group was much more delayed compared to our study.

In our study all patients received 4 liters/ min of oxygen throughout the procedure. It was observed that during the procedure, two patients in each group were apnoeic transiently, immediately following bolus injections. These patients started breathing immediately after gentle tapping or calling out their names. Respiratory depression was observed more in the MF group. Five patients in the propofol group and two in the MF group experienced airway obstruction. Clinically no patient had respiratory rate less than 10 per minute. The mechanism of respiratory depression in the midazolam fentanyl group was due to the significant blunting of the hypoxic ventilatory drive resulting in hypoventilation and decrease in the respiratory rate. In T.W. Weherman study mean percentage decline in the oxygen desaturation was greater in the propofol group (5% +/- 3%) than the midazolam group (3% +/- 2%).<sup>10</sup> A drop in saturation less than 90% was seen in 11/98 patients in P group compared to 8 in the midazolam group. In our study, the mean percentage decrease in saturation (P 1.83 +/- 5.62% vs MF 1.37 +/- 3.22) was equivalent in both the groups and insignificant.

Vargo et al observed a decrease in in mean arterial blood pressure in both the groups with no significant difference.<sup>11</sup> Hypotension was seen in 6/38 in P group and 3/37 in the M group. In 2004 Ian et al did a prospective study in 500 patients for upper GI endoultrasoundography.<sup>12</sup> Propofol was given as bolus 25-45 mg followed by infusion 25mcg/kg/min. There was no hypotension, tachycardia or bradycardia. He studied only young and healthy ASA 1 and 2 patients. In our study propofol was given as bolus top ups and maintained a 100 mcg/kg/ min and hence the hypotension.

In our study we found that 14 patients of the propofol group had hypotension compared to three in the MF group, which was statistically significant. Four patients in the P group had severe hypotension which needed treatment. There has been a statistical significant decrease in the arterial pressures (systolic and diastolic) from their baselines in both the groups. However mean decrease in the SBP in the MF group was 14.54 mmHg which was clinically insignificant as compared P group in which the mean decrease was 33.27 mmHg. Statistically it was seen that the mean percentage decline in SBP in the P group was significantly more than the MF group (23.26% in the P group compared to 11.03% in the MF group). There was statistical decrease in heart rate from the baseline in both groups, but it was not clinically relevant. There was no incidence of bradycardia or arrhythmias. It is known that a induction dose of propofol causes 20-30 % decrease in blood pressure. Midazolam and fentanyl both decrease the systemic vascular resistance and can cause decrease in blood pressure. But they do not depress the myocardium as compared to propofol. We have included in our study ASA 3 patients. These patients may not be able to compensate for the vasodilatory actions of propofol. Thus clinically in an endoscopy suite propofol can cause unacceptable hypotension in ASA 3-4 patients.

23% of the patients in the P group complained of pain on injection of the drug propofol. All patients in both the groups except one in the MF group were pain free postoperatively. Pain in the postoperative period could be due to abdominal distension, especially in prolonged cases or some therapeutic procedure like sphincterotomy. Post operative nausea vomiting is an important frequent complication in GI endoscopies. Only two patients had nausea in the P group and one of them vomited. Propofol has an antiemetic property and fentanyl even though being an opioid has the least emetogenic effect.

The endoscopists were very satisfied with sedation in both groups (80.67% MF vs 75.57% in P group) the difference was insignificant. The endoscopists were not blinded in our study which could be responsible for greater and similar satisfaction score. These finding were similar to the study done by Eszter Sego et al.<sup>13</sup>

### Limitations of study

In our study amnesia was assessed only by subjective questionnaire. Sophisticated techniques like the visual memory test were not used. We have not included in this study home readiness and other psychomotor tests which assess discharge criteria.

### CONCLUSION

We conclude that both the groups are of merit and safe. Quality of sedation is more ideal with propofol, with deeper sedation than required. An additional feature of propofol is its early recovery. Haemodynamic variations (more with propofol) and respiratory complications are seen with both groups. These can marginalised completely with eternal vigilance and timely correction

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# A Study to Know Correlation among De-Pigmentation of Body Areas and Sex of Vitiligo Patients with their Self Esteem and Impact of Vitiligo on Quality of Life

Divyesh Vernwal<sup>3</sup>, D. K. Sharma<sup>1</sup>, Swapnil Agrawal<sup>2</sup>, Divya Sharma<sup>2</sup>, C. S. Sushil<sup>1</sup>, D. K. Vijayvergia<sup>1</sup>

## ABSTRACT

**Introduction:** Vitiligo is a skin disorder characterized by patches of depigmented skin. It has impact on self esteem and quality of life. Present study was done to know correlation between different body areas of de-pigmentation in vitiligo patients, sex of vitiligo patients with their self esteem and also impact of vitiligo on different domains of life which affect overall quality of life.

**Material and methods:** 100 vitiligo patients and 100 subjects as control group were evaluated for self-esteem and quality of life by Rosenberg's Self-Esteem Scale (RSES), WHO Quality of Life – Bref's Scale (WHOQOL-BREF'S). Data were tabulated, analyzed and suitable statistics applied (i.e. chi square, T-test).

**Results:** vitiligo patients report significantly low self-esteem, compared to lighter skinned individuals. 59%, 29%, and 12% vitiligo patients suffered from low, normal and high self esteem respectively. Vitiligo patients had developed poor body image for himself, due to which they faced unexpected psychosocial traumas and made negative view for life, which declined Quality of life in various life domains.

**Conclusion:** Vitiligo generates psychological distress, violates self confidence, self esteem, disrupts social relationship and creates stress-vitiligo vicious cycle.

**Keywords:** quality of life, self confidence, self esteem, vitiligo.

## INTRODUCTION

Vitiligo is a common, acquired, idiopathic skin disorder characterized by one or more patches of depigmented skin due to the loss of cutaneous melanocytes with no other texture changes. It is considered a significant problem in India. Skin diseases are associated with psychological abnormalities including anxiety, depression, psychosomatic symptoms including pain and discomfort, embarrassment, social inhibition and suicidal ideation. Effective treatment of vitiligo need to accompany improvement in self-esteem, affect, shame, embarrassment, body image, social assertiveness and self-confidence.

Psycho-dermatologic disorders fall into three categories. (1) Psycho-physiologic disorders (e.g., acne, vitiligo, psoriasis and eczema) are skin problems, not directly connected to the mind but react to emotional states, as stress. (2) Primary psychiatric disorders that result in self-induced cutaneous manifestations. e.g. trichotillomania and delusions of parasitosis. (3) Secondary psychiatric disorders that results in psychological problems. e.g. decreased self-esteem, depression or social phobia.

The highest incidence of the condition has been recorded in Indians from the Indian subcontinent, followed by Mexico and Japan. Vitiligo, in India, is referred as "ven kushtam" meaning white leprosy.<sup>1,2</sup> Parameters used to assess the severity of vitiligo are area of involvement, disfigurement, progression of disease/disease stability, potential for re-pigmentation and psycho-

social impact. The patients of vitiligo report embarrassment, helpless and low self esteem leading to emotional stress and social isolation, particularly if the disease develops on exposed areas of the body. These feelings can affect their relationships with friends, co-workers and even family members, which in turn increases the risk of depression and other psychosocial disorders.<sup>3-6</sup>

Vitiligo patients developed an exaggerated perception of disfigurement that usually leads to a distorted self-image, lack of confidence which may induce shame and avoidance of social relationships. Vitiligo had major impact on the quality of life (QOL) of patients. Skin determines our appearance and any patches may cause considerable influence on patients' psychological well-being. It causes cosmetic disfigurement and leading to psychological trauma to the patients. Moreover, many patients suffer from poor body image and low self-esteem, which results in social lives that are quite distressful. Present study was planned with the aim to study the impact of vitiligo on self esteem and quality of life of patients.

## MATERIAL AND METHODS

The present study was a single centre, cross sectional, single interview study that was approved by the institutional ethical board. 100 Vitiligo patients attending OPD in department of Dermatology, Government Medical College, Kota (Rajasthan) were selected randomly, who were aged 13 years and above, ready to give informed consent and literate enough to understand the questionnaire constituted study group and 100 suitably matched subjects preferably the relatives of the patients constituted the control group, who had no known dermatological or psychiatric disorders. Subjects with mental retardation, psychotic disorder, dementia, delirium and other amnestic disorders and who had not given consent after preliminary interview were not included in the study.

The selected patients (study group) and controls (control group) were interviewed in detail and were evaluated on three tools. First tool was specially designed semi structured proforma to collect identification data, socio-demographic data, past history of psychiatric illness, illness characteristics, clinical

<sup>1</sup>Professor, <sup>2</sup>Senior Resident, <sup>3</sup>Resident, Department of Psychiatry, Government Medical College, Kota, Rajasthan, India

**Corresponding author:** Dr. Divyesh Vernwal, 'BUNIYAAD VILLA', front of S.P. Bungalow, Police Line Road, Bahraich(U.P.), India

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diagnosis (confirmed by Dermatologist). Second tool was Hospital Rosenberg's Self-Esteem Scale (RSES) developed by sociologist Dr. Morris Rosenberg. It is a ten-item Likert-type scale with items answered on a four-point scale to reflect self esteem of respondents about their feelings, and third tool was World Health Organization Quality Of Life- Bref (Hindi Version) WHOQOL-BREF for quality of life assessment in the four domains, which were (i) physical health, (ii) physiological well-being, (iii) social relations, (iv) environment.

## STATISTICAL ANALYSIS

Information and data so collected were tabulated, analyzed and subjected to suitable statistical methods (mean, percentages and Chi square test) and conclusions were drawn.

## RESULTS

Table-1 shows distribution of comparative impairment of self esteem between male and female on the basis of Rosenberg self esteem scale (RSES). It was evident that patients had scored < 15 on RSES scale indicating low self esteem and patients had scored 15-25 on RSES scale indicate normal self esteem while patients scored >25 on RSES scale indicate high self esteem. In our study 33% female and 67% were male vitiligo patients. Among 33% female vitiligo subjects, it was evident that 70% female patients (approx. ¾ population of female) had scored < 15 on RSES scale indicating low self esteem, While 12% female patients had score 15-25 on RSES scale which indicate normal self esteem and only 18% female patients scored >25 on RSES scale which indicate high self esteem. Similarly among 67% male vitiligo subjects, It was evident that 54% male patients (approx. ½ male population) had also scored < 15 on RSES scale indicating low self esteem, While 12% male patients had scored 15-25 on RSES scale which indicate normal self esteem and Rest 18% male patients scored >25 on RSES scale which indicate high self esteem.

Score on rosenberg self esteem scale	Female (N=33)	Male (N=67)
<15(Low Esteem)	23(70%)	36(54%)
15– 25 (Normal)	4(12%)	25(37%)
>25(High Esteem)	6(18%)	6(9%)
$\chi^2 = 7.36$ , P = 0.025, d/f = 2, Significant		

**Table-1:** Distribution showing relation of self esteem with gender difference According To Rosenberg self esteem scale (RSES)

Score on rosenberg self esteem scale	On exposed areas	On covered areas	On both areas	Total (N=100)
<15(Low Esteem)	29 (50%)	2 (3%)	28(47%)	59
15– 25 (Normal)	11 (38%)	1 (3%)	17(59%)	29
>25(High Esteem)	4(33%)	0(0%)	8(67%)	12
$\chi^2 = 45.99$ , P < 0.00001, d/f = 4, Highly Significant				

**Table-2:** Distribution According To Rosenberg self esteem scale (RSES)

Domains for Quality of life	Mean score and S.D.( $\pm$ )		Unpaired t test		
	Study Group	Control Group	T score	P value	Significance
Physical	50.43 $\pm$ 27.23	76.09 $\pm$ 8.61	-7.719	<0.00001	Highly significant
Psychological	45.70 $\pm$ 32.09	72.93 $\pm$ 12.69	-6.821	<0.00001	Highly significant
Social relationship	48.41 $\pm$ 35.91	79.02 $\pm$ 12.61	-6.967	<0.00001	Highly significant
Environmental	53.01 $\pm$ 28.92	66.36 $\pm$ 11.19	-3.719	<0.00040	Significant
Total	197.55 $\pm$ 120.75	294.58 $\pm$ 34.44	-6.622	<0.0001	Highly significant

**Table-3:** Distribution According to Quality of life by WHOQOL – BREF's Scale



Table-2 shows distribution correlation between Rosenberg self esteem scale (RSES) scores and body areas of de-pigmentation. It was evident that 44 patient had de-pigmentation only on exposed areas, 3 patients had de-pigmentation only on covered areas while Rest 53 vitiligo patients had de-pigmentation on both exposed and covered body parts. It was evident that 59 patients had score < 15 on RSES scale indicating low self esteem, among them 28 (47%) had vitiligo spots on both body areas, 29 (50%) had vitiligo spots only on exposed body parts and 2 (3%) patients had only on covered body areas respectively. While 29 patients had score 15-25 on RSES scale which indicate normal self esteem had respective figures 17 (59%), 11 (38%) and 1 (3%) and Rest 12 patients scored >25 on RSES scale which indicate high self esteem and their respective figures were 8 (67%), 4 (33%) patients. The difference among these three groups were statistically highly significant ( $P<0.00001$ ), i.e. vitiligo patients significantly had low self esteem in whom vitiligo patch was on the exposed body areas of patients. Table-3 describes the quality of life of both groups as evaluated through WHOQOL – BREF. It is evident that mean score (0 – 100) in the study group in physical, psychological, social relationship and environmental domain was 50.43, 45.70, 48.41 and 53.01 while in the control group it was 76.09, 72.93, 79.02 and 66.36 respectively. Domain scores of both the groups were in descending order for physical, psychological, social relationship and environmental domain. The QOL scores in all the domains were significantly higher in control group as compared to study group with mean score 197.55 vs 294.58.

## DISCUSSION

It was seen that lowering of self-esteem and self-confidence of vitiligo patient's was related to age of onset of disease and chronicity of disease. Childhood-onset vitiligo was found to be correlated with important psychosocial trauma and leads to negative self-esteem. With the increasing significance of consultation liaison psychiatry, we also have to focus on psychosocial management of such chronic dermatological illness. More awareness is being created among physicians and evidence of effective treatment for psychiatric disorder is reducing the negative attitudes towards psychiatric disorders.

This study was undertaken to find correlation between different

body areas of de-pigmentation with the self-esteem of vitiligo patients. We also made comparative assessment of self esteem impairment in females and male. To assess self esteem standard scale was used. It was a semi structured interview and all available information including patient information, informant's information was used to decide severity of impaired self esteem. The result of distribution of comparative impairment of self esteem between male and female that approx.  $\frac{3}{4}$  population of female and approx.  $\frac{1}{2}$  male population indicating low self esteem which was supported by Wang X et al<sup>4</sup> who found that Men affected more than women (0.71% vs. 0.45%, p<0.01). On the contrary Hita Shah et al<sup>3</sup> in their study on 365 patients found that females (68.4%) were affected more than males (31.6%) in a ratio of 2.1:1. However Handa and Kaur<sup>7</sup>, Lu T et al<sup>8</sup> and most of the researchers reported that males and females affected with almost equal frequency. The reason why females outnumbered males in some studies seemed presumably due to the fact that social stigma and marital concerns prompted women to seek early consultation.

On studying association between self esteem and body area of de-pigmentation, it was observed that difference among these three groups were statistically highly significant (P<0.00001), i.e. vitiligo patients significantly had low self-esteem in whom vitiligo patch was on the exposed body areas of patients. Our findings were supported by finding of Özlem Devrim Balaban et al<sup>9</sup>, Podaralla Ramakrishna et al<sup>10</sup> which report lower self-esteem in vitiligo patients compared to lighter skinned individuals. Childhood-onset vitiligo was found to be correlated with important psychosocial trauma leading to negative self-esteem. It is showing that more the vitiligo on the exposed body areas of patients lower the self esteem, that is self esteem inversely proportional to the vitiligo area on exposed body areas.

Impact on different domains of life which affect overall quality of life in vitiligo patient was also studied. Though there are generic as well as disease specific instrument available to assess QOL, WHOQOL-BREF was used in this study. This scale measures QOL and it's easy to administer. It has been used in a variety of medical conditions. This instrument has minimum possible confounding influence on socio-cultural differences.

Quality of life is "the subjective satisfaction expressed or experienced by an individual in his physical, mental and social situations". Various measures both generic as well as disease specific have been used to assess QOL. The different domains of quality of life which were analysed, include the following: Physical health, Physiological well-being, Social relations and Environment. We had taken total of every domain and grand total of all domains for analysis. On tabulation we found that domain scores of both the groups were in descending order for physical, psychological, social relationship and environmental domain. The QOL scores in all the domains were significantly lower in study group as compared to control group with mean score 197.55 vs 294.58. So quality of life was significantly worst for all the domains in study group. This finding was comparable to previous study done by Sangma LN et. al,<sup>11</sup> who showed that Quality of life (QOL) in vitiligo patients declined more severely, and there was more incidence of depression compared to the control group. These changes were critical for the psychosocial life of the affected people. Similar results had drawn by Mishra N et. al.<sup>12</sup>

## CONCLUSION

It can be inferred that vitiligo patients have low self esteem and confidence. Vitiligo generates psychological distress and disrupts the social relationship, which creates a vicious stress-vitiligo cycle. Results in this study indicated that majority of vitiligo patients had low self esteem, which was significantly impaired in patients having vitiligo on exposed areas. Vitiligo affects QOL in majority of vitiligo patients and such patients require more sympathetic attitude from a dermatologist and society.

In view of the lack of too much studies in our country concerning impaired self esteem and quality of life in Vitiligo, our attempt to have a close look at self esteem and quality of life in a reasonable sample of Vitiligo patients may serve a platform for future research.

### Limitations of the study

This study was a point prevalence study and it included all cases from Government hospital located in an urban centre, hence the results cannot be generalized. So a prospective study with a large sample from different centres and also considering rural population may be carried out to explore psychiatric morbidity of different population affected by vitiligo. Similarly effect of treatment of vitiligo on psychiatric morbidity was not taken in to consideration in this study. Therefore a case-control prospective study should be planned, which may demonstrate improvement in standard of living, if any after successful treatment of vitiligo.

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# Florid Cemento-Osseous Dysplasia with Multiple Impacted Supernumerary Teeth in Maxilla and Mandible – A Case Report

Jayanta Chattopadhyay<sup>1</sup>, Soumi Ghanta<sup>2</sup>

## ABSTRACT

**Introduction:** Florid cemento-osseous dysplasia is a benign, fibroosseous and multifocal dysplastic lesion of the jaw and consists of cellular fibrous connective tissue with bone and cementum-like tissue.

**Case report:** This clinical report describes a nonfamilial case of Florid cemento osseous dysplasia (FCOD) accompanied by osteomyelitis in a 41-year old male patient. Orthopantomograph revealed multiple radiopaque cementum-like masses distributed throughout the maxilla and mandible. There were multiple impacted supernumerary teeth present in both jaws. Blood investigation did not detect any abnormality in serum alkaline phosphatase level. Antibiotics were given for osteomyelitis. No impacted teeth were extracted as they were asymptomatic. After that, patient is followed up at regular intervals with reinforcement of good oral hygiene to prevent osteomyelitis.

**Conclusion:** Clinicians should be aware of the radiographic manifestation of such conditions and knowledge to recognize and differentiate from other conditions similar to their appearance.

**Keywords:** Florid-cemento osseous dysplasia, Fibroosseous lesion, Impacted teeth, Osteomyelitis.

## INTRODUCTION

The term osseous dysplasia refers to the abnormal development and disordered production of bone and cementum like tissue. Waldron considered these lesions to be fibroosseous lesions arising from periodontal ligament. These osseous dysplasias are categorized as periapical (surrounds the periapical region of tooth), focal (single lesion) and florid cemento osseous dysplasias. The word 'florid' refers to wide spread, extensive manifestation of the lesions. Florid cemento-osseous dysplasia (FCOD), previously called *gigantiform cementoma*, *multiple cemento-ossifying fibroma*, *sclerosing osteitis*, *multiple enostosis* and *sclerotic cemental masses of the jaws*, was first described by Melrose et al.<sup>1</sup> It is a benign, fibro-osseous and multifocal dysplastic lesion of the jaw and is usually asymptomatic and occurs most often bilaterally. It consists of cellular fibrous connective tissue with bone and cementum-like tissue.<sup>2,3</sup> It may/may not cause cortical expansion. There is a tendency for secondary infection leading to osteomyelitis due to avascular nature of these bony lesions.<sup>2</sup>

A search of the literature showed that only a few cases have been reported concerning the familial form of FCOD associated with multiple impacted teeth. However, very few examples were found of the nonfamilial form of FCOD associated with multiple impacted teeth. Here we present details of a very rare case of nonfamilial FCOD associated with multiple impacted teeth in both jaws accompanied by osteomyelitis.

## CASE REPORT

A 41 year-old male patient reported to the dental department of

Narayana Multispeciality Hospital with a complaint of a pain and discharging of pus in the left lower posterior teeth region. He gives history of extraction of the mandibular left posterior teeth two years back due to mobility and pus discharge. The extraction event was associated with delayed healing. Patient also gives previous history of extraction of maxillary left anterior and posterior teeth and mandibular anterior teeth 3 years back due to caries. Family and medical history were non-contributory. There was no history of swellings or bony deformity elsewhere in the body. The familial history was taken and some of the family members were examined, but no familial aspects of the disease could be established. On extraoral examination, facial asymmetry was present and the length from angle of mandible to midline of left side was more than that of right side. Intraoral examination revealed a mild diffuse swelling extending from 36 to 38 region causing expansion of buccal cortical plate and mildly lingual cortical plate. On palpation it was hard and tender. There was discharging of pus present distal to 36 region (Figure-1). 37 and 38 were missing. Left lower first molar was tender to percussion. On further examination 23, 26, 43 were missing (Figures-2,3). However, the alveolar mucosa with respect to the missing teeth was normal. The bucco-palatal width of 22 to 26 region was more than that of right side (Figure-2). Orthopantomograph revealed multiple sclerotic masses scattered in both the jaws (Figure-4). These sclerotic masses were present above the inferior alveolar canal in mandible. The areas of mixed radiolucent and radiopaque pattern involving both the jaws are also notified. Moth eaten type of radiopacity was present distal to left lower first molar. There were multiple impacted supernumerary teeth present in both maxilla and mandible. Most of the impacted teeth seemed to be pushed through the periphery of the jaws by the expansile lesions. Blood investigations did not detect any biochemical abnormalities. Serum alkaline phosphatase was normal. Based upon this clinical and radiographic finding, this condition was diagnosed as nonhereditary type of florid cemento-osseous dysplasia with osteomyelitis and multiple impacted teeth. Biopsy was not done as the case can be diagnosed on the basis of the characteristic features seen on the radiographs. Antibiotics were given for osteomyelitis. No impacted teeth were extracted

<sup>1</sup>Professor and Head, Department of Oral Pathology and Microbiology, Awadh Dental College and Hospital, Jamshedpur, <sup>2</sup>Senior Lecturer, Department of Oral Medicine and Radiology, Haldia Institute of Dental Sciences and Research, Haldia, India

**Corresponding author:** Dr. Soumi Ghanta, C/O- Dr. Anjan Kumar Ghanta, Vill- Barbarisha, P.O.- Kolaghat, Dist- Purba Midnapur, PIN- 721134, West Bengal, India

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**Figure-1:** Intraoral view- Presence of pus discharge in left mandibular posterior region



**Figure-2:** Intraoral view of maxillary arch- Missing 23 and 26; more bucco-palatal width from 22 to 26 region as compared to right side.



**Figure-3:** Intraoral view of mandibular arch



**Figure-4:** Orthopantomograph revealed multiple sclerotic masses scattered in both the jaws and moth eaten type of radiopacity was present distal to left lower first molar. Multiple impacted supernumerary teeth were also present in both the jaws.

as they were asymptomatic. Patient is followed up at regular intervals.

## DISCUSSION

Exuberant fibro-osseous lesions occurring in multi-quadrants of the jaws were designated as gigantiform cementomas or familial multiple cementomas in the first edition of the World Health Organization's Histological Typing of Odontogenic Tumours, Jaw cysts and Allied Lesions.<sup>4</sup> Florid osseous dysplasia was first suggested by Melrose et al in 1976.<sup>2,4,5</sup> After that Waldron proposed the term florid cemento osseous dysplasia (FCOD) because of closely resemblance of dense sclerotic masses with cementum.<sup>4</sup> It is defined by Robinson to be an abnormal reaction of bone to irritation or stimulation. Melrose pointed out non-inflammatory feature of these lesions because they failed to resolve after elimination of presumed irritants. Eversole and Cho et al supported the progenitor role of periodontal ligament fibroblasts for adjacent hard tissue cells. These lesions are characterized by replacement of bone by connective tissue matrix in which the matrix displaying varying degrees of mineralization in the form of woven bone or cementum-like round basophilic acellular structures. FCOD is most commonly seen in middle aged females.<sup>2,5,6</sup> The present case of a 41-year-old male patient may represent the first of such a rare combination of features being reported in the Indian literature.

FCOD has a tendency for bilateral, symmetrical involvement. It occurs most often in the mandible, but may occur in all four quadrants of the jaws.<sup>2,3,6</sup> All four quadrants were involved in the present case. It is most often asymptomatic and detected through routine radiographic examination. Symptoms such as dull pain or drainage of pus may occur. This lesion is susceptible to osteomyelitis because of exposure of densely sclerotic cemental masses to the oral environment from progressive alveolar atrophy under a denture, traumatically induced ulceration of alveolar mucosa or tooth extraction or biopsy. So, biopsy is not indicated. Clinical and radiological features are most important for diagnosis. FCOD rarely shows cortical expansion<sup>1-3,6</sup> which was present in our case.

Few reported cases of familial form of FCOD have been found in the English literature which appears to be inherited as an autosomal dominant trait with variable phenotypic expression. Unlike the sporadic cases, the familial form is characterized by more expansile lesions and tends to occur in younger individuals.<sup>5,7</sup> In the present case, no familial aspects of the disease could be established. The case had multiple impacted teeth with cortical expansion in both jaws. The case was painless except left side of mandibular posterior region which was secondarily infected leading to osteomyelitis. Very few reported cases of FCOD with multiple impacted teeth were found and most of them were familial in nature.<sup>2</sup> The nonfamilial form of FCOD very rarely shows such a combination.

The radiographic appearance of FCOD depends on the degree of maturation of the lesion. The most common radiographic presentation is multiple confluent sclerotic masses admixed with well defined areas of a mixed radiolucent-radiopaque pattern located usually in the tooth-bearing regions. Over time, the lesions tend to become increasingly radiopaque. The lesion may present different radiographic features in different stages. The classic appearance includes diffuse, lobular, irregular-shaped radiopacities throughout the alveolar process.<sup>1,2,5,8</sup> They do not involve the inferior border, except through direct

focal extension and do not occur in the rami.<sup>2,5</sup> In the present case, multiple sclerotic masses were scattered in both the jaws. These sclerotic masses were present above the inferior alveolar canal in mandible. Computed tomography (CT) can be used to differentiate FCOD from lesions that exhibit a similar sclerotic appearance on conventional radiographs. Enostosis or exostosis exhibits well defined high-density masses on axial CT images than on occlusal radiographs, and they are found to be continuous with cortical plates.<sup>5</sup>

The histomorphology shows a spectrum of progressive features depending upon the stage of development. In the initial stages there is unencapsulated proliferation of cellular fibrous connective tissue containing numerous small calibre blood vessels. In the more advanced stages, mineralized tissue consisting of woven and lamellar bone and cementum like tissue may appear pagetoid with prominent resting and reversal lines.<sup>2,6</sup>

Biopsy is not indicated as FCOD lesions are susceptible to infection leading to osteomyelitis due to avascular nature of altered tissues. Clinical and radiological features are most important to diagnose FCOD.<sup>2</sup>

FCOD lesions should be differentiated from other similar appearing sclerotic lesions on conventional radiographs. Paget's disease manifests as cotton-wool appearance involving multiple bones such as maxilla, mandible, spine, femur, skull, pelvis and sternum and produces elevated alkaline phosphate levels whereas florid cemento-osseous dysplasia is centred above the inferior alveolar canal in mandible and serum alkaline phosphatase level is within normal limit. FCOD usually does not involve other bones. FCOD usually does not involve other bones.<sup>2,5,7</sup> No biochemical alterations and other bone involvement were found in this case presented. Differential diagnosis of FCOD should also include chronic diffuse sclerosing osteomyelitis, which can be a complication of the disease.<sup>5</sup> Chronic diffuse sclerosing osteomyelitis is a primary inflammatory condition of the mandible presenting with cyclic episodes of unilateral pain and swelling. It shows a single area of diffuse sclerosis containing small, ill-defined osteolytic areas, whereas florid cemento-osseous dysplasia is seen as multiple round or lobulated opaque masses. Chronic diffuse sclerosing osteomyelitis is not confined to tooth-bearing areas. It may involve the body of the mandible from the alveolus to the inferior border and may extend into the ramus. Florid cemento-osseous dysplasia has been interpreted as a dysplastic lesion arising in tooth-bearing areas.<sup>2,5,7</sup> This lesion does not appear to be developmental in nature such as fibrous dysplasia, nor does it show the characteristics of neoplasia such as ossifying fibroma.<sup>3</sup> Odontogenic tumors, especially cemento-ossifying fibroma, usually exhibit more buccolingual expansion than does FCOD.<sup>4</sup> Rare possibilities include Gardner's syndrome. Clinical examination and patient data may be crucial in differentiating the lesions. Gardner's syndrome, which can include multiple enostoses, usually is associated with intestinal polyposis and is hereditary. Multiple osteomas frequently are associated with them.<sup>2,9</sup> Florid cemento-osseous dysplasia has no other skeletal changes or tumours that are seen in this syndrome.<sup>6</sup>

There is no need for any treatment in an asymptomatic patient. Antibiotics are generally not effective in FCOD due to poor tissue diffusion, but regular follow up is mandatory due to the susceptibility to infection and fracture of the jaws.<sup>2,5,8</sup>

Instructions to keep good oral hygiene should be given to control periodontal disease and prevent tooth loss. Reevaluation with panoramic radiographs should be done in every 2 or 3 years in an asymptomatic patient and dental CT imaging should be considered if new symptoms or signs develop.<sup>3,5,6,9</sup> No treatment is required unless the patient is esthetically concerned or becomes symptomatic. Management of the symptomatic patient is more difficult because of development of chronic inflammation and infection within densely mineralized tissue.<sup>2,5,6</sup> In such cases, administration of antibiotics is indicated, but sometimes it may not respond to antibiotics due to the avascular nature of the lesion, requiring surgical debridement and enucleation.<sup>1,2,5</sup> However saucerization and extensive surgical resection are probable treatment options for extensive and symptomatic lesions. All efforts should be made to preserve the teeth because of protracted healing after tooth extractions.<sup>2,5</sup> There is no satisfactory treatment for this condition till date.

## CONCLUSION

Mostly florid cemento osseous dysplasias are asymptomatic and are found during routine radiographic examination. Clinicians should be aware of the radiographic manifestation of such conditions and knowledge to recognize and differentiate from other conditions similar to their appearance.

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# Diagnostic Role of CSF-ADA in Differential Diagnosis of Meningitis

Sharad Jain<sup>1</sup>, Anand Sharma<sup>2</sup>, Rashmi Nayak<sup>3</sup>

## ABSTRACT

**Introduction:** Among the patients with meningitis, tubercular meningitis is an important cause of morbidity and mortality in India and other developing countries. Due to lack of early diagnosis, fatality is high in positive cases and sequel of disease may be distressing and disabling in the non-fatal cases. The estimated mortality due to tubercular meningitis in India is 1.5/100,000 population. Many literature has shown that CSF- ADA levels can differentiate various types of meningitis. Aim of the present study was to evaluate whether ADA levels can be used to differentiate various types of meningitis in suspected meningitis cases.

**Material and methods:** A total of 138 clinically suspected cases of meningitis admitted to NSCB medical college hospital Jabalpur were studied. All the cases were examined clinically and their CSF and blood samples were obtained for various investigations after taking consent in written Performa. CSF ADA levels were measured in all cases using Spectrophotometric method.

**Result:** Statistically significant higher values of CSF- ADA were observed with Tubercular Meningitis compared to Pyogenic Meningitis and Viral meningitis cases ( $p<0.001$ ). The sensitivity and specificity was 96.4% and 96.4% respectively when a cut-off value of ADA of 11U/l was used. The PPV, NPV and accuracy of ADA test in diagnosing Tubercular Meningitis was 97.6, 94.6 and 96.4 respectively.

**Conclusion:** We concluded that CSF- ADA level can be used as simple, rapid, inexpensive test for early diagnosis of tubercular meningitis and differentiating it from pyogenic and viral meningitis.

**Keywords:** CSF-ADA, Differential Diagnosis of Meningitis

## INTRODUCTION

Among the patients with meningitis, tubercular meningitis is an important cause of morbidity and mortality in India and other developing countries. Due to lack of early diagnosis, fatality is high in positive cases and sequel of disease may be distressing and disabling in the non-fatal cases. Global burden of tuberculosis is still high, particularly in developing countries; and globally, there were an estimated 9.27 million new cases (139/100,000 population) of tuberculosis in 2007, and the number of prevalent cases was 13.7million (206/100,000 population).<sup>1</sup> 9 Incidence rates of tubercular meningitis are age specific and range from 31.5/100,000 (<1 year) to 0.7 per 100,000 (10-14 year) in the Western Cape Province, South Africa.<sup>2</sup> The estimated mortality due to tubercular meningitis in India is 1.5/100,000 population.<sup>3</sup> Adenosine deaminase is an enzyme of purine metabolism pathway that catalyzes hydrolytic deamination of adenosine to inosine and ammonia. ADA has 2 isoenzymes ADA1 and ADA2. ADA2 is the major component (73%) of the activity of total ADA in the serum of healthy persons. ADA has much greater affinity for adenosine and foundonly in lymphocytes, macrophages and monocytes, which release it when stimulated in the presence of live organisms.<sup>4</sup>

Many literature has shown that CSF ADA levels can differentiate

various types of meningitis. Various investigators have shown that the levels of ADA could be sensitive and specific in diagnosis of tubercular meningitis.<sup>5-7</sup> Aim of the present study is to evaluate whether ADA levels can be used to differentiate various types of meningitis in suspected meningitis cases.

## MATERIAL AND METHODS

A total of 138 clinically suspected cases of meningitis admitted to NSCB medical college hospital Jabalpur were studied. All the cases were examined clinically and their CSF and blood samples were obtained for various investigations after taking consent in written Performa. The present study was approved by the scientific and ethics committee of NSCB Govt. medical college and hospital Jabalpur(MP)

Following investigations were done-

- Hematological- Hb, TLC.
- Biochemical- RBS.
- CSF- Physical examination, biochemical(Protein, sugar), Microscopic examination, bacteriological exam(AFB and Gram stain)
- Neuroimaging
- CSF ADA level using Spectrophotometric method

### Inclusion criteria

Patient of all age group with suspected sign, symptoms and clinical features suggestive of meningitis.

### Exclusion criteria

- Patient already on treatment of meningitis
- Patients with acute infection at sites other than CNS.
- Patient in whom lumbar puncture is contraindicated
- Associated sever hepatic dysfunction
- Females on oral contraceptives and intrauterine device
- Sever dyslipidemia and patients on steroid treatment.

**Estimation of ADA in CSF:** Turbidimetry method was used for ADA estimation.

## STATISTICAL ANALYSIS

The data were analyzed using chi square test with the help of SPSS 20 software. The critical levels of significance of the results were considered at 0.05 levels i.e.  $P<0.05$  was considered significant.

## RESULT

In the present study 138 patients of clinically suspected

<sup>1</sup>Associate Professor, <sup>2</sup>Resident, <sup>3</sup>Assistant Professor, Department of Pathology, NSCB Medical College, Jabalpur(MP), India

**Corresponding author:** Dr. Rashmi Nayak, Type V/1 T and D Circle Colony BSNL, Cantt, Sadar, Jabalpur (MP) India

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meningitis were included of which there were 83 cases of Tubercular Meningitis, 24 cases of Viral meningitis and 31 cases of Pyogenic Meningitis.

In the present study the lowest age was <1 month and the highest was 75yrs. The mean age of study group was 24.16year. Table-1 describes the age wise distribution of cases with maximum No of cases (35) in age group 30-45yrs followed by second peak in age group <0-5 and 15-29yrs age group with 33 cases in each group. The mean age for TBM was  $26.96 \pm 19.49$ , mean age for VM was  $20.17 \pm 16.99$  and mean age for PM was  $19.76 \pm 21.55$ . Statistically no significant difference was seen ( $p>0.05$ ).

Table-2 shows gender wise distribution in meningitis cases. There were 73.5% male and 26.5% females in TBM 62.5% male and 37.5% females in VM and 61.3% male and 38.7% females in PM group. Overall male case were more in number compared to female in our study however there were no statistically significant difference seen ( $p>0.05\%$ ).

Table-3 depict the ADA values in meningitis cases. Value of ADA were  $12.28313 \pm 2.034748$  in Tubercular Meningitis,  $2.658065 \pm 0.349069$  in Pyogenic Meningitis cases and in Viral Meningitis cases value were  $1.991667 \pm 0.239414$ . Statistically significant higher values were observed with Tubercular Meningitis compared to Pyogenic Meningitis and Viral Meningitis cases ( $p<0.001$ ). The sensitivity and specificity was 96.4% and 96.4% respectively when a cut-off value of ADA of 11U/l was used. The PPV, NPV and accuracy of ADA test in diagnosing TBM was 97.6, 94.6 and 96.4 respectively.

## DISCUSSION

In developing countries like India where tuberculosis is very common early diagnosis of TBM and institution of correct therapy early in the course of disease can prevent serious neurological manifestations and can considerably reduce the morbidity and mortality. On routine CSF examination many a time it is difficult to differentiate between TBM and viral meningitis. The only confirmatory test for TBM is demonstration of tubercle bacilli in AFB smear and on culture. But AFB smear is not positive in all cases and culture takes 4-6 weeks, which can delay the treatment and serious complication can develop. So there is need for rapid confirmatory test for

early diagnosis of TBM. Our study aimed at evaluating the diagnostic role of CSF ADA level in TBM. In the present study out of total 138 patients, 83 patients were diagnosed as tubercular meningitis based on the clinical features and CSF analysis. The mean ADA activity was  $12.28 \pm 2.03$  U/l in the tubercular meningitis group,  $2.65 \pm 0.34$  in pyogenic meningitis group and  $1.99 \pm 0.23$  in the viral meningitis group. Comparing the ADA activity, the difference was found to be statistically significant ( $p<0.001$ ) in the tubercular meningitis compared to non tubercular meningitis. The sensitivity and specificity was 96.4% and 96.4% respectively when a cut- off value of ADA of 11 U/l was used. CSF- ADA levels were considerably higher in tubercular meningitis compared to viral meningitis and pyogenic meningitis. The results were concurrent with the other studies.<sup>8-11</sup> Choi SH et al studied ADA activity in CSF of 182 patients with meningitis. The mean ADA level in tubercular group was  $12.7 \pm 7.5$  U/l and it was significantly higher than the other groups ( $3.10 \pm 2.9$  U/l;  $p<0.001$ ). The sensitivity and specificity was 83.0% and 95.0% respectively when a cut-off value of 7 U/l was used.<sup>5</sup> Pettersson et al reports sensitivity of 100.0% and specificity of 99.0% when a cut-off value of 20 U/l was used, but in that study there were only 3 enrolled tubercular meningitis patients.<sup>6</sup> Chotmongkol V et al identified a CSF ADA level of 15.5U/l as the best cut-off value to differentiate tubercular meningitis and non-tubercular meningitis, with sensitivity of 75% and specificity of 93.0%.<sup>7</sup>

In our study, we found that the mean value of CSF ADA was  $2.65 \pm 0.34$  in pyogenic meningitis. Some studies have reported a lower efficacy of this test and show an overlap between tubercular meningitis and bacterial meningitis.<sup>12,13</sup> So we used the higher cut-off value of 11U/l in order to increase the sensitivity of ADA. In our study the level of ADA in CSF is considerably high in tubercular meningitis compared to pyogenic and viral meningitis at a cut-off of 11U/l. So we concluded that CSF-ADA level can help in the differentiation of tubercular meningitis from non-tubercular meningitis. However, they should be interpreted judiciously in the light of the patients' clinical manifestations and the CSF physical, biochemical and microscopic characteristics.

## CONCLUSION

We concluded that CSF-ADA activity was higher in patients with tubercular meningitis as compare to pyogenic and viral meningitis. So it can be used as simple rapid inexpensive test for differentiating tubercular from pyogenic and viral meningitis

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Age(years)	TBM (n=83)	VM (n=24)	PM (n=31)
<0-5	14(16.9%)	6(25.0%)	13(41.9%)
6-14	9(10.8%)	5(20.8%)	2(6.5%)
15-29	22(26.5%)	4(16.7%)	7(22.6%)
30-45	25(30.1%)	7(29.2%)	3(9.7%)
46-59	5(6.0%)	1(4.2%)	4(12.9%)
>60	8(9.6%)	1(4.2%)	2(6.5%)
Mean±SD	$26.96 \pm 19.49$	$20.17 \pm 16.99$	$19.76 \pm 21.55$

Table-1: Age distribution in cases of meningitis

Sex	TBM (n=83)	VM (n=24)	PM (n=31)
Male	61(73.5%)	15(62.5%)	19(61.3%)
Female	22(26.5%)	9(37.5%)	12(38.7%)

Table-2: Gender wise distribution in cases of meningitis

	TBM (n=83)	PM (n=31)	VM (n=24)
ADA (U/L)	$12.28313 \pm 2.034748$	$2.658065 \pm 0.349069$	$1.991667 \pm 0.239414$

Table-3: Levels of ADA in Meningitis

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# Seroprevalence of HBsAg, Anti-HCV and Co-infection among Liver Disease Patients: A Prospective Observational Trial

Amarjit Kaur Gill<sup>1</sup>, Vivek Mittal<sup>2</sup>, Vanita Mittal<sup>3</sup>, Narinder Kaur<sup>4</sup>, Amandeep Kaur<sup>5</sup>, A K Maria<sup>6</sup>, Rajinder Singh<sup>7</sup>

## ABSTRACT

**Introduction:** The blood borne pathogens which are of considerable public health concern are HBV (Hepatitis B virus), HCV (Hepatitis C virus) and Co-infection. The mechanism of transmission for these are similar but the risk is much higher for HBV and HCV due to high prevalence of their carrier and high infectivity stages. Study aimed to detect the prevalence of HbsAg, anti HCV and Co infection in liver disease patients and to analysis the risk factors associated with liver disease patients.

**Material and Methods:** The study included patients of all age groups, visiting OPDs or admitted to the wards of Medicine, who were diagnosed as patients of liver disorders from 1<sup>st</sup> April 2014 to 30th Sept 2015 in AIMS, Bathinda.

**Results:** Out of 100 cases studied, 70 (70%) patients were males and 30 (30%) patients were females and almost 58 patients had history of single whereas 30 patients had history of multiple risk factors like treatment from quacks, alcohol addiction, exposure to blood transfusion, history of dental procedures, history of previous surgical procedure, history of tattooing done and visiting barbers respectively. And out of studied patients, 6 (100%) patients were HBsAg positive and 44 patients were anti HCV positive cases.

**Conclusion:** It is concluded from the present study that HBV and HCV are the major factors in the development of liver diseases with a prevalence of 6% and 44% respectively in patients with liver illnesses.

**Keywords:** HBsAg antigen, Anti-HCV, Seroprevalence, Risk factors, Hepatitis, Hepacard

## INTRODUCTION

The world has entered into a new millennium but there is a growing burden of blood borne diseases particularly in the developing nations. The blood borne pathogens which are of considerable public health concern are HBV (Hepatitis B virus), HCV (Hepatitis C virus) and Co-infection.<sup>1,2</sup>

**Hepatitis B:** Etiological agent HBV belong to hepadenavirus family. Its incubation period is 60-90 days, most common in 15–29 yrs of age but it can infect any age group. This virus spreads through body fluids and parenteral route i.e by transfusion of blood and blood products, from mother to fetus and by sexual route. The outcome of infection with HBV varies from complete recovery to progression to chronic hepatitis and rarely death from fulminant disease.<sup>3,4</sup>

DNA polymerase activity, HBV DNA, and HBe Ag which are representative of viremic stage of hepatitis B, occur early in incubation period along with HBsAg.<sup>3-5</sup>

**Hepatitis C:** HCV belongs to genus hepacivirus in family of flaviviridae. HCV causes acute hepatitis of which many progress to liver cirrhosis with increased risk of HCC. It spreads by direct contact with an infected person's blood i.e needle

stick injuries, cuts with sharps, use of contaminated blood and sexual intercourse. It is prevalent throughout the world, with a prevalence as high as 10 % in certain populations in Africa.<sup>6-8</sup>

**Co-Infection:** The two hepatotropic viruses share same modes of transmission, coinfection with the two viruses is not uncommon, especially in areas with a high prevalence of HBV infection and among people at high risk for parenteral infection.<sup>9,10</sup>

Study aimed to detect the prevalence of HbsAg, anti HCV and Co infection in liver disease patients and to analysis the risk factors associated with liver disease patients.

## MATERIAL AND METHODS

After obtaining approval from the Institutional ethical committee and written informed consent, the present observational study was conducted in the Department of Microbiology in collaboration with Department of Medicine of AIMS, Bathinda.

The study included a total of 100 patients of all age groups who were diagnosed as patients of liver disorders and either HCV positive or HBsAg positive or both, from 1<sup>st</sup> April 2014 to 30th Sept 2015 and who were just diagnosed as liver disease but no viral markers positive were excluded from the study in this period of study.

These patients either were visiting as OPD patients or admitted to the wards of Medicine, AIMS, Bathinda. After taking detailed history of patient about the risk factors, sign and symptoms, complete investigation were done and noted in the performa.

After taking consent, 6ml of blood sample was taken under complete aseptic conditions. Then it was added to two EDTA vacutainer (3ml each). One blood sample was tested in the department of Microbiology for viral markers and 2<sup>nd</sup> was tested for routine investigations and LFTs.

<sup>1</sup>Professor and HOD, <sup>4</sup>Associate Professor, <sup>5</sup>Assistant Professor,

<sup>3</sup>Resident, Department of Microbiology, <sup>2</sup>Associate Professor, Department of Anaesthesiology, <sup>6</sup>Professor and HOD, Department of Medicine, <sup>7</sup>Professor and HOD, Department of Biochemistry, Adesh Institute of Medical Sciences and Research (AIMS), Bathinda, Punjab, 151001, India

**Corresponding author:** Dr. Vivek Mittal, Associate Professor, Department of Anaesthesiology and Intensive Care, AIMS, Adesh University, Bathinda, Punjab. 151001, India

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## Method

**Test for Detection of HBsAg:** Technique used-Hepacard for detection of HBsAg ( J mitra and Co.kits).

**1) HBV elisa test:** Hepalisa a solid phase enzyme linked immunosorbent assay (ELISA) based on the “Direct Sandwich” principle.

**2) HCV elisa test:** The 3rd generation HCV Microlisa is based on a highly sensitive technique, Enzyme Linked Immunosorbent Assay which detects antibodies against HCV in human serum and plasma.

**3) Biochemistry tests:** Another half of the sample were sent to the biochemistry department for LFT and CBC and results were recorded in the proforma.

- |                         |                     |
|-------------------------|---------------------|
| 1. SGOT                 | 2. SGPT             |
| 3. Alkaline phosphatase | 4. Bilirubin levels |
| 5. Sr. Proteins         | 6. Hb               |
|                         | 7. TLC              |

(These tests had been done using the Erba kits).

## STATISTICAL ANALYSIS

Microsoft Excel and Microsoft word (version 7) were used to generate the tables and figures. Results are based on descriptive statistics. The result was present on mean  $\pm$  (S.D.) median (interquartile range) or number of patients as appropriate. For statistical comparison t test and chi-square tests were used and ‘P’ value  $< 0.05$  was considered statistically significant

## RESULTS

The following observations were made in the study of seroprevalence of hepatitis B surface antigen and anti- HCV antibodies in liver disease patients conducted in Department of Microbiology of Adesh hospital, Bathinda from 1<sup>st</sup> April 2014 to 30 September 2015. In our study, we took 100 liver disease patients and our findings were as following;

### Demographic profile

**a) Age Distribution:** 55(55%) patients were in the age group of 41-60 years, 29 cases(29%) were in the age group of 21-40 years, while 16 cases ( 16%) were in the age group of 61-80 years. The age ranged from 20-80 years with mean age of 42.50 yrs.

**b) Sex Distribution:** 70 (70%) patients were males and 30 (30%) patients were females, with male to female ratio being 2.3:1.

**c) Residence Distribution:** 32(32%) patients were from urban areas and 68(68%) patients were from rural areas.

**d) Occupation Distribution:** 70(70%) cases were male patients and 30(30%) were female patients. Male patients were, farmers 42(60%), followed by drivers 12(17.14%), business men 11(15.7%), Govt /pvt. job holder 4(5.7%) and labourers

1(1.4%) respectively. Whereas, Female patients were house wives 25(83.33%), followed by 5(16.67%) patients were Govt/ Pvt. Job holders.

### Risk Factors in Patients of Liver Diseases

12 patients had no history of risk factors. Whereas 58 patients had history of single risk factor exposure and 30 patients had multiple risk factor exposure

**a) Single Risk Factors:** Out of 58 patients, 46 were male patients and 12 were female patients. Whereas 7 patients had history of treatment from quacks, 33 had the history of alcohol addiction, 4 had history of exposure to blood transfusion and 5 had history of dental procedures, while 5 had history of previous surgical procedure, 3 had tattooing done, while 1 had history of visiting barbers respectively.

**b) Multiple Risk Factors:** Out of 30 patients 18 were male patients and 12 were female patients. whereas 5 patients had history of treatment from quacks and blood transfusion, 5 patients had history of IV drug abuse and alcohol ingestion, 10 patients had history of treatment from quacks and alcohol ingestion, 4 patients had a history of blood transfusion and alcohol ingestion, while 4 had history of dental procedures and treatment from quacks, 2 had history of sexual exposure and alcohol consumption respectively.

### HBsAg positivity in relation to Liver Diseases

6 (100%) patients were HBsAg positive. Out of these, 3(50%) patients were of viral hepatitis, 2(33.33%) patients were of alcoholic hepatitis and 1(18.18%) patient was of cirrhosis respectively (Table-1).

### Anti-HCV positivity in relation to Liver Diseases

44 (100%) patients were anti HCV positive cases. Maximum positivity was seen in patients of cirrhosis of liver i.e. 22 (50%) patients were anti HCV positive, followed by patients of viral hepatitis 10 (22.72%), then patients of alcoholic liver disease 6 (13.63%) and 3 (6.81%) patients each of fatty liver and chronic liver disease (Table-1).

### HBsAg positivity in relation to Various High Risk Factors

6 positive HBs Ag patients to various risk factors as exposure of patients to single risk factors or multiple risk factors as per their occupation and life style (Table-2).

### Anti-HCV Positivity In Relation To Various High Risk Behavior

In Table-2, out of 100 liver disease patients, we showed the relation of 44 anti-HCV positive patients to various risk factors as exposure of patients to single risk factors or multiple risk factors as per their occupation and life style.

### CO -Infection of HBV and HCV In Liver Disease

Out of total 100 patients, 48 patients were positive, 30 patients

Disease	No. of cases	HBsAg positivity	Percentage (x/6)(x=+case)	Anti HCV positivity	Percentage (x/44)
Fatty liver	5	0	0	3	6.81%
Viral hepatitis	25	3	50	10	22.72%
Alcoholic hepatitis	29	2	33.3	6	13.63%
Cirrhosis	33	1	18.18	22	50%
Chronic liver disease	8	0	0	3	6.81%
Total	100	6	100	44	100%

Table-1: HBsAg and Anti-HCV positivity in relation to Liver Diseases



Risk factor	Total Cases	M	F	Total HBsAg +ve cases	Total Anti-HCV+ve cases
No risk factor	12	6	6	0	0
IV drug user	0	0	0	0	0
IV drug user + Alcohol ingestion	5	5	0	1	4
Treat from Quacks	7	4	3	0	7
Treat from Quacks + Blood trans.	5	2	3	2	4
Treat from Quacks + Alcohol ingestion	10	5	5	1	4
Blood transfusion	4	1	3	0	3
Blood trans + Alcohol ingestion	4	4	0	0	2
Sexual trans + Alcohol ingestion	2	2	0	0	0
Alcohol ingestion	33	33	0	1	5
Dental extraction	5	0	5	1	5
Dental extraction + Treatment from Quacks	4	0	4	0	4
Surgical intervention	5	4	1	0	3
Tattooing	3	3	0	0	2
Barber	1	1	0	0	1
Total	100	70	30	6	44

**Table-2:** Various High Risk Behavior in relation to HBsAg and Anti -HCV positive cases

were male and 18 patients were female. Whereas out of these 48 patients, 4 patients were only/exclusively HBsAg positive, 42 patients were only/exclusively anti-HCV positive and Co-infection was found in 2 cases, both were male patients.

## DISCUSSION

Present study comprised of 100 patients of liver disease who attended OPD or were admitted in wards of department of Medicine in Adesh medical college, Bathinda, Punjab. The HBsAg and anti -HCV antibodies were tested in these patients. In the present study (2015), out of 100 patients, the age ranged from 21-80 years with a mean $\pm$ SD of 42.50 $\pm$ 10.8 whereas Singh et al<sup>16</sup> from Chandigarh found that out of 100 patients the age ranged from 16-75 years with a mean  $\pm$  SD of 46.5 $\pm$ 16.46, Chakravarti et al<sup>17</sup> from Delhi found that out of 130 patients, the age ranged from 16-72 years with a Mean  $\pm$  SD of 43.5 $\pm$ 17 and Gill et al<sup>20</sup> from Patiala found that out of 100 patients, the age ranged from 12-75 years with a Mean  $\pm$  SD of 41.15 $\pm$ 16.46. The P value is  $\geq 0.05$  and insignificant.

We found that male to female ratio was 2.3:1, whereas Gill et al<sup>20</sup> in their study, done in patiala, found that male to female ratio was 1.9:1, Chakravarti et al<sup>17</sup> in their study, found that male to female ratio was 3.7:1, Singh et al<sup>16</sup> in Manipur, in their study, found that male to female ratio was 2.3:1 and Kumar et al<sup>14</sup> in their study, done in Aligarh, found that male to female ratio was 1.6:1.

In present study(2015),out of 100 patients, 68(68%) patients were from rural areas and 32(32%) patients were from urban areas, whereas Gill et al<sup>20</sup> reported that out of 100 patients, 54(54%) patients were from rural areas and 46 (46%) patients were from urban areas and Ayele et al<sup>22</sup> reported that out of 120 patients, 29(24.2%) patients were from rural areas and 91 (75.8%) patients were from urban areas

In the present study (2015), maximum male personnel were farmers, followed by driver, business men, govt./pvt. job holders and laborer, whereas female patients were housewives, whereas Gill et al<sup>20</sup> reported that majority of their study group male personnel were labourers, farmers, business men, govt/ pvt. job holders, students and health care worker, while in female patients, were housewives followed domestic helpers and student.

This study included 100 cases with liver disease comprising of 5 cases of Fatty liver, 25 cases of Viral hepatitis, 29 cases of Alcoholic hepatitis and 33 cases of Cirrhosis and 8 cases of Chronic liver disease whereas Devi et al<sup>15</sup>, in their study, included 100 cases with liver disease comprising 30 cases of Viral hepatitis, 36 cases of Alcoholic hepatitis and 33 cases of Cirrhosis and Gill et al<sup>20</sup> found, in their study that out of 100 cases with liver disease comprising 27 cases of Viral hepatitis, 38 cases of Alcoholic hepatitis and 35 cases of Cirrhosis.

Out of 100 liver disease patients, 12 patients had no history of risk factors. Whereas 58 patients had history of single risk factor exposure and 30 patients had multiple risk factor exposure. Whereas, Singh et al<sup>16</sup> founded, Out of 100 patients, 30 patients had history of blood transfusion and 15 patients had history of alcohol ingestion, Devi et al<sup>15</sup>, out of 100 cases of hepatic diseases, 34 patient had history of risk factors like blood transfusion, IV drug abuser (IDU) and multiple sexual contact etc. Gill et al<sup>20</sup> founded that out of 100 cases of liver disease, 28 had history of risk factors. like blood transfusion, drug addicts, needle prick, perinatal transmission and history of sexual contact. So, Devi et al<sup>15</sup>, Singh et al<sup>16</sup> and Gil et al<sup>20</sup> all studied 100 cases of liver diseases, but in their maximum patients, the common mode of transmission was by blood transfusion followed by IV drug abusers but in present study maximum cases had history of alcohol consumption (47) followed by treatment from quacks (26), so the difference in study was may be due to difference in the type of patients under study.

In the present study, out of 100 liver disease patients, 6 patients were HBsAg positive. Out of 100 liver disease patients, 6 patients were HBsAg positive, so prevalence was 6%. The results of the present study in regards to HBsAg prevalence were comparable to study of Mathur et al<sup>12</sup> who had prevalence 5.9% and Singh et al<sup>16</sup> had 4%. While Gill et al<sup>20</sup>, Ayele et al<sup>22</sup> and Sharma et al<sup>23</sup> reported higher prevalence of HBsAg i.e 18%, 35.8% and 36.3% respectively. It may be due to higher prevalence of HBsAg in those areas.

In our study, we found multiple risk factors like IV drug abusers + alcohol consumption, blood transfusion + treatment from quacks, blood transfusion+ alcohol consumption and dental procedures+ treatment from quacks were the major risk factors. In the present study, Out of 100 liver disease cases, 44(44%)

Author	Year of Study	Place	IV drugs	Blood Trans.	Treat. Quacks	Sexual Trans.	Dental / tatto	Sx Inv./ Nedl Prick	Multi Risk factor
Arora et al <sup>19</sup>	2007	Amritsar	3.5%	7.14%	-	3.57%	-	7.14%	17.8%
Gill et al <sup>20</sup>	2009	Patiala	16.6%	5.5%	-	5.5%	-	5.5%	
Saravanan et al <sup>21</sup>	2009	Chennai	23.2%	-	26.7%	8.9%	37.5%		61.6%
Sharma et al <sup>23</sup>	2014	Farrukhabad	1.8%	6.4%	-	5.5%	9.1%	50%	-
Present study	2015	Bathinda	-	-	-	16.6%	16.6%	-	66.6%

**Table-3:** HBsAg positivity in relation to High risk factors

Auth.	Yrs.	Place	IV Drug Addict %	Blood Trans. %	Treat From Quacks %	Alcohol Addict %	Dental/ tattoo/ Barber %	Sexual Trans.%	Sx Inv/ Ndl. Stick%	Multi Risk Factors%
Sood et al <sup>13</sup>	2002	Ludhiana	-	18.2	-	15.5	20	-	16.7	
Arora et al <sup>19</sup>	2007	Amritsar	7.7	-	-	-	-	7.7	15.35	46.15
Gill et al <sup>20</sup>	2009	Patiala	17.4	13.2	-	-	-	-	4.4	-
Saravanan et al <sup>21</sup>	2009	Chennai	19.4	-	25.3	-	43.3	10.4	-	64.1
Sharma et al <sup>23</sup>	2014	Farrukhabad	8.4	8.3	-	-	8.3	8.3	42	-
Pr.study	2015	Bathinda	-	6.9	18.4	11.5	18.4	-	6.9	46

**Table-4:** Anti-HCV positivity in relation to high risk behaviour

patients were anti HCV positive cases. Whereas Devi et al<sup>15</sup> had 30%, Singh et al<sup>16</sup> found 48%, Seyad et al<sup>18</sup> found 40.7%, Saravanan et al<sup>21</sup> found 43% and Gill et al<sup>20</sup> found 23% anti-HCV positive cases (Tables-3,4).

In the present study, out of total 100 patients, Co-infection were found in 2 cases, both were male patients. Whereas, Devi et al<sup>15</sup> found HCV positivity around 5%, Singh et al<sup>16</sup> found 5%, Gill et al<sup>20</sup> found 3%, Saravanan et al<sup>21</sup> found 5.9% and Sharma et al<sup>23</sup> found 0.33%.

### Limitations of the study

This is a basically a prospective observational study, with a relatively smaller sample size. So some biases and pitfalls may have been left while designing and executing the study trial

### CONCLUSION

In the present study that HBV and HCV are the major factors in the development of liver diseases with a prevalence of 6% and 44% respectively in patients with liver illnesses. Maximum liver disease patients being in age group 41-60. Whereas, 2% of patients had Co-infection with HBV and HCV, which can be attributed to low prevalence of HBV as well as to the prevalence of occult HBV in HCV infected patients. HCV infection appears to have a suppressive effect on the replication of HBV which could be another reason for low HBV prevalence and co-infection.

The major risk factors associated were found to be alcohol consumption and treatment from quacks and blood transfusion. So alcohol consumption could be an aggravating factor for causing impaired liver functions in addition to HBV and HCV. The transmission of HCV could be curtailed by the awareness of the general public about his mode of transmission.

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# Comparitive Study between Minicholecystectomy Versus Lap Cholecystectomy

Sanjeev Singla<sup>1</sup>, Mamta Singla<sup>2</sup>, Sundeep Singla<sup>3</sup>, Gaurav Thami<sup>1</sup>, Pushpinder Malik<sup>4</sup>, Nivesh Aggarwal<sup>5</sup>

## ABSTRACT

**Introduction:** Open cholecystectomy is still the most common operation performed in our country. Amount of trauma inflicted by surgeon is directly proportional to the length of incision. There emerged a clear trend towards smaller incision which leads to development of mini-cholecystectomy in 1982. But with the introduction of lap cholecystectomy in the year 1987, the surgical community witnessed a revolution in basic ideology. Aim of the study was to compare post operative pain, wound infection and duration of hospital stay with mini-cholecystectomy and lap cholecystectomy and to determine the rate of conversion to standard open cholecystectomy from lap cholecystectomy and mini-cholecystectomy.

**Material and methods:** 100 Patients were randomly divided at time of induction of anesthesia into one of two groups i.e. mini-cholecystectomy and lap cholecystectomy. Incision length was kept 4-5 cm in mini-cholecystectomy.

**Results:** Pain was estimated by pain score. Mean operating time was 50 minutes for mini cholecystectomy and 119 min for lap cholecystectomy. Conversion rate to standard open cholecystectomy in mini-cholecystectomy was 8% and 6% in lap cholecystectomy. Wound infection rate was 4% in both group of patients.

**Conclusion:** Pain score of patients undergoing laparoscopic cholecystectomy was less as compared to patients who underwent mini-cholecystectomy. However there was not much difference in rate of conversion to standard open cholecystectomy and rate of wound infection in both groups but hospital stay of lap cholecystectomy patients was less as compared to mini-cholecystectomy.

**Keywords:** laparoscopic cholecystectomy, mini-cholecystectomy, comparison

## INTRODUCTION

As lap cholecystectomy was introduced in the year 1987, the surgical community witnessed a revolution in basic ideology. It has many advantages over conventional cholecystectomy such as use of smaller incision, cosmetically better and no muscle is cut. This leads to less morbidity, decreased pain and early mobility.

But open cholecystectomy is still the most common operation performed in our country because it avoids infrastructural and instrumental costs, the need to train large number of surgeons who are already in practice and is bereft of many problems inherent with lap cholecystectomy.

Surgical community has realized that surgical incision contributes to morbidity and mortality.<sup>1</sup> Amount of trauma inflicted by surgeon is directly proportional to the length of incision and division of muscles. There emerged a clear trend towards smaller incision which lead to development of mini-cholecystectomy in 1982.<sup>2</sup> So the study was done to compare post operative

pain, wound infection and duration of hospital stay with mini-cholecystectomy and lap cholecystectomy and to determine the rate of conversion to standard open cholecystectomy from lap cholecystectomy and mini-cholecystectomy.

## MATERIAL AND METHODS

This study was conducted at BPSGMC Khanpur, kalan between december 2013 to december 2014. Ethical clearance from local review board and informed consents from patients was taken as required. 100 patients based on inclusion exclusion criteria were randomly divided at time of induction of anesthesia into one of two groups i.e. mini-cholecystectomy and lap cholecystectomy.

**Inclusion criteria:** All patients above 10 years of age group having cholithiasis, visiting to the OPD, were included in the study.

**Exclusion criteria:** All patients having H/O jaundice, pancreatitis, empyema, mucocele, CBD stones were excluded from study.

Incision length was kept 4-5cm in mini-cholecystectomy. A subcostal transverse incision was given in all cases of mini-cholecystectomy. After cutting anterior rectus sheath rectus muscle was split 2-3 cm right of linea alba. Posterior rectus sheath was exposed after splitting and retracting the rectus muscle. This was then divided vertically and peritoneal cavity was opened. This was done so as to have better comparative results as many studies have shown that it is the cutting of rectus muscle which is responsible for pain and morbidity.<sup>3,4</sup> Lap cholecystectomy was done by using standard four ports. All patients were subjected to investigations for confirmation of diagnosis and anesthesia fitness. In the postoperative period all patients were interviewed and observation were noted as described below

## STATISTICAL ANALYSIS

SPSS 13 was used for statistical analysis. We calculated mean, standard deviation for categorical data. Statistical comparison was done with the help of t test.

<sup>1</sup>Associate Professor, <sup>4</sup>Assistant Professor, <sup>5</sup>Professor, Department of Surgery, BPS Government Medical College Khanpurkalan Sonepat,

<sup>2</sup>Professor, Department of Surgery, Muzaffarnagar Medical College, Muzaffarnagar, <sup>3</sup>Assistant Professor, Department of Medicine, Rajshree Medical Research Institute, Bareilly, India

**Corresponding author:** Dr Sanjeev Singla, Associate Professor, Department of Surgery, BPS Government Medical College Khanpurkalan, Sonepat, India

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## RESULTS

Table-1 shows age and sex distribution of mini-cholecystectomy and lap cholecystectomy patients. It was found to have more patients of cholithiasis between age group 26 to 55 years. No sedation was required or given to any of the patients of either group. Immediately after surgery on day zero 10 patients had nausea and vomiting in both groups. Nausea and vomiting was not seen in any patient of either group after day zero.

### Mean operating time

Patients who underwent mini-cholecystectomy had a mean operating time of 50 min while patients in whom lap cholecystectomy was done time taken was much longer as compared to mini-cholecystectomy. Mean operating time for lap cholecystectomy was 119 min.

### Wound infection rate

Wound infection in both group of patients was noted. 2 (4%) patients of mini-cholecystectomy had minor serous discharge from wound site. In lap chole group 2 (4%) patients develop wound infection in the epigastric port site.

### Conversion to standard open cholecystectomy

4 (8%) patients of mini-cholecystectomy group had to be converted to standard open cholecystectomy. In lap cholecystectomy only 3 (6%) patients had to be converted to standard open cholecystectomy

### Hospital stay

Hospital stay of both group of patients was noted and mean was calculated to have comparison. Mean hospital stay of mini-cholecystectomy patients was 4.3 days while that of lap cholecystectomy patients had mean hospital stay of 3.16 days.

## DISCUSSION

**Age:** Mean age of mini-cholecystectomy patients and lap cholecystectomy patients was 40.40 and 42.82 with p value >0.05 and t value .7072 as shown in Table-1. Average age of presentation was fourth decade which is also the reported age of peak incidence by other surgeons.<sup>5-7</sup> In both groups patients were of same age group without any statistical significant difference. Measurement of pain was done by simple pain, sedation and nausea scoring system as given by Dr. Ann Coleman.<sup>8</sup>

**Pain score:** Patients of lap cholecystectomy suffered from less pain as compared to mini-cholecystectomy as mean pain score for lap cholecystectomy was less as compared to mini-cholecystectomy as shown in Table-2. This decrease in pain in lap cholecystectomy is mainly as no muscle is cut and only small 4 skin incisions at different places are given.

**Mean operating time:** Mean operating time was 50 min for mini-cholecystectomy and 119min for lap cholecystectomy in our study. Study done by Axel Ros et al<sup>9</sup> had shown similar timing for lap cholecystectomy (108min) and mini-cholecystectomy (48min). Mean operating time for lap cholecystectomy was more as compared to mini-cholecystectomy. This was because it takes time to start the procedure in lap cholecystectomy as we are to set and test the instruments, camera, telescope, suction, electrocautery etc. before starting the surgery and another reason was because lap cholecystectomy was in the initial stages of development and the time decreases as the experience was gained. Similar findings have been noted by Majeed et al.<sup>10</sup>

Age(in yrs)	Mini-cholecystectomy		Lap cholecystectomy	
	M	F	M	F
10-25	5	0	5	0
26-40	21	1	20	17
41-55	18	1	17	17
56-70	5	1	4	11
>70	1	0	1	0
Mean age	40.40		42.82	
Standard Deviation	13.02		12.66	
Pvalue >.05, t value .7072				

Table-1: Age distribution

Day	Pain score	lapcholecystectomy I	mini cholecystectomy
1	0	0	0
	1	24	4
	2	26	23
	3	0	23
Mean		1.420	2.560
P value <0.001 t value 7.756			
2	0	9	1
	1	38	22
	2	3	25
	3	0	2
Mean		.932	1.610
p value <0.001 t value 6.463			
3	0	24	3
	1	26	44
	2	0	3
	3	0	0
Mean		.589	1.136
p value <0.001 t value 7.318			
4	0	45	16
	1	5	34
	2	0	0
	3	0	0
Mean		.143	.769
value <0.001, t value 7.315			

Table-2: Value of pain score in patients of both groups

**Wound infection rate:** There was not much difference in the infection rate of patients in both groups. Infection rate in both groups was 4%. While wound infection rate in various other studies<sup>11-13</sup> varies from 2.2% to 5.9%. However in patients of lap cholecystectomy group it was the epigastric port site which got infected most of the time. It may be because we remove gallbladder from epigastric port and while removing there occurs some spillage of bile into the wound.

**Conversion rate:** There was not much difference in the rate of conversion in both groups. In mini-cholecystectomy group length of incision had to be increased in 4 cases. Out of 4 cases incision extended in two cases was because of obesity, one was because of difficult dissection in calot's triangle and another was because of empyema gallbladde. In lap cholecystectomy group conversion to open was done in 3 cases. Out of 3 cases one was because of CBD injury and another 2 were because of frozen calot's triangle.

**Hospital stay:** Hospital stay of patients of both groups was

noted. In our study mean hospital stay for mini-cholecystectomy patients was 4.3 days and lap cholecystectomy patients was 3.16 days. Similar studies conducted by Majeed A.W. et al<sup>10</sup> and McGinn FP<sup>14</sup> et al had reported no difference in the hospital stay of both group of patients while study conducted by McMohan AJ et al<sup>15</sup> had reported shorter hospital stay for patients of lap cholecystectomy group.

## CONCLUSION

In this era of expensive health care, any strategies that decreases duration of morbidity and disability and reduce length of hospitalization arouse tremendous interest among medical community. There is clear indication that on average these patients took one day more for recovery and discharge from hospital as compared to patients undergoing lap cholecystectomy. This leads to availability of more beds for patients without any increase in physical infrastructure which can be used to treat other patients. This is especially useful for developing countries which have limited resources and less number of beds per thousand population. Therefore lap cholecystectomy is definitely better than mini-cholecystectomy because of less pain, morbidity and reduced hospital stay.

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# Study of Prevalence of Thyroid Dysfunction in Patients with Type 2 Diabetes Mellitus

Navneet Agrawal<sup>1</sup>, Manoj Gulati<sup>2</sup>

## ABSTRACT

**Introduction:** Type 2 diabetes mellitus and thyroid dysfunction shares the common endocrinopathies. Thyroid dysfunction complicates diabetes management and related complications. The present study was performed to find the prevalence of thyroid dysfunction in patients with type 2 diabetes mellitus (Type 2 DM).

**Material and Methods:** The present retrospective study included 100 patients of Type 2DM who were coming to Diabetes Obesity & Thyroid Centre, Gwalior for consultation. A brief history and examination was done, blood samples were taken and sent to Thyrocare labs, Mumbai for investigations including thyroid function tests and HbA1c.

**Results:** Most of the patients belong to age group of  $\geq 50$  years (66%) with mean age of  $54.63 \pm 8.85$  years and there was male predominance. Mean T3 (ng/dl), T4 ( $\mu$ g/dl), TSH ( $\mu$ IU/ml) and HbA1c (%) level was  $99.75 \pm 20.58$ ,  $9.32 \pm 1.93$ ,  $4.20 \pm 4.51$  and  $7.58 \pm 0.72$  respectively. In present study, 27.8% had associated thyroid dysfunction, out of that 15.2% had subclinical hypothyroidism, 10.6% had clinical hypothyroidism and 2% had hyperthyroidism.

**Conclusion:** Thyroid hormone dysfunction is common in patients with type 2 DM and as it affects the metabolic control, there is a need for thyroid estimation in type 2 diabetics.

**Keywords:** thyroid dysfunction, type 2 diabetes mellitus, triiodothyronine, thyroxine, thyroid stimulating hormone

## INTRODUCTION

The connection between thyroid dysfunction and diabetes mellitus is reported by different clinical trials around the world. Diabetes affects thyroid functions at various levels and thyroid hormones influence carbohydrate metabolism and pancreatic functions to variable extents. In patients with diabetes, thyroid function is significantly altered such as thyrotropin-releasing hormone (TRH) release from hypothalamus and conversion of T4 to T3.<sup>1</sup>

A study on 7097 type 1 diabetes mellitus (T1DM) patients reported a prevalence of 9.5% of thyroid dysfunction.<sup>2</sup> A clinic based study comprising of both T1DM and type 2 diabetes mellitus (T2DM) patients (1310 patients) reported a higher prevalence (13.4%) of thyroid dysfunction.<sup>3</sup>

In a patient with diabetes, the most common type of thyroid dysfunction is hypothyroidism. It results in reduced hepatic glucose production which means a reduced insulin dose is required in a patient with hypothyroid diabetics.<sup>4</sup> On the other hand impaired insulin stimulated glucose utilization in peripheral tissues has been reported in both clinical and subclinical hypothyroidism which accounts for insulin resistance. So, hypothyroidism predisposes to hypoglycemia, and at the same time, causes insulin resistance.<sup>4</sup>

Also in patients with T2DM, hyperthyroidism is reported to be more common compared to normal people. In many patients, uncontrolled hyperthyroidism may be the reason for poor

glycemic control and recurrent diabetic ketoacidosis.<sup>5</sup>

In response to hyperthyroidism gut absorption of glucose is increased along with endogenous glucose production.<sup>5</sup> The present study was a clinic based analysis to find the prevalence of thyroid disorders in patients with T2DM.

## MATERIAL AND METHODS

It was a retrospective analysis of 100 patients of T2DM who came for consultation at Diabetes, Obesity and Thyroid centre, Gwalior. Before the start of the study, informed consent was taken from the patients and the ethical approval was taken from the local authorities.

Patients with history suggestive of T2DM of either sex on oral hypoglycemic agent and/or insulin, even not taking any medication for diabetes were included. Diagnosis of T2DM was done as per the criteria suggestive by American Diabetes Association. HbA1c of  $\geq 6.5\%$  was considered as diabetic. A brief history regarding details of diabetes, glycemic control, family history of diabetes and thyroid disorders and other comorbidities was taken and blood samples were send to Thyrocare Lab Mumbai for investigations.

Thyroid functions were classified as Normal, (thyroid-stimulating hormone (TSH) =  $0.30 - 5.5 \mu$ IU/ml; thyroxine (T4) =  $4.5 - 12.0 \mu$ g/dl and triiodothyronine (T3) =  $60 - 200$  ng/dl), Hypothyroidism (total T4  $< 4.5 \mu$ g/dl and TSH  $> 5.5 \mu$ IU/ml), Subclinical hypothyroidism (T4 is within normal limits but TSH  $> 5.5 \mu$ IU/ml) and Hyperthyroidism (serum TSH  $< 0.3 \mu$ IU/ml).

## STATISTICAL ANALYSIS

All the data were analyzed using IBM SPSS version 20 software. Analysis was performed using chi-square test and independent sample student t test. P values  $< 0.05$  was considered to be significant.

## RESULTS

In present study, most of the patients were above the age group of  $\geq 50$  years (66%). Mean age of study population was  $54.63 \pm 8.85$  years. There were 36% female and 64% males. The mean average blood glucose of study population was  $206.09 \pm 52.08$  mg/dl.

<sup>1</sup>Diabetologist, Department of Diabetes, Obesity and Thyroid Centre,

<sup>2</sup>Consultant, Department of Physician, Parivaar Hospital, Gwalior, India

**Corresponding author:** Dr Navneet Agrawal, 33, Lalitpur Colony, Near Shankar Chowk, Lashkar, Gwalior 474001, India

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<b>Thyroid Dysfunction</b>		<b>Total patients (%)</b>	<b>HbA1c % (mean±SD)</b>
Hypothyroidism	TSH (>5.5μIU/ml)	10.6	8.82 ± 0.62
	T3(T3 <60 ng/dl)		
	T4 (<4.5μg/dl)		
Subclinical hypothyroidism	TSH (>5.5μIU/ml)	15.2	7.98 ± 0.56
	T3 (60-200 ng/dl)		
	T4 (4.5 - 12.0 μg/dl)		
Hyperthyroidism	TSH (<0.3 μIU/ml)	2	6.84±1.02
	T3 (>200 ng/dl)		
	T4 (>12.0 μg/dl)		

TSH; thyroid-stimulating hormone, T3; triiodothyronine, T4; thyroxine, HbA1c; glycated hemoglobin

**Table-1:** Distribution of thyroid dysfunction and HbA1c in study population

Mean T3 (ng/dl), T4 (μg/dl), TSH (μIU/ml) and HbA1c (%) level was 99.75±20.58, 9.32±1.93, 4.20±4.51 and 7.58 ±0.72 respectively.

## DISCUSSION

Diabetes mellitus is serious health related problem affecting a large number of populations worldwide. The associations between diabetes and thyroid disorders have long been reported and they have been shown to mutually influence each other.<sup>1</sup>

In present study, there was a male predominance with mean age of study group being 54.63±8.85 years. The present study recorded a high prevalence of thyroid dysfunction (27.8%) in patients with type 2 DM, as also reported in a study done by Diez et al in Spain, who have reported 32.4% prevalence of thyroid dysfunction.<sup>6</sup>

Another study done by Perros et al had reported a prevalence of 13.4% in patients with diabetes.<sup>3</sup> Radaideh et al did a similar study in Jordan and reported that the overall prevalence of thyroid dysfunction in T2DM patients to be 12.5%.<sup>7</sup> In present study 15.2% had subclinical hypothyroidism and 10.6% had clinical hypothyroidism.

Reports have shown that onset of diabetes come approximately one decade before the diagnosis of thyroid dysfunction.<sup>9</sup>

Bharat et al did a similar study on 60 diabetic patients and reported higher TSH level ( $P<0.05$ ) and lower T4 level ( $P<0.05$ ) in patients with diabetes as compared to normal patients. They found similar T3 level in both the group ( $P>0.05$ ).<sup>10</sup> In present study also hypothyroidism was more prevalent in diabetic patients, which is similar to the study done by Islam et al and Suzuki et al.<sup>11, 12</sup>

Demitrost et al observed that 16.3% had subclinical hypothyroidism, 11.4% had hypothyroidism and 1.5% were hyperthyroidism cases in their study.<sup>13</sup> Our data is in accordance with their findings.

The reason behind the abnormal thyroid hormone level in diabetic patients may be due to insulin which increases the free T4 level while it decreases the T3 level by stopping the T4 to T3 conversion and reduced TRH synthesis in diabetic patients.<sup>12</sup> reports have also shown that glycaemic control is also determined by insulin which is reported to regulate TSH and TRH level.<sup>14</sup>

A disturbance in thyroid level may also exaggerate chances of cardiovascular disease in patient with diabetes by inter-relationships with insulin resistance, dyslipidaemia and endothelial dysfunction.<sup>10</sup>

Inability to diagnose abnormal thyroid hormone levels in

patients with diabetes is often a reason for poor diabetic management.<sup>15</sup> If a patient is showing unexplained alteration in metabolic control, thyroid function tests should be performed.<sup>16</sup>

## Study limitation

The present study was done with small number of patients; a large randomized clinical trial is required to confirm the findings of the present study.

## CONCLUSION

The prevalence of thyroid dysfunction in patients with T2DM in present study was 27.8%. 15.2% had subclinical hypothyroidism, 10.6% had clinical hypothyroidism and 2% had hyperthyroidism. All patients with type 2 DM should be selectively screened for thyroid dysfunction to achieve a good metabolic control.

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# Role of Implant Angles in Hemiepiphysiodesis using 8 Plate for Correction of Angular Deformity Around Knee

Anurag Baghel<sup>1</sup>, Narendra Singh Kushwaha<sup>2</sup>, Shailendra Singh<sup>3</sup>, Raghav Pratap Singh<sup>4</sup>, Santosh Kumar<sup>5</sup>

## ABSTRACT

**Introduction:** Knee joint being crucial weight bearing region may be exposed to pathological mechanical load due to Mal-alignment causing early osteoarthritis of the knee joint. Correction by surgical treatment like hemiepiphysiodesis with eight plate is necessary and proves beneficial depending upon the degree of deformity. The aim of this study was to evaluate the total change of Tibiofemoral Angle (TFA), Mechanical Axis Deviation (MAD) and implant angles and the relationship between implant angles and TFA and MAD during the correction of deformity.

**Material and methods:** we carried out our study in 15 patients having knee angular deformities like genu varum and genu valgus. These patients were surgically managed using eight-plate guided growth. Correction of deformity was measured by radiological assessment. Certain growth and implant angles were measured radiographically like- tibio femoral angle, mechanical axis deviation and Implant angles. Every patient was properly under surgical, medical management and post operative follow up.

**Results:** Proximal and Distal implant angles showed negative correlation with Mechanical axis deviation in Genu varum and Genu valgum cases which was statistically significant ( $p<0.001$ ). Tibio femoral angle improved for valgum deformity from  $22.210\pm 2.390$  to  $6.340\pm 2.620$ . Mechanical axis deviation improved for valgum deformity from  $3.63\pm 0.35$  cm to  $0.73\pm 0.43$  cm (6%).

**Conclusion:** Implant angles increases in their values and their increment retards as the deformity comes near to correction values. These implant angles show that physes is growing and both plate and physes are working normal.

**Keywords:** genu varum, genu valgum, hemiepiphysiodesis, implant angle

## INTRODUCTION

Knee joint being crucial weight bearing region may be exposed to pathological mechanical load due to Mal-alignment causing early osteoarthritis of the knee joint. Correction by surgical treatment is necessary depending upon the degree of deformity. Most physiological deformities peak between 1 and 3 years (varus) or between 3 and 6 years (valgus) and resolve spontaneously.<sup>1</sup>

Pathological angular deformities can be either idiopathic or due to congenital syndromes such as skeletal dysplasia. In contrast to physiological deformities, pathological deformities manifest as the underlying disease progresses and acts on skeletal growth, leading to a gradual mechanical axis displacement.<sup>2</sup> Correction of genu valgum and genu varum by eight plate application is safe and effective.<sup>3</sup>

There are two implant angles – proximal implant angle and distal implant angle.<sup>4</sup> Proximal implant angle is the angle subtended by proximal screw of eight plate with the long axis of shaft of plate (Figure-1). Distal implant angle is the angle subtended by distal screw with long axis of plate (Figure-1).

We placed the plate on convex side of deformity (Tension bend wiring). We put the screws at an angle of more than  $90^\circ$  (i.e. implant angle should  $\geq 90^\circ$ ) so as to avoid the damage to physes. These screws put the resistance to growth of physes and so slows down the growth of physes of the side where plate is applied, but not on the opposite side. But these screws don't put permanent resistance to growth of physes as they are not locked in plate.<sup>5</sup> They are movable in the plate, so when physes grows the implant angle increases and thus these screws put partial resistance to growth. So these screws give guided growth arrest to physes attributed to thin non locking mechanism in plate<sup>5,7</sup>. The aim of this study was to evaluate the total change of Tibiofemoral Angle (TFA), Mechanical Axis Deviation (MAD) and implant angles and the relationship between implant angles and TFA and MAD during the correction of deformity.

## MATERIAL AND METHODS

This study population composed of total 15 patients from the department of orthopaedic surgery, KGMU, Lucknow. 5 Patients had genu varum deformity with unilateral as well as bilateral limbs involvement irrespective of gender. 10 Patients had genu valgum deformity with randomly involved unilateral or bilateral limbs, irrespective of gender. Only patients with open physes of bone were included in the study with the age group of 2 to 14/16 years (14 for female and 16 for male).<sup>6</sup>

Patients with potential growth on opposite side of physes and Mechanical Axis Deviation (MAD) in zone 2 or 3 with gait disturbance, knee pain, medial or lateral thrust were included.<sup>7</sup> Patients with mature bone having closed physes or suffering from any kind of physiological deformity were excluded. Correction of deformity was measured in terms of the following radiological criteria:

Tibiofemoral Angle (TFA) 2. Mechanical Axis Deviation (MAD) 3. Proximal Implant Angle (PIA) 4. Distal Implant Angle (DIA) were also measured.

PIA and DIA tells about functioning of the growth plate (Physes) and clinical Improvement in functional status and symptoms of patients.

Implant angles, MAD and tibio-femoral angle were measured

<sup>1</sup>Lecturer, Department of Orthopaedic Surgery, Government Medical College, Kannauj, <sup>2</sup>Associate Professor, <sup>3</sup>Assistant Professor, Department of Orthopaedic Surgery, <sup>5</sup>Professor, Department of Orthopaedic Surgery, KG Medical University, Lucknow, <sup>4</sup>Director, Ayushman Hospital, Dhampur, Uttar Pradesh, India

**Corresponding author:** Dr. Anurag Baghel, House no. MS-52, Sector D, Aliganj, Pin- 226024, Lucknow, Uttar Pradesh, India

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Variables	Pre Op				Post Op				% change	p value
	At 0 month	After 2 month	After 4 month	After 6 month	After 8 month	After 10 month				
TFA	13.17 ± 1.42	9.33 ± 1.50 <sup>ns</sup>	5.83 ± 1.89*	2.50 ± 1.75**	-2.33 ± 1.74***	-6.00 ± 0.58***			145.6%	p<0.001
MAD	3.22 ± 0.16	2.63 ± 0.25 <sup>ns</sup>	1.80 ± 0.35**	1.07 ± 0.29***	0.40 ± 0.19***	0.00 ± 0.00***			100.0%	p<0.001
PIA	99.67 ± 0.61	101.17 ± 0.65 <sup>ns</sup>	105.00 ± 0.86 <sup>ns</sup>	113.00 ± 1.65***	115.00 ± 1.97***	117.67 ± 4.84***			15.3%	p<0.001
DIA	93.33 ± 1.33	94.00 ± 1.15 <sup>ns</sup>	98.00 ± 1.03 <sup>ns</sup>	105.50 ± 1.59***	110.67 ± 1.02***	114.67 ± 0.33***			18.6%	p<0.001

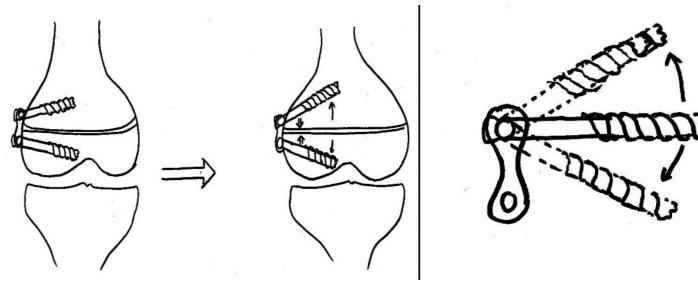
<sup>ns</sup>p>0.05 or \*p<0.05 or \*\*p<0.01 or \*\*\*p<0.001 - as compared to Pre Op

**Table-1:** Pre and post treatment changes in angular deformity around knee joint in patients with genu varum

Variables	Time	TFA	MAD	PIA	DIA
Time†	1.00				
TFA	-1.00***	1.00			
MAD	-1.00***	0.99***	1.00		
PIA	0.98***	-0.97***	-0.98***	1.00	
DIA	0.98***	-0.98***	-0.98***	0.99***	1.00

\*\*\*- p<0.001, TFA: Tibio Femoral Angle, MAD: Mechanical Axis Deviation, PIA: Proximal Implant Angle, DIA: Distal Implant Angle

**Table-2:** Inter correlation between mean response of variables over the periods in patients with genu varum



**Figure-1:** Showing varied degree of Implant Angle

by computer software. Patients were only allowed for movement after proper healing and when they got rid of post surgical pain. Clinico-radiological Follow-up was done every second month till deformity was fully corrected and 8 plate was removed when once MAD came 0°. Radiographic imaging of patients was done by exposing patella forward with X ray beams parallel to the ground and towards the knee.<sup>8</sup> Due to unavailability of large X ray films we made the scanogram by joining 2 or 3 films together by computer software and then we measured different parameters on it.

We evaluated this system and mechanism by measuring change in implant angle, TFA, MAD and their interrelationship.<sup>9,10</sup>

All patients were evaluated clinico-radiologically pre-operatively. Implant angles were calculated at immediately after operative procedure. Subsequently patients were evaluated at every 2<sup>nd</sup> month till MAD ≈ 0 cm and then the plate was removed. For radiological evaluation scanogram was done. MAD and all angles were measured by computer software.

## STATISTICAL ANALYSIS

Statistical analysis was done using ANOVA and post hoc tests. Data are summarized as Mean ± Standard Deviation. Comparison between Groups was carried out by one way repeated measures analysis of variance using general linear models. Bonferroni post hoc was used for contrasts and to analyze mean difference. Pearson correlation method was used to assess association between the variables. Simple linear regression was done to assess relative association between time and response of treatment. P<0.05 was considered statistically significant.

## RESULTS

The mean age of patients in Genu Varum was between 3-10 yrs with mean (± SD) 6.50 ± 2.66. There were six limbs of five patients of Genu varum deformity (five males, one female, one bilateral, four unilateral) which were evaluated. After treatment TFA showed change of 145.6 % and MAD showed a change of 100%. PIA showed a change of 15.3% and DIA showed a change of 18.6% as Summarized in Table-1. ANOVA revealed significant improvement in all variables (p values < 0.01 or < 0.001).

Variables	Pre Op				Post Op				% change	p value
	At 0 month (n=14)	After 2 month (n=14)	After 4 month (n=14)	After 6 month (n=14)	After 8 month (n=14)	After 10 month (n=14)	After 12 month (n=7)			
TFA	22.21 ± 2.39	20.00 ± 2.19 <sup>ns</sup>	16.79 ± 1.96 <sup>ns</sup>	13.71 ± 1.89 <sup>ns</sup>	10.57 ± 1.65**	7.50 ± 1.58***	6.34 ± 2.62***		61.4%	p<0.001
MAD	3.63 ± 0.35	3.09 ± 0.37 <sup>ns</sup>	2.39 ± 0.37 <sup>ns</sup>	1.66 ± 0.33**	0.97 ± 0.32***	0.55 ± 0.29***	0.73 ± 0.43***		79.9%	p<0.001
PIA	97.93 ± 0.99	99.93 ± 0.99 <sup>ns</sup>	102.71 ± 1.01*	107.36 ± 1.14***	110.64 ± 1.04***	114.50 ± 0.95***	117.71 ± 0.99***		16.8%	p<0.001
DIA	85.71 ± 1.89	88.93 ± 1.49 <sup>ns</sup>	93.64 ± 1.54*	98.07 ± 1.76***	102.64 ± 1.53***	106.71 ± 1.50***	110.43 ± 2.66***		22.4%	p<0.001

<sup>ns</sup>p>0.05 or \*p<0.05 or \*\*p<0.01 or \*\*\*p<0.001 - as compared to Pre Op. TFA: Tibio Femoral Angle, MAD: Mechanical Axis Deviation, PIA: Proximal Implant Angle, DIA: Distal Implant Angle

**Table-3:** Pre and post treatment changes in angular deformity around knee joint in patients with genu valgum

Variables	Time	TFA	MAD	LDFA	MPTA	PIA	DIA
Time†	1.00						
TFA	-0.98***	1.00					
MAD	-0.97***	1.00***	1.00				
PIA	1.00***	-0.97***	-0.97***	0.99***	-0.98***	1.00	
DIA	1.00***	-0.98***	-0.98***	0.99***	-0.99***	1.00***	1.00

\*\*\*- p<0.001, TFA: Tibio Femoral Angle, MAD: Mechanical Axis Deviation, PIA: Proximal Implant Angle, DIA: Distal Implant Angle, Time†: in months

**Table-4:** Inter correlation between mean response of variables over the periods in patients with genu valgum

### To see the association between the variables

The mean response of the variables over the periods (months) were correlated with each other and summarized in Table-2. Table-2 also showed significant ( $p<0.001$ ) and negative (inverse) correlation of TFA and MAD with time while significant ( $p<0.001$ ) and positive (direct) correlation of PIA and DIA with time. Further, PIA and DIA both showed significant ( $p<0.001$ ) negative correlation with MAD (Table-2).

### A total of 10 patients (7 males, 3 female) of Genu Valgum deformity were evaluated.

There were fourteen limbs (ten patients) of genu valgum deformity (five males, one female, one bilateral, four unilateral) which were evaluated. Mean age ranged from 3 – 10 years with the mean $\pm$ SD  $6.50\pm2.66$  years. After treatment TFA showed change of 61.4 % and MAD showed a change of 79.9%, PIA showed a change of 16.8% and DIA showed a change of 22.4% (Table-3). ANOVA revealed significant improvement in all variables ( $p$  values  $< 0.01$  or  $< 0.001$ ).

### To see the association between the variables

The mean response of the variables over the periods (months) were correlated with each other and summarized in Table-4. Significant ( $p<0.001$ ) and negative (inverse) correlation of TFA and MAD with time while significant ( $p<0.001$ ) and positive (direct) correlation of PIA and DIA with time. Further, PIA and DIA both showed significant ( $p<0.001$ ) negative correlation with MAD (Table-4).

## DISCUSSION

Angular deformities of knee corrected by osteotomy can result in failure due to complications. Hemipiphysodesis for knee deformity correction using common 8-plate procedure is beneficial. This surgical method is thought to exhibit less hardware failure, easier to apply with lesser complications such as hardware breakage and migration. It is also seen in our study that this technique if used on adolescents have fairer and faster rate of correction. The age group of children in this study was below 16 years. Therefore, the majority were adolescents which correlates with the study by Stevens PM<sup>5</sup>. In previous literature nobody estimated relation between rate of correction by physis level or age using this treatment method. We found rates of correction were fast when the distal femoral and proximal tibial physes were treated concurrently, or when the technique was used in children under the age of 16 years. This age factor proved beneficial as it gave advantage to reduces the need for osteotomy for knee deformities.<sup>3</sup>

In this study all plates were applied to femoral side of deformity. After 8 plate application, deformity got corrected MAD came to center of the knee joint, pain was relieved, Child started to play with his peers as he could run or walk normally without any gait

disturbance.

We evaluated role of angles for deformity correction by measuring them through radiographs.

1. TFA changed from  $22.210\pm 2.390$  to  $6.340\pm 2.620$  in valgum deformity. For varum deformity it changed from  $13.17^{\circ}\pm 1.42^{\circ}$  to  $6.00^{\circ}\pm 0.58^{\circ}$ . Study done by Guzman and Boero<sup>11</sup> correlated with our findings.
2. MAD improved for valgum deformity from  $3.63\pm 0.35$  cm to  $0.73\pm 0.43$  cm. The total correction for varum deformity was from  $3.22\pm 0.16$  cm to 0 which was in contrast to the study done by Rolf D. Burghardt, John E. Herzenberg, Shawn C. Standard<sup>4</sup> since the total correction of valgus and varus deformity in their study was 3.07 cm and 3.88 cm respectively.
3. We measured two other angles-proximal implant angle and distal implant angle which was based on the study done by Anastasios D. Kanellopoulos et al, in pigs. Proximal implant angle is angle subtended by proximal screw with the plate and similarly distal implant angle is angle between screw and plate. If both the angles increases it shows that physis is growing and is functional and no harm had been done to physis during surgery or post-operatively.
4. The PIA in our study increased for valgus and varus deformity from  $97.93^{\circ}\pm 0.99^{\circ}$  and  $99.67^{\circ}\pm 0.61^{\circ}$  To  $117.71^{\circ}\pm 0.99^{\circ}$  and  $117.67^{\circ}\pm 4.84^{\circ}$ .
5. The DIA increased for valgus and varus deformity from  $85.71^{\circ}\pm 1.89^{\circ}$  And  $93.33^{\circ}\pm 1.33^{\circ}$  To  $110.43^{\circ}\pm 2.66^{\circ}$  and  $114.67^{\circ}\pm 0.33^{\circ}$  respectively. The PIA and DIA correlated well with the time and other variables.

Eight plate was removed when MAD came to 0 and TFA was around 7 degree of valgus (adult value). We did not encounter complications related to implant as it occurs with Blount's staple in which there is migration of the staple leading to permanent damage to physis.

Osteotomies were avoided since the deformity was corrected in short span of time. Patients were mobilized as soon as they became comfortable with post operative pain. No post operative POP cast was given.

## CONCLUSION

During the study we concluded the role of implant angles in hemipiphysodesis using 8 plate. The implant angles increase in their values and their increment retards as the deformity comes near to correction values. These implant angles reveal that physis is growing and both plate and physis are working normal.

Their relation with deformity correction i.e. MAD and TFA is linear (more or less). Due to this collinear relation we can say that all parameters go hand in hand. If one parameter changes

other parameter also changes with the same pace.

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# Study of Opportunistic Intestinal Parasitic Infections in HIV Seropositive Patients at a Tertiary Care Teaching Hospital in Karnataka, India

Rajeshwari Prabhakar Rao<sup>1</sup>

## ABSTRACT

**Introduction:** Opportunistic intestinal parasitic infections are the major source of diarrheal disease in developing countries, mainly in Human Immunodeficiency Virus (HIV) infected patients. The aim of this study was to determine the intestinal parasites in HIV seropositive patients with and without diarrhea

**Material and Methods:** The study was conducted during January 2015 - December 2015. A total of 200 stool samples from 100 HIV seropositive patients were examined microscopically for the presence of ova and cysts using wet mount preparations and stained smears. Out of 100 patients, 63 had prolonged diarrhea for more than 4 weeks, 10 had acute diarrhea of lesser than 7 days and 27 were asymptomatic cases, who attended out-patient department. Patients with and without diarrhea participated in the study after giving consent. Enteric pathogens were detected in 49 (49 %) of the 100 patients.

**Results:** The parasites identified were *Cryptosporidium* (21), *Isospora belli* (7), *Cyclospora* (4), *Microsporidia* (2), *Entamoeba histolytica* (9), Hookworm (6). Intestinal parasites in chronic diarrhea were significantly higher than acute diarrhea (42% vs. 6%;  $P < 0.05$ ). Parasitic pathogens are frequently associated with HIV seropositive patients with diarrhea in Southern India.

**Conclusions:** Intestinal opportunistic parasitic infections were detected in 49 % among HIV-seropositive patients. Early detection of opportunistic intestinal parasitic infections will help in the management and will improve the quality of life of HIV infected individuals.

**Keywords:** Chronic diarrhea, HIV, Opportunistic parasites, *Cryptosporidium*, intestinal parasites

*stercoralis* or an opportunistic pathogen, e.g., *Cryptosporidium*, *Isospora*, *Cyclospora* and *Microsporidia*. In case of immunocompetent hosts, only some individuals harboring pathogenic intestinal parasites suffer from symptomatic disease, but the scenario has changed with the advent of HIV/ AIDS. In HIV/ AIDS patient, the rate of infection with a particular intestinal parasite depends on the endemicity of a particular intestinal parasite in the community.<sup>4,5</sup> As the parasitic diarrheal diseases in HIV/ AIDS patients is on the rise, the present study was conducted on HIV seropositive patients with or without history of diarrhea.

## MATERIAL AND METHODS

The study was conducted in the department of Clinical microbiology of Srinivas Institute of Medical Science and Research Centre, Mukka, Surathkal, Mangalore, between January 2015 to December 2015, after obtaining essential institutional ethical clearance. A total of 200 stool samples from 100 patients were examined for intestinal parasites. Fresh stool samples of patients were examined both macroscopically and microscopically in the laboratory.

A total of 100 HIV seropositive patients from skin, medicine and Integrated counselling and testing centre (ICTC) attached with microbiology department were included in this study. After giving consent, 100 patients with and without diarrhea participated in the study and provided two consecutive stool samples. Before sample collection, patient information was obtained such as name, age, sex, occupation, clinical history including history of diarrhea, antibiotic and antiparasitic treatment history. Patients on antiparasitic and antibiotic treatment were not included in the study.

Stool samples were collected in clean wide mouthed, leak proof plastic containers from each patient. Processing of stool samples was done for investigation of intestinal parasites. As per the standard protocol, parasites were detected. Both saline and iodine preparation as well as wet preparation from formal ether concentrated samples were examined microscopically for the presence of protozoan trophozoites and cysts, helminthic ova and larvae. To detect intestinal coccidian parasites, smears

<sup>1</sup>Associate Professor, Department of Microbiology, Srinivas Institute of Medical Science and Research Centre, Mukka, Surathkal, Mangalore, India

**Corresponding author:** Dr. Rajeshwari Prabhakar Rao, Associate Professor of Microbiology, SIMS and RC, Mukka, Surathkal, Mangalore, India

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## INTRODUCTION

Microbial health threats are once more a source of concern due to emerging infectious diseases. In some cases, these diseases are resurgent, like tuberculosis. Some emerging infectious diseases are completely new to humans, such as cryptosporidiosis, isosporiasis, cyclosporiasis and microsporidiosis. Emergence of human diseases is due to various factors, depending upon the particular disease.<sup>1,2</sup> The factors may be environmentally acquired or due to genetic immune deficiencies on the part of the host. One such example is the epidemic of acquired immune deficiency syndrome (AIDS), which has made us vulnerable to opportunistic infections.<sup>3</sup>

In Human Immunodeficiency Virus (HIV) infected individuals, enteric infections occur with increased frequency and some of these are more likely to be persistent, severe, recurrent and associated with extraintestinal manifestations. In developing countries, intestinal parasitic infections are a major cause of morbidity. Common parasites associated with HIV infected persons are either well-established enteric pathogens, e.g., *Entamoeba histolytica*, *Giardia lamblia* and *Strongyloides*

were prepared from stool samples and stained with modified acid fast method.<sup>6</sup>

## STATISTICAL ANALYSIS

Microsoft Excel and Microsoft Word (version 8.1) were used to generate the tables. Results are based on descriptive statistics.

## RESULTS

In this study, a total of 200 stool samples from 100 HIV seropositive patients were examined for intestinal parasitic infections. Out of 100 seropositive cases, 73 were symptomatic cases and 27 were asymptomatic patients. The symptomatic patients were further divided into two groups according to the duration of diarrhea as acute (10) and chronic diarrhea (63). Among the total seropositive patients, 49 (49%) showed intestinal parasitic infections, which include 42% from chronic diarrhea stool samples, 6% from acute diarrhea samples and 1% from the stool of asymptomatic cases. Among the total seropositive patients, 98% of the parasites were identified from

symptomatic patient samples and 2% parasites in asymptomatic cases (Table-1).

In the present study, five types of intestinal protozoal cysts and one helminthic ova were observed and the most common among them was *Cryptosporidium parvum* (21), followed by *E. histolytica* (9), *Isospora belli* (7), Hookworm (6), *Cyclospora* (4) and *Microsporidium* (2). Out of the total 100 patients in the study, majority were males (75%, 75/100). Remaining 25% (25/100) were females. Age distribution in this study group showed that the lowest age of the case whose stool was examined was 20 years and highest age was 65 years. The age distribution results showed that maximum number of intestinal parasites were identified from the age group 20 -30 years followed by 31-40, 41-50 and > 51 year age groups. The study showed that more than 95% of intestinal parasites were identified in young and middle age group of patients, i.e., between 20-50 years. In the age group greater than 51 years, only 2% of the intestinal parasites were observed (Table-2).

Total no. of HIV seropositive patients	No. of patients	Positive for intestinal parasitic infection (%)	P value
Symptomatic patients (73)			
Acute diarrhea	10	6	< 0.05
Chronic diarrhea	63	42	
Asymptomatic patients (27)	27	1	
Total	100	49	

Table-1: Distribution of intestinal parasitic infections in HIV seropositive cases

Age	No. of cases	Distribution of Parasites						Total no. of intestinal parasites
		<i>C. parvum</i>	<i>I. belli</i>	<i>Cyclospora</i>	<i>Microsporidia</i>	<i>E. histolytica</i>	Hookworm	
20-30	28	7	5	2	1	4	3	22
31-40	49	8	1	1	1	4	2	17
41-50	19	5	1	1	0	1	1	9
> 51	4	1	0	0	0	0	0	1
Total	100	21	7	4	2	9	6	49

Table-2: Intestinal parasites in different age groups

Parasites	Symptomatic cases		Asymptomatic cases (%)	Total parasites (intestinal) (%)
	Acute diarrhoea (%)	Chronic diarrhoea (%)		
<i>C. parvum</i>	1	19	1	21
<i>I. belli</i>	1	6	0	7
<i>Cyclospora</i>	0	4	0	4
<i>Microsporidia</i>	0	2	0	2
<i>E. histolytica</i>	2	7	0	9
Hookworm	2	4	0	6
Total	6	42	1	49

Table-3: Intestinal parasites identified in HIV seropositive patients

Author	Place	Year	Isolation rate (%)
Pape et al. <sup>9</sup>	Peru	1990-1993	57.33
Punpoowong et al. <sup>19</sup>	Thailand	1994-1995	50
Abaza et al. <sup>20</sup>	Egypt	1995	23
Prasad et al. <sup>12</sup>	Lucknow, India	1995-1998	50
Brandomisio et al. <sup>11</sup>	Italy	1998	27.92
Escobedo and Nunez. <sup>3</sup>	Cuba	1999	51
Mohandas et al. <sup>13</sup>	Chandigarh, India	2002	30
Kumar et al. <sup>14</sup>	Chennai, India	2002	30.67
Mathur M.K et al. <sup>1</sup>	Jamnagar, India	2009-2010	50.36
Present study	Mukka, Mangalore, India	2015	49

Table-4: Comparative study of intestinal parasitic infections in HIV seropositive patients

This study showed that about 69.4% of the identified intestinal parasites were coccidian parasites, whereas 30.6% were the other protozoans and helminths. *C. parvum* 21 (42.85%) was the most common coccidian parasite identified. In this study, only two cases showed *Microsporidial* cyst, a least commonly identified parasitic cyst. *E. histolytica* was detected in 9% and *Hookworm* ova were detected in 6% cases (Table-3)

## DISCUSSION

The emergence and pandemic spread of AIDS is the greatest challenge to public health in modern times. HIV infection is a serious problem in the present day. A high rate of infection is found in many regions of the world, including the Southeast Asia. Association of AIDS pandemic with intestinal parasitic infections is now a serious concern.<sup>7,8</sup>

In the present study, 49% of intestinal parasites were identified from the stool samples of HIV seropositive patients. In a study conducted by Pape et al. from Peru, 57.33% of parasites were identified. This was high when compared to our studies. In 1993, Cotte et al. in France reported the prevalence of intestinal parasitic infections to be 70.6%, which was very high when compared to our studies. Brandonisio et al. in Italy reported the prevalence of intestinal parasitic infections in HIV/ AIDS patients to be 27.92%.<sup>9-11</sup>

Intestinal parasitic infections have been reported from different parts of India. Prasad et al. from Lucknow reported the prevalence of intestinal parasitic infestation in HIV seropositive patients to be > 50%.<sup>12</sup> In the study conducted by Mohandas et al. from Chandigarh observation was on 120 HIV seropositive patients and reported the prevalence of intestinal parasitic infestations to be 30%.<sup>13</sup> In another study conducted on 150 HIV/ AIDS patients by Kumar et al. in 2002, the prevalence of intestinal parasitic infestations was found to be 30% in Chennai.<sup>14</sup> The difference in prevalence of intestinal parasitic infestations can be due to the difference in the geographical distribution of parasites, personal hygiene and sanitary habits. Other factors for difference in prevalence may be due to selection of cases with different immune status and difference in stool examination method. The patients may be infected with multiple intestinal parasites because of poor sanitary conditions.

In our study, the most common parasite was *Cryptosporidium* and was found in 21% HIV seropositive patients. Other studies have revealed similar findings. In Brazil, Moura et al. in the year 1989, found the prevalence of *Cryptosporidium* to be 18.2% whereas in another study conducted in Brazil by Cimerman et al. in the year 1999, the prevalence was reported to be 7%. Chacin et al. in Venezuela found *Cryptosporidium* in 41.3% of HIV/ AIDS patients. Anand et al. from Manipur in the year 1996 reported the prevalence of *Cryptosporidium* as 46.6%.<sup>15-18</sup> Prasad et al. reported the prevalence of *Cryptosporidium* in Northern India to be 11% during 1995-98.<sup>12</sup> In another study, conducted in Chandigarh by Mohandas et al. in 2002, found *Cryptosporidium* in 13% of HIV seropositive patients.<sup>13</sup> In a study conducted by Kumar et al. in Chennai, 12% of the stool samples were positive for *Cryptosporidium*.<sup>14</sup> *Cryptosporidium* was found to be the etiological agent of diarrhea in 10-20% of patients with AIDS worldwide.<sup>17</sup>

In USA and Europe, *Isospora* is an uncommon cause of diarrhea in AIDS patients (about 2%). This was low when compared to

our studies, where 7% of the total stool samples were found to be positive for *I. belli*. Prevalence of *I. belli* in some of the countries are Brazil (9.9%), Zaire (12%), Zambia (16%) and Haiti (12%) *I. belli* is commonly isolated in patients with AIDS and chronic diarrhea.<sup>16</sup> Coccidian parasite *Cyclospora* was a common finding in Haiti (11%), but was not a common isolate in our study (4%). In US and Tanzania, < 1% of patients with AIDS and chronic diarrhea were positive for *Cyclospora*.<sup>16,18</sup> Studies from different parts of the world show varying prevalence rates with marked geographical variations. Stools of all HIV seropositive patients with diarrhea should be thoroughly investigated to identify intestinal pathogens for proper management (Table-4).

## CONCLUSION

Parasitic infection is a common finding in HIV associated chronic diarrhea cases. The present study has shown that *Cryptosporidium* is the most important emerging pathogen in HIV infected patients with diarrhea in Southern India. Simple direct, concentrated and stained smear examination of stool can help in identification of enteric parasites in majority of patients. The current finding emphasizes the need for early detection of opportunistic intestinal parasitic infections among HIV seropositive patients. This will help the clinicians to decide appropriate management strategies.

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# A Retrospective Study of Wilms Tumour in Our Institute

N. Anil Kumar<sup>1</sup>, Satish Bezawada<sup>2</sup>, S. Venkata Chaitanya<sup>2</sup>, S.R. Sree Gouri<sup>3</sup>, Prasad Pulla<sup>2</sup>

## ABSTRACT

**Introduction:** Wilms tumor (WT) accounting for 6-7% of all childhood cancers is the most common renal tumour in childhood. We conducted this study to review the outcome of multimodality treatment of Wilms' tumor at our institute.

**Material and Methods:** The clinicopathological profile of 8 cases of Wilms' tumor between 2011- 2015 were studied with NWTS (National Wilms' Tumor Study Group) protocol. Data was retrospectively analyzed to determine the outcome of treatment which consisted of unilateral Radical Nephrectomy followed by radiotherapy and chemotherapy based on histopathological staging of the tumor.

**Results:** Eight patients were diagnosed and confirmed histopathologically as Wilms' tumor between june 2011 through june 2015 and outcomes correlated with age, laterality of tumour, sex, stage at presentation and histology. Favourable histology including focal anaplasia was found in 62.5% while unfavourable histology was elicited in 37.5% of the cases. On follow up, six out of eight patients are doing well while one had pulmonary metastasis and one expired.

**Conclusion:** We successfully managed cases of wilms tumour with comparable results of other studies.

**Keyword:** Wilms tumour

## INTRODUCTION

Wilms' tumor (nephroblastoma) is the most common primary malignant renal tumor of childhood.<sup>1,2</sup> This embryonal tumor develops from remnants of immature kidney. Wilms tumor accounts for 6 to 7% of all childhood cancers.<sup>3</sup> In children less than 15 years of age, the annual incidence rate is about 7 to 10 per million.<sup>1,2</sup> The treatment of Wilms' tumor has been improved in the past two decades, with the aid of multimodal therapy protocols.<sup>4-6</sup> The radical changes in multimodality management of wilms tumour off late transferred to a better outcome of these lethal cases. Though there are many studies conducted world wide, studies conducted in India per se are sparse. Hence, we conducted this study to evaluate the results of Wilms' tumor obtained in our Centre.

## MATERIAL AND METHODS

Eight patients were studied in the period between june 2011 and june 2015 in Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh.

The clinical profile, presenting features, the stage of tumor, histopathologic results, and the survival rates were noted down. In all patients, histopathological classification and clinical staging were done according to the NWTS Group.<sup>7</sup> At our centre, patients are also treated as per NWTS protocol where in patients with unilateral Wilm's tumor were treated surgically, followed by adjuvant chemotherapy and/or radiation.

### Inclusion criteria

All the patients who were diagnosed as Wilm's tumor and who underwent management as per NWTS protocol between June 2011 and June 2015 were included in study.

### Exclusion criteria

Patients who had preoperative radiotherapy and/or chemotherapy were excluded from study.

### STATISTICAL ANALYSIS

These patients data was coded into a Microsoft Excel spreadsheet (Redmond, WA) and results were expressed as percentages, median or mean.

### RESULTS

Of these 8 patients, 4 were males and 4 were females (M/F = 1:1). Median age of presentation was 48 months. The modes of presentation are shown in Table-1. Abdominal mass and/or abdominal distension was the most common presenting symptom which was seen in 6 (75%) cases. Other symptoms and signs included abdominal pain in 1 patient (12.5 %), hematuria in 1 patient (12.5%). There were no bilateral cases in our study. Left kidney was affected in 5 (62.5%), and the right one in 3 (37.5%) cases. The distribution of 8 operated patients according to the surgical stage was: stage I 12.5%, stage II 37.5%, stage III 25%, stage IV 25%, and stage V 0%. Favorable histology was diagnosed in 62.5% and unfavorable histology in 37.5% of the patients. The relapse-free and overall 4 year survival rates were 75% and 87.5%, respectively.

### DISCUSSION

Wilms' tumor is the most common renal tumor of infancy and childhood. It affects one child per 10,000 worldwide before the age of 15.<sup>1,2</sup>

The male/female predominance varied with geography of study. In our study the incidence of tumor was similar in males and females which was similar to that of Europe. Studies from America reported a female predominance.<sup>5,6</sup>

The median age of presentation in our study was 48 months. This was similar to many other studies like the South African study where the median age of 39 months<sup>11</sup> and the GFAOP group where the median was 36 months.

Abdominal mass and/or distension was the most common mode of presentation (75%) which was similar to that of United Kingdom Children's Cancer Study Group (UKCCSG) where 74% of cases presented with abdominal mass.

Our study showed a predilection towards the left side (62.5% of

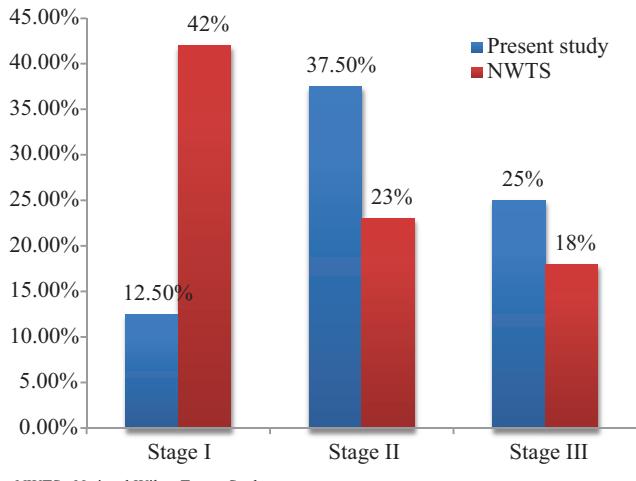
<sup>1</sup>Associate Professor, <sup>2</sup>Post graduate, Department of Urology, <sup>3</sup>Assistant Professor, Department of Obstetrics and Gynaecology, Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, India

**Corresponding author:** Dr. Nallabothula Anil Kumar, Associate professor, Dept of Urology, SVIMS, D.No.5/5/346, 1st floor 2nd house, Near Sneha Hospital, Sarojini Devi Layout, Tirupati, Andhra Pradesh State, India.

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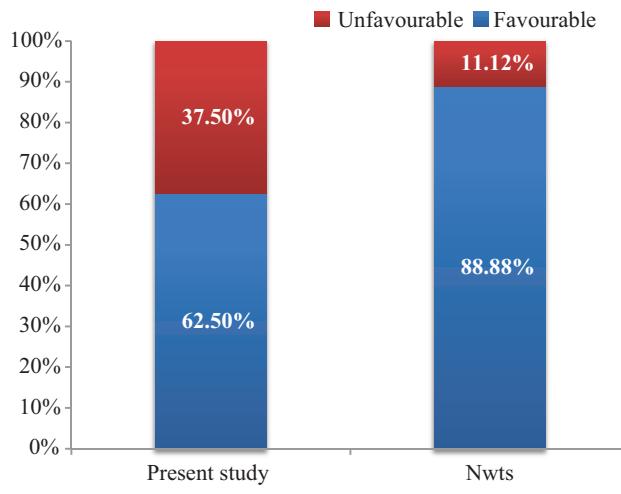
Presenting sign/symptom	No of cases	Percentage
Abdominal mass and abdominal distension	06	75%
Hematuria	01	12.5%
Abdominal pain	01	12.5%
Bilateral disease	00	00%
Congenital anomalies	00	00%

Table-1: Mode of presentation of Wilms tumor in this study



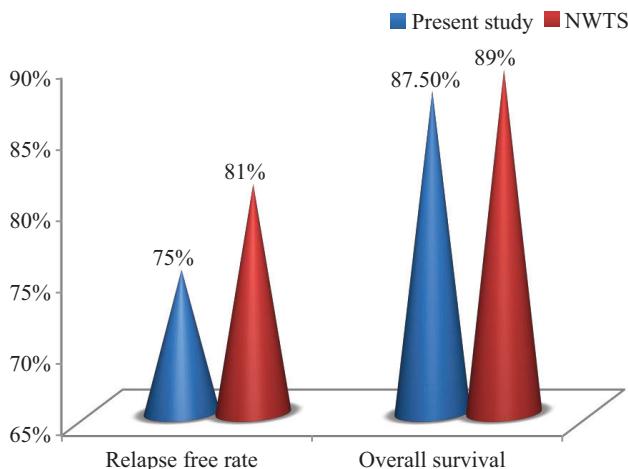
NWTS - National Wilms Tumor Study

Figure-1: Distribution of surgical stages



NWTS - National Wilms Tumor Study

Figure-2: Histopathology findings



NWTS - National Wilms Tumor Study

Figure-3: Relative relapse-free survival rate and overall survival rate

cases) which was compatible with the report of Lemerle et al, but in contrast to Mott et al who reported the similar right and left kidney involvement.<sup>13,14</sup>

When surgical stages of our patients were compared with that of NWTS3, we found that in NWTS3, stage I patients constituted 42% of all patients<sup>8</sup>, while it was 12.5% in our study. Stage II patients constituted 37.5% of our study population compared with 23% in NWTS3 patients. Stage III patients constituted 25% of our study population compared with 18% in NWTS3 patients.<sup>8</sup> This difference in stage distribution might be due to the fact that in developing country like India often patients have delayed approach to health care facility complemented with lack of adequate number of tertiary care centres and lack of screening facilities for early diagnosis.

62.5% of our patients had favorable and 37.5% had unfavorable histology compared to favourable histology of 88.88% and unfavourable histology of 11.12% in NWTS.<sup>8</sup>

Relative relapse-free survival rate and overall survival rate at 4 years in our study were 75% and 87.5%, respectively which were little lower to NWTS3 (81% relapse free survival and 89% overall survival rate) and United Kingdom Wilms' tumor Study 1 (UKWS 1 (overall survival rate of 83% at 6 years) ) results.<sup>10</sup> This might be due to lower percentage of stage I cases and higher percentage of stage II cases in our study.

## CONCLUSION

The present study establishes our success in managing wilms tumour in developing country with comparable relapse free and overall survival rates of studies from developed world. Lack of cytogenetic investigation was one of the pitfall in our study. A larger sample size would provide better insight with respect to the general finding of these results.

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# Evaluation of Prognostic Parameters for Assessment of Efficacy of Steroid Therapy at Day 7 in Patients with Severe Alcoholic Hepatitis

B. Ramesh Kumar<sup>1</sup>, K. Ravikanth<sup>2</sup>, K. Panduranga Rao<sup>3</sup>

## ABSTRACT

**Introduction:** Alcoholic Hepatitis (AH) is an acute inflammatory condition occurring in patients with alcoholic abuse. Currently steroids are the treatment modality in it so the present study was done to evaluate factors associated with poor response to steroid therapy in patients with severe alcoholic hepatitis and compare prognostic parameters in predicting efficacy of steroid therapy at day 7.

**Material and Methods:** This is a prospective comparative study conducted for a period of 2 years, Data was collected prospectively of 55 patients with diagnosis of severe alcoholic hepatitis who satisfied inclusion/exclusion criteria.

**Results:** Alcoholic hepatitis remains associated with high short term mortality in hospitalized patients. The 30 day mortality of severe AH in the current study was 40%. Alcoholic hepatitis was most common in males between 40-50 years old. With median age of  $46.9 \pm 7.7$  (31 – 60) years. Edema/ascites were noted in 78.2%, liver decompensation in 76%, cirrhosis in 34.5% and portal hypertension was present in 67.2% patients. The clinical complications consisted of Asterixis and HE in 40%, HRS and renal failure in 18.2% and 40% patients developed infections. HRS, HE, LFTs, RFTs, Na<sup>+</sup> and all scores including MDF, MELD, CTP showed significant association with in hospital mortality at 30 days on univariate analysis.

**Conclusion:** The CTP, MELD, DF, GAHS, UKELD, and ABIC, as well as those of MDF, MELD obtained at day7 had excellent positive and negative predictive values on ROC curve analysis but at a higher cut-off value.

**Keywords:** Prognostic Parameters, Steroid Therapy, Alcoholic Hepatitis

Gastroenterology, Osmania General Hospital. This study was approved by ethics committee of the hospital. Written informed consent was obtained from all the subjects included in the study.

**Inclusion Criteria:** Patients aged 18 years or older, clinical alcoholic hepatitis with serum albumin >5mg/dl, History of heavy alcohol abuse (>40 g/d for male and >20 g/d for female) present until 1 month of onset of symptoms, AST/ALT ratio >2 with an AST level >45 (1.5 times upper limit of normal) but <500 U/L or ALT <300 U/L and AST/ALT ratio >2, other causes of liver disease including chronic viral hepatitis (Hepatitis B or C), Biliary obstruction, Hepatocellular carcinoma, Discriminant function (DF)  $\geq 32$  ( $DF = 4.6 \times prothrombin\ time + (serum\ bilirubin)$ ).

**Exclusion Criteria:** Abstinence of >2m prior to admission, or a previous index admission, Duration of clinically apparent jaundice >3 months, Co-existent chronic liver disease (NASH, Iron load, biliary or autoimmune), Evidence of chronic viral hepatitis (Hepatitis B or C), Biliary obstruction, Portal vein thrombosis (PVT), Hepatocellular carcinoma, Recent history of herbal medication/hepatotoxic drug exposure, Evidence of current malignancy (except non-melanotic skin cancer), Use of either prednisolone or PTX within 6 weeks prior to admission, AST >500 U/L or ALT >300 U/L (not compatible with AH), Patients dependent upon inotropic support (except Terlipressin). Data was collected prospectively of 55 patients with diagnosis of SAH who satisfied inclusion/exclusion criteria. Detailed clinical history was taken particularly with reference to history of alcohol intake, quantity, duration, pattern, and type of liquor, binge episodes. Patients were assessed at admission for severity of liver disease and presence of complications like ascites, jaundice, HE, variceal haemorrhage, SBP, and/or HRS and daily progress notes were recorded. MELD, CTP, DF scores were calculated on admission. In patients placed on CS, presence of contraindications to steroid treatment and the exact date of initiation of steroid therapy were all recorded. Lille score, change in bilirubin, increase in creatinine were documented at 7 days in patients who received steroids. Thus, these three scores were validated separately in a subgroup of patients with severe AH (admission DF  $\geq 32$ ) treated with corticosteroids, using clinical and biochemical parameters obtained on the day

<sup>1</sup>Associate Professor, <sup>2</sup>Post Graduate, <sup>3</sup>Professor, Department of Gastroenterology, Osmania Medical College, Hyderabad, India

**Corresponding author:** Dr. B.Ramesh Kumar, Associate Professor, Department of Gastroenterology, Osmania Medical college, Hyderabad, India

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before treatment start and the evolution in bilirubin at day 7 of treatment with steroids. The data was collected for each patient until the end-point of either hospital discharge or in-hospital mortality.

Therapy for severe AH defined by MDF >32 consisted of either Corticosteroids(CS) or Pentoxifylline (PTX), the choice between the two was based on clinical evaluation, presence of infection, development of complications, associated other comorbidities and was in accordance with hospital protocol.

## STATISTICAL ANALYSIS

Baseline characteristics of study population was compared by using Chi-squared test for categorical data and Student t-test or Mann–Whitney U test for continuous data, as appropriate. Data are presented as mean with standard deviation, median (interquartile range) or number (%) and all reported *P* values are two-tailed.

## RESULTS

Total patients admitted with diagnosis of alcoholic hepatitis and evaluated for inclusion in the study (N=90). 35 patients were excluded. Reasons for exclusion were 1 patient had abstinence, 1 patient had duration of jaundice > 2 m, 16 patients had

bilirubin <5 mg/dl, 4 patients had ionotropic support, 7 patients had ALT <45 or >500, AST/ALT <2, 1 patient had associated HCV infusion, 5 patients had Hbsg positive, Final number of patients included were 55. Out of 55 patients, 29 patients were treated with PTX, 26 patients were initially treated with CS. Most included patients were male except for one female patient. Demographic characteristics of the patients are shown in Table-1.

The mean TLC was 11,400/mm<sup>3</sup> and mean PMN leukocytosis was 74.4%. The mean total bilirubin was 13.4 mg/dl, the mean AST, ALT and SAP were 192, 85 U/L and 209 U/L respectively. Mean albumin was 2.5g/dl and mean INR was 1.9 (mean PT-24.8) with a control time of 13 sec. Mean Urea and Creatinine levels at admission were 42 mg/dl and 1.4 mg/dl whereas mean Na<sup>+</sup> was 130.7meq/L. The prognostic scores calculated with variables obtained at time of admission revealed mean MDF of 67.2+/-31.4 (range 35.9-142.5), mean CTP of 9.2+/-1.7(range7-13) and MELD of 26+/-5.6 (range 20.1- 40) (Tables-2,3).

In patients with severe alcoholic hepatitis who were treated with steroids (Table-4), presence of history of CLD, clinical signs of edema, asterixis, splenomegaly, presence of infection, MOD, sepsis and complications of HE but not HRS or SBP were associated with significant mortality and worsening of clinical disease with increased mortality at thirty days after starting steroid therapy. Increase in creatinine and bilirubin at day 7 were also associated with increased mortality and higher values (worsening) at day 7 than on day 1 after being started on steroid therapy and were associated with increased mortality and death at 30 days (*p*<0.005) and were comparable to lille

Variables	Mean ± SD (range)	
Age	46.9±7.7	(31-60 years)
Male	54	(98.2)
Duration of hospital stay	15.76 ± 6.5	(5-40 years)
Alcohol (g/day)	138.45 ± 34.5	(80-220)

Table-1: Demographic details of cases included (n=55)

	Alive		Dead		<b>t value</b>	<b>P value</b>
	<b>Mean</b>	<b>SD</b>	<b>Mean</b>	<b>SD</b>		
Alcohol g/d	122.42	26.93	162.50	30.93	5.094	.000
Duration yr	15.73	7.38	15.82	5.03	.050	.960
Hb	12.05	1.70	9.47	2.02	5.109	.000
TLC	10757.58	2539.57	12386.36	2232.72	2.443	.018
PMN	72.82	6.03	76.86	5.62	2.504	.015
Platelet	156848.48	60807.13	128272.73	45869.57	1.875	.066
Bilirubin	10.71	1.44	17.55	3.38	10.330	.000
ALT	72.73	23.48	103.50	28.96	4.335	.000
AST	159.79	47.93	242.00	66.63	5.325	.000
SAP	165.33	68.02	276.41	61.94	6.145	.000
TP	5.92	0.26	5.59	0.21	5.025	.000
Albumin	2.69	0.33	2.24	0.31	5.048	.000
PT	20.73	2.18	31.00	4.48	11.336	.000
INR	1.56	0.18	2.36	0.34	11.476	.000
Urea	34.82	5.89	52.91	10.70	8.071	.000
Creatinine	1.18	0.10	1.84	0.73	5.065	.000
RBS	89.91	22.46	91.95	35.70	.261	.795
Na <sup>+</sup>	133.21	5.86	127.05	4.82	4.098	.000
K <sup>+</sup>	4.06	0.77	4.29	0.99	.985	.329
MDF	45.44	9.38	99.92	23.09	12.173	.000
CTP	8.12	1.05	10.91	1.11	9.416	.000
MELD	22.08	1.45	31.79	4.16	12.378	.000
NA_MELD	24.73	3.28	34.36	3.27	10.67	.000
ABIC	6.97	0.82	8.87	0.97	7.864	.000
GAHS	8.03	0.73	10.36	0.85	10.90	.000
UKELD	61.34	3.90	70.07	4.46	7.682	.000

Table-2: Clinical features at Time of admission stratified according to survival

score in sensitivity and specificity.

On assessment of parameters to evaluate efficacy of steroid therapy at day 7, Lille score at cut off of 0.48, rise in creatinine of more than 0.15 and a rise in bilirubin of 3.5mg at day 7

compared to values calculated on day 1, were all associated with good positive predictive value of 100 while NPV was best for rise in serum creatinine. A lille score of 0.48 had a sensitivity of 75% and specificity of 100% with an area under ROC of

	Alive		dead		t value	p value
	Mean	Std. Deviation	Mean	Std. Deviation		
Age	42.8	6.6	52.3	7.7	-2.94	.008
Alcoholic	127.2	24.9	140.0	24.5	-1.09	.287
Duration	13.7	6.5	19.3	3.6	-1.99	.059
Hb	12.3	1.6	10.6	2.9	1.87	.075
TLC	11344.4	1525.9	11800.0	737.6	-.70	.493
PMN	75.1	3.5	76.5	2.7	-.88	.389
Platelet	170222.2	68310.3	102833.3	34527.8	2.30	.032
Bil	10.7	1.5	16.2	3.5	-5.66	.000
ALT	70.3	20.8	95.7	24.9	-2.47	.022
AST	155.5	45.7	213.7	63.6	-2.45	.023
SAP	156.1	67.8	230.0	63.3	-2.35	.028
TP	6.0	.2	5.6	.2	3.87	.001
ALBUMIN	2.8	.3	2.4	.4	3.32	.003
PT	20.4	2.2	27.3	3.2	-5.93	.000
INR	1.5	.2	2.1	.2	-6.20	.000
UREA	32.9	5.5	44.8	2.7	-5.10	.000
CREAT	1.2	.1	1.4	.1	-3.85	.001
RBS	83.4	16.4	110.5	63.1	-1.72	.099
NA	134.9	5.3	128.3	4.0	2.78	.011
K	4.2	.7	4.1	.9	.21	.839
MDF	44.0	9.1	81.3	17.9	-6.76	.000
CTP	7.8	.9	10.0	.9	-5.35	.000
MELD	21.8	1.4	27.9	2.3	-7.92	.000
CR_INC	.0	.1	.8	.6	-6.43	.000
BIL_DIFF	1.9	1.4	-4.3	2.2	7.96	.000
MDF7	33.2	7.8	102.5	32.6	-8.65	.000

**Table-3:** Baseline parameters and patient demographics/clinical features at time of admission in patients treated with steroids stratified according to survival/death:

	total	Alive	dead	Pts with (alive/dead)	P-value
Jaundice	24	18	06	7 (3/4)	0.02
Fever	24	18	06	10 (8/2)	0.64
Anorexia	24	18	06	14 (8/6)	0.02
Ascites	24	18	06	13 (7/6)	0.01
Edema	24	18	6	14(8/6)	0.02
Anorexia	24	18	06	17(13/4)	0.8
Asterixis	24	18	06	5 (1/4)	0.00
GI bleed	24	18	06	1 (0/1)	0.7
Splenomegaly	24	18	06	8 (4/4)	0.05
HE	24	18	06	5 (1/4)	0.003
HRS	24	18	06	1 (0/1)	0.7
SBP	24	18	06	1 (0/1)	0.7
MOF	24	18	06	4 (0/4)	0.00
Infection	24	18	06	5 (1/4)	0.001
Sepsis	24	18	06	6 (0/6)	0.00

**Table-4:** Clinical features and other complications associated with mortality in those treated with steroids

Test Result Variable(s)	AUROC	Asymptotic Sig. <sup>b</sup>	Best cut off	sensitivity	specificity	PPV	NPV
CR_INC	1.000	.002	0.15	100	100	100	100
BIL_DIFF	.916	.003	3.5	100	93.8	100	94.4
LILLE	.852	.033	0.48	75	100	100	85.7

**Table-5:** Sensitivity and specificity and best cut-off values for parameters used for assessment of efficacy of steroid therapy at day 7 and ROC curve

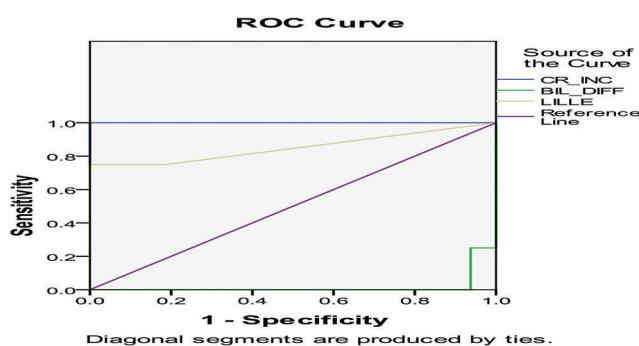


Figure-1: ROC curve

0.852, while creatinine rise was the best indicator of increased mortality risk with continued steroid therapy with a sensitivity and specificity of 100% and area under ROC of 1.00 (Figure-1).

## DISCUSSION

In this cohort, most of patients were male (98.6%). Worldwide, men are more likely than women to drink excessively. Proportion of patients who meet criteria for alcohol dependence is greater in men than in women and men consistently have higher rates of alcohol-related deaths and hospitalizations than women. In our study mean age was  $46.9 \pm 7.7$  (31 – 60) years and is consistent with many other studies which also showed SAH to be most common in males between 40-50 years old. The clinical profile and complications during admission in this study included all 55 patients with clinical jaundice; anorexia was significant in 74.5% while fever was documented in 34.5% only. Edema and ascites were noted in 78.2 % (43 out of 55). Out of total 55 patients 42 (76%) patients had one or more features of liver decompensation at the time of admission. 19(34.5%) patients had evidence of Cirrhosis at time of admission and portal hypertension was present in 37 (67.2%) patients. All patients in the study had severe alcoholic hepatitis (MDF >32). Asterixis and HE were documented in 40% (22 out of 55) patients at admission, while HRS/ renal dysfunction was documented in 10 patients (18.2%) and 22 patients developed infections (40%). 11 had urinary tract infection, 2 had pneumonitis, 2 had diarrhoea and 4 oesophageal candida infection. SBP was documented in a total of 5 patients (9%). GI bleed was noted in 18 (32.7%) patients and overall, the 30d mortality in our cohort was 40%, which is consistent with previous studies reporting short-term mortality ranging to 14.4–27%.<sup>1-3</sup> In a study by Tijera et al<sup>4</sup>, main clinical risk factor associated with mortality in patients with SAH, were concomitant cirrhosis demonstrated by USG and the development of HE. Whereas, in our study only HRS was significantly associated with mortality on univariate analysis, also HE, ascites, sepsis and age did not show high significance compared to HRS(HR-0.135 (p<0.05)). Zhao JM, et al<sup>5</sup> evaluated factors related to mortality in patients with severe hepatitis for several causes, they found that mortality was higher in patients with cirrhosis compared with non-cirrhotic patients (40% vs. 4.3%, P = 0.002) and results of multivariate conditional logistic regression analysis indicated that HE, serum creatinine levels are risk factors for death. This is corroborated by very high significance of CTP (HR-607.5(p<0.01)) in this study, which had most significance among all the scores evaluated at time of admission. Bilirubin, ALT, AST, SAP, PT/INR, Urea and creatinine all showed significance (p<0.05). Finally, recently,

Orntoft N W<sup>6</sup>, et al found that most deaths within the first 84 days after admission in patients with alcoholic hepatitis resulted from liver failure(40%), infections(20%), or HRS(11%). Most patients without cirrhosis died of causes related to alcohol abuse, whereas most patients with cirrhosis (n = 675) died of liver failure, infections, or VB. In our study 22 patients developed infections (40%); 11 had UTI, 2 had pneumonitis, 2 had diarrhoea and 4 had oesophageal candidiasis. SBP was documented in a total of 5 pts (9%). GI bleed was noted in 18(32.7%) patients. 15(27%) patients had features of SIRS at time of admission, out of these, associated infection was detected in 9 pts but 6 pts did not have any evidence of infection, suggesting SIRS of non-infectious etiology likely sec to SAH itself. Only HRS was significantly associated with mortality on univariate and multivariate analysis, also HE, ascites, sepsis and age did not show high significance compared to HRS. However, other authors have reported bacterial infections as a main cause of death.<sup>7,8</sup>

Immune system dysfunction is reported in patients with SAH. Neutrophils are an essential component of the innate immune response and key players in the pathogenesis of alcoholic hepatitis. Jaeschke H, et al<sup>9</sup> found decreased neutrophil phagocytic capacity correlating with disease severity. Mookerjee RP, et al<sup>10</sup>, also demonstrated neutrophil dysfunction in patients with alcoholic hepatitis. Regard to infections found in our patients, is noteworthy that the most frequent was UTI followed by Candida, an explanation for this finding could be the potential side-effects of corticosteroids compounded by malnourished status.

The Lille score is a combination of six variables including a dynamic one, i.e. the evolution in bilirubin following 1 week of corticosteroid treatment. Within our cohort, use of the Lille model proved an accurate predictor of both 30d (AUROC 0.81). Our findings are coherent with those of a recent prospective assessment, in which, however, diagnosis of AH relied completely on clinical criteria.<sup>20</sup> In this study, Lille score showed sensitivity of 75% and specificity of 100% at a cut off value of 0.48 for increased short term mortality and poor response to therapy with CS. As of today, the Lille model represents one of the best currently validated dynamic criterion for the assessment of mortality in AH, and the only one linked to specific stopping rules for corticosteroid management: in poor responders (Lille >0.45) discontinuation of corticosteroids is recommended, particularly when Lille >0.56. Paradoxically in a few cases, Lille score showed a value of zero (<0.45) even when the bilirubin at day 7 had increased mildly compared to bilirubin at day 7 in patients started on CS. A very important variable in the Lille score is the level of serum bilirubin at 7 days after start treatment with corticosteroids. The decrease in the bilirubin level is a crucial determinant of response to treatment. In a study by Bargalló-García A, et al<sup>19</sup> MELD score, urea and bilirubin values one week after admission were independently associated with both in-hospital survival (OR = 1.14, 1.012 and 1.1, respectively), and survival at 6 months (OR = 1, 15; 1.014 and 1.016, respectively). In patients treated with Corticosteroids, bilirubin, TP/Albumin, PT/INR, Urea, creatinine showed significantly higher values in those who died compared to those who survived.

Amongst the prognostic scores, all the scores also showed

higher values in those who died compared to those who survived ( $p<0.05$ ) including Lille score, change in bilirubin at 7days and increase in creatinine. Age, Bilirubin, total protein/albumin, PT/INR, Urea, Creatinine were associated with increased mortality risk ( $p<0.005$ ) in those treated with steroids. Presence of decompensated cirrhosis, elderly in age, renal injury, and malnourished status were also found to be significant in patients who responded poorly to steroids. HRS did not yield significant P-value likely secondary to the fact that very few patients were eligible for initiation of steroids.

For efficacy of steroid therapy at day 7, Lille score at cut off of 0.48, rise in creatinine of more than 0.15 and a rise in bilirubin of 3.5mg at day 7 compared to values calculated on day1, were all associated with good positive predictive value of 100 while NPV was best for rise in serum creatinine. AUROC analysis of parameters that were evaluated on 7<sup>th</sup> day for response to treatment with steroids showed highest sensitivity and specificity for increase in creatinine with a cut-off value of 0.15mg increase on 7<sup>th</sup> day with an AUROC of 1.00. Lille score with a cut-off of 0.48 had specificity of 100% and PPV of 100 for poor response to steroids after 7 days. Currently, importance is laid on response criteria to corticosteroids, or non-improvement at 7-days if liver transplantation is considered, as the PPV of most scores in earlier studies was insufficient to establish a poor prognosis at admission.

## CONCLUSION

Alcoholic hepatitis remains associated with high short term mortality in hospitalized patients. The 30 day mortality of severe AH in the current study was 40%. Alcoholic hepatitis was most common in males between 40-50 years old. Edema/ascites were noted in 78.2%, liver decompensation in 76%, cirrhosis in 34.5% and portal hypertension was present in 67.2% patients. The clinical complications consisted of Asterixis and HE in 40%, HRS and renal failure in 18.2% and 40% patients developed infections. For assessment of efficacy of steroid therapy at day 7, Lille score at cut off of 0.48, rise in creatinine of more than 0.15 and a rise in bilirubin of 3.5mg at day 7 compared to values calculated on day1, were all associated with good positive predictive value of 100 while NPV was best for rise in serum creatinine.

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# Study of Cervical Lymphadenitis, Correlation between Clinical Features, FNAC and Histopathology of Cervical Lymphadenitis

Naresh Kumar Vemulapalli<sup>1</sup>, Pradeep Kumar Chitumalla<sup>2</sup>

## ABSTRACT

**Introduction:** Chronic granulomatosis disease, particularly cervical lymph node tuberculosis, is endemic in various parts of the world. Present study was taken up to know the incidence and etiological factors of cervical lymphadenopathy and to know the correlation between clinical presentation, FNAC and histopathology of cervical lymphadenitis.

**Material and Methods:** This study includes 50 patients of cervical lymphadenopathy cases were studied taking detailed clinical history, physical examination and investigations, FNAC and biopsy were done.

**Results:** The commonest cause of cervical lymphadenopathy is Tuberculosis (68%) and the next most common cause is chronic non specific lymphadenopathy (30%). The commonest age group affected is 2<sup>nd</sup> and 3<sup>rd</sup> decades. Females (60%) Males (40%). A definite history of contact with tuberculosis was obtained only in 18% in this series. 74% of the patients in this series were from low income group and 66% lived in overcrowded conditions. Tuberculous lymphadenopathy was found more in urban population (76%) than in rural population (24%). In our study the specificity and sensitivity of FNAC of tuberculous cervical lymphadenopathy is 94 and 77 respectively. Totally out of 50 cases 24 cases were suspected to have tuberculosis from the clinical features by adding FNAC as the diagnostic modality we diagnosed 28 cases with help of histopathology diagnostic accuracy reached to 34 case with tuberculosis.

**Conclusion:** It can be concluded that FNAC is a reliable diagnostic tool in invasive surgical procedures undertaken in the diagnosis of tuberculous adenitis.

**Keywords:** Cervical Lymphadenitis, Clinical Features, FNAC and Histopathology, Cervical Lymphadenitis

## INTRODUCTION

Neck consists of 300 lymph nodes<sup>1</sup> nearly 1/3 of the total lymph nodes of the body the enlargement of these nodes is significant because of many etiologic factors. Any infection of the upper respiratory tract can be associated with cervical adenitis, in adolescents infectious mononucleosis may begin with diffuse adenopathy. Chronic granulomatosis disease, particularly cervical lymph node tuberculosis, is endemic in various parts of the world. Sarcoidosis often affects Mediastinal and tracheal lymph nodes but cervical adenopathy is also common. Histoplasmosis, coccidioidomycosis and actinomycosis can also produce cervical lymphadenopathy. Salivary gland infection can also produce cervical lymphadenopathy. Massive lymphadenopathy in young and children is seen in reactive lymphoid lymphoplasia.<sup>2</sup> Malignant metastasis can also be the cause of cervical lymph node enlargement. Lymphoma also present as cervical lymphadenopathy. Among the different infective and inflammatory conditions of cervical lymphadenopathy tuberculosis is the most commonly found because of the high prevalence of the disease in our country.

Cervical lymph node involvement is the common extra-pulmonary manifestation of tuberculosis. It is commonly encountered in daily surgical out patient department in our country. Tuberculosis is a disease of great antiquity and has even been found in Egyptian mummies.<sup>3</sup> It remains a major disease on a worldwide basis. Fortunately by effective host defense mechanism and improved social conditions have brought down the disease to low levels in developed countries. It is still common in developing countries like India. The risk is highly increased in immunocompromised patients. Tuberculous lymphadenopathy commonly affects adolescents and young adult's children are also affected.<sup>4</sup> Common age of affected children is 0-5 years. Neck lymph nodes are the commonly affected. Mycobacterium bovis was considered to be the causative agent of tuberculous lymphadenopathy in the past. But now mycobacterium tuberculosis is responsible for most of the tuberculous lymphadenopathy and mycobacterium bovis in some of the cases. This study comprises of 50 cases of cervical lymphadenopathy taken from Prathima hospital, Karimnagar during the period 2011 to 2014. This study was done to know the incidence and etiological factors of cervical lymphadenopathy, the distribution according to age, sex, urban-rural population, socioeconomic conditions of patients. This study mainly focuses on inflammatory and infective causes, correlation between clinical features, FNAC, histopathology and specificity and sensitivity of FNAC cervical lymphadenopathy.

## MATERIAL AND METHODS

This study included 50 patients who attended the surgical OPD of Chalmeda Ananda Rao Institute of Medical Sciences, Karimnagar between August 2015 – March 2016. In this series 50 cases were studied taking detailed clinical history, physical examination and investigations. After physical examination and arriving at clinical diagnosis confirmation was done by FNAC and biopsy. Lymph node biopsy was the most important of these.

**Inclusion criteria:** Cases of inflammatory and infective were taken

**Exclusion criteria:** Cases of secondary's in neck and lymphomas were excluded.

Details of patients as name, age, sex, religion, address,

<sup>1</sup>Assistant Professor, <sup>2</sup>Associate Professor, Department of General Surgery, Chalmeda Ananda Rao Medical College, Karimnagar, Telangana, India

**Corresponding author:** Dr. Pradeep Kumar Chitumalla, Associate Professor, Department of Surgery, Chalmeda Ananda Rao Institute of Medical Sciences, Karimnagar, Andhra Pradesh, India.

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occupation of the patients were noted. Cases were taken at random and only cases who gave consent for lymph node biopsy were taken for study. All patients were given anti-tuberculous drugs using DOTS strategy with 2 months intensive therapy and 4 months with continuation phase therapy with drugs isoniazid, rifampicin, ethambutol and pyrazinamide.

## STATISTICAL ANALYSIS

Statistical analysis was done by calculating sample percentage value. No correlation was done, as this study involves only descriptive analysis.

## RESULTS

Tuberculous lymphadenopathy was the commonest cause of cervical lymphadenopathy with 68% followed by chronic nonspecific lymphadenopathy with 30% and fungal infection 2% (Table-1).

The results of a study series of fine needle aspiration (FNA) biopsies from the head and neck region of 50 patients has been reviewed in order to evaluate the efficacy of this method in the diagnosis of tuberculous lymphadenopathy (TBLN). Of the 35 patients whose fine needle aspiration cytology (FNAC) showed granulomatous changes, 50 had subsequent surgery and histological confirmation of the cytological appearance. 34 had TBLN, thus the specificity of FNAC was 94 per cent in diagnosing tuberculous related granulomatous lymphadenopathy. One false positive FNAC was reported histologically to be non specific. Of the 50 patients, 34 patients had subsequently TBLN confirmed histologically. Of these 34 patients, FNA from 34 showed granulomatous changes or acid fast bacilli (AFB), thus the sensitivity of FNAC in detecting tuberculous lymphadenopathy was 77 per cent. All the 50 patients who presented to the outpatient department were subjected to through clinical examination, FNAC and histopathology (Table-2).

Out of the 50 patients 24 were suspected to have tuberculous

Aetiology	Number	Percentage
Tuberculous Lymphadenopathy	34	68
Non Specific Lymphadenopathy	15	30
Fungal Infection	1	2
Age Distribution		
0-10	1	2
11-20	20	40
21-30	13	26
31-40	11	22
41-50	3	6
51-60	1	2
>60	1	2
History of contact with tuberculosis		
No history of contact	41	82
Definite history of contact	9	18
Sex Distribution		
Male	20	40
Female	30	60
Income Group		
Low (<2000)	37	74%
Middle (2000-6000)	12	24%
High (>6000)	1	2%

Table-1: Demographic details of study

Living Conditions	Number		Percentage
	Area	Number	
Overcrowding (4 or more persons living in one room)	33		66%
Less than 4 persons living in one room	17		34%
Aetiology	Urban	25	50
	Rural	9	18
Chronic non-specific 32%	Urban	15	30
	Rural	1	2
Symptoms			
Swelling in the neck	50		100
Axillary Swelling	2		4
Inguinal Swelling	2		4
Fever	15		30
Loss of weight	20		20
Loss of appetite	20		40
Soar throat	1		2
Cough	1		2
Discharging sinus	1		2
Cold abscess	4		8
Old sinus scar	1		2
Pain	3		6
Caries tooth	1		2
Lymph nodes			
Unilateral right	16		32
Left	20		40
Bilateral	14		28
Other group of lymph nodes	5		10

Table-2: Living conditions, incidence of cervical lymphadenopathy in urban and rural areas, symptoms.

Group of lymph nodes	
Sub-mandibular and Submantal	16%
Upper anterior and deep cervical	28%
Upper posterior deep cervical	40%
Lower antero and deep cervical	28%
Lower posterior deep cervical	24%

Table-3: Group of lymph nodes.

cervical lymphadenopathy. All the patients were subjected to FNAC AND histopathology with the help of FNAC we were able to make out the diagnosis of tuberculosis to 28 patients with the help of FNAC and histopathology combined we could diagnose tuberculosis in 34 patients out of 50 patients in our study. In our study series the sensitivity and specificity of FNAC of tuberculous cervical lymphadenopathy was 77 and 94.

## DISCUSSION

The total number of cases studied were 50 who attended the surgical outpatient department of Chalmeda Ananda Rao Institute of Medical Sciences Hospital, Karimnagar.

**Aetiology of cervical lymphadenopathy:** It can be seen from the study that tuberculous lymphadenopathy was the commonest cause of cervical lymphadenopathy with 68% followed by chronic nonspecific lymphadenopathy with 30% and 2% fungal infection.

**Age Incidence:** In 50 cases the disease commonly affected the

2<sup>nd</sup> decades with 19% and 3<sup>rd</sup> decades with 18% respectively. 4% of cases affected were in this group in the present study. In Wilson's<sup>7</sup> series of 100 cases the common age group of patients was in the 2<sup>nd</sup> and 3<sup>rd</sup> decade followed by the 4<sup>th</sup> decade with 25%, 32% and 13% respectively. In B.P trivedi's<sup>9</sup> series of 235 cases also the commonest age group of presentation was in the 2<sup>nd</sup> and 3<sup>rd</sup> decade with 44% and 35%.next common age groups affected were 1<sup>st</sup> and 4<sup>th</sup> decade with 10% and 8%respectively. In S.P.pamra<sup>5</sup> series of 322 cases the commonest age group affected were 2<sup>nd</sup> and 3<sup>rd</sup> decades with 25% and 35%. In the present study chronic nonspecific adenopathy affected were 2<sup>nd</sup> decade 18% and 3<sup>rd</sup> decade 8% respectively. Commonest age group affected is between 11and 20,21, and 30 closely followed by 31 and 40 years nonspecific lymphadenopathy commonly affects the age group of 11to 20,21 to 30 and less commonly 1 to 10. The causative agent in this age group is atypical mycobacterium. In adults the causative agent is most commonly the mycobacterium tuberculosis. Only 5% are due to atypical mycobacterium. In one study of 343 children with reported lymphadenitis due to atypical mycobacterium 136 were of 3 years or younger age.194 were younger than 5 years –only 5 children were younger than 1 year. It cannot be assumed that all cervical lymphadenopathy in children were caused by atypical mycobacteria. About 5 -10% of childhood lymphadenopathy was due to mycobacterium tuberculosis. In another series studied by Hooper<sup>10</sup>, tuberculous lymphadenopathy was most common in the age group of 20 to 40 years. In the Prabhakar's series earliest presentation was in a 9 month old infant and late age of occurrence was 90 years the average age being 33.6 years. The average age of presentation was 37 years.

**History of Tuberculosis:** There was no definite history of contact with tuberculosis in 82% of cases. A define history was obtained in only in 18% of cases. In S.K.Sen series of tuberculous cervical lymphadenopathy of 386 cases, 78.8% cases had no history of contact with tuberculosis, 19.1% had definitive history of contact with tuberculosis.

**Sex Incidence:** There was increased incidence of tuberculous cervical lymphadenopathy in females than males. All the studies in the past show a definite increased incidence of cervical lymphadenopathy in females. The incidence was more in Trivedi series 57% (1953), Jone's series 58% (1953), S.K Sen's series 58.6% (1955) and S.D.Pamra<sup>5</sup> series 57.08% (1987). In the present study it was present in Males 48% and females 52%. The increased incidence in females may be because of the wide prevalence of malnourishment in females. The other factors influencing the higher incidence in females are overcrowding, lack of education, early marriage, pregnancy, large families, and poor socioeconomic conditions.

**Incidence in different income groups:** The Economic and living conditions were taken into consideration to find out the incidence of cervical lymphadenopathy in the studied series. In this study series, 74% of the patients belonged to the low income group, 24% belonged to the middle income group. Only 2% of patients belonged to the higher income group. In S. K. Sen's series, 65.9% belonged to the low income group and 31.6% belonged to the middle income group. Only 2.5% were of the higher income group. The majority of the patients belong to the lower socioeconomic status and lesser number of patients

were in middle income group. The higher economic status group was the least affected. This shows living conditions of the patients, here 66% of patients in this study lived in overcrowded conditions i.e 4 or more than 4 persons lived in one room. In S.K.sen's series 76.7% lived in overcrowded conditions.

**Incidence in urban and rural areas:** 50% of the patients had tuberculous lymphadenopathy and belongs to urban areas. 18% of the patients had tuberculosis and belongs to rural area. 30% patients belonged to urban areas and 2% of the patients' belonged to rural areas. Overcrowding is an important factor for the spread of tuberculosis having higher incidence in urban areas.

**Presenting symptoms of the studied series:** All patients in the present study had cervical lymph node swelling. Other presenting symptoms were weight loss and loss of appetite (20%), fever (30%), axillary and inguinal swellings (4%), cold abscesses (8%), pain (6%), sore throat, cough, discharging sinus, old sinus scars and caries tooth (2%).

**Group of lymph nodes involved:** There was unilateral involvement of node in 72% of cases. Right side was affected in 32% and left side was affected in 40% of cases bilateral involvement in 14% of the cases. In 10% of cases other groups of lymph nodes were affected. In S.K.sen series there was bilateral neck node involvement in 54.5%, unilateral in 45.5% and neck nodes associated with other group of lymph nodes in 28.5% of cases.

**Various groups involved in cervical lymphadenopathy:** It is evident that the upper anterior deep cervical group of nodes are the most commonly involved. Jugulodigastric nodes were the commonest in this group because tonsils are the common route of entry for the tuberculous bacilli. In the present study upper posterior deep cervical nodes were the commonest (40%) affected.

**Chest Radiography findings:** Generalized tuberculosis is very common and may or may not be associated with a known focus in the body. In faber's series 20% had associated active lesion on chest x-ray and in S.D purohit's<sup>6</sup> series 33% of patients had associated active pulmonary tuberculosis as shown by chest x-ray.

The higher incidence was found in faber's series (20%), lowest in wilmont's<sup>8</sup> series (5%) in the present study the incidence was 16%. The disease is mainly confined to the cervical group of lymph nodes. When the primary complex occurs in the lungs, the disease may also be generalized with lesions elsewhere in the body. The behaviour of these nodes closely resembles that of the peripheral adenitis following infection or injury at the drainage site.

**Biopsy:** It is the confirmatory diagnostic aid. It was done in all the cases. Only histologically proved cases of tuberculous lymphadenopathy and chronic non specific lymphadenopathy were included in the the present study. No case of Sarcoidosis was reported in this study. In the present series 68% were caseating lymphadenitis, 32% were non caseating lymphadenitis or non specific lymphadenitis. Anti tubercular treatment was started in all patients with proven tuberculous lymphadenopathy. Limited excisional surgery was done in 2 patients who had sinuses. Aspiration was done in 4 patients who had cold abscesses, under

cover of anti tuberculous therapy. All cases were followed up for 6 to 9 months after starting chemotherapy.

**Follow Up:** All the cases of tuberculous lymphadenopathy were advised to take the antitubercular drugs regularly for 6 to 9 months and advised to come back for regular monthly follow up. Most of the patients responded well for chemotherapy. A few patients were lost for follow up.

**Response to treatment:** In the present study most of the patients responded to short course chemotherapy with four drugs. A few were lost for follow up. Surgery was limited in patients with cold abscesses and sinuses along with ATT.

## CONCLUSION

It can be concluded that FNAC is a reliable diagnostic tool in helping invasive surgical procedures undertaken in the diagnosis of tuberculous adenitis. The Ziehl-Neelsen stain to identify AFB should be incorporated as an adjunct to increase the diagnostic accuracy of tuberculous lymphadenitis. From our study there is a definite correlation between clinical features, FNAC and histopathology as we can diagnose tuberculous cervical lymphadenopathy with more cases being confirmed with the disease after histopathology.

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# Coagulation Parameters in Pre-eclamptic and Eclamptic Patients - A Comparative Study of 90 Cases

Upam Kr. Sharma<sup>1</sup>, Reena Kouli<sup>2</sup>, Ramesh Sonowal<sup>3</sup>, Projnan Saikia<sup>4</sup>

## ABSTRACT

**Introduction:** Pregnancy Induced Hypertension (PIH) is one of the most common disorders seen in human pregnancies. In roughly half of the cases the disorder progresses into pre-eclampsia, a dangerous condition that can prove fatal to expectant mothers. Early assessment of severity of pre-eclampsia and eclampsia is necessary to prevent maternal and fetal morbidity and mortality. Hence, this study was undertaken with the objective to compare the coagulation parameters of women with pre-eclampsia and eclampsia.

**Material and Methods:** Total 90 PIH cases in their third trimester of pregnancy comprising of 30 Mild Pre-eclampsia, 30 Severe Pre-eclampsia and 30 Eclampsia patients were enrolled for the study. Coagulation parameters such as BT, CT, PT, aPTT, platelet count were studied in these patients. Data were analyzed using MS Excel 2007 and GraphPad Prism 7.

**Results:** There was statistically significant increase in the BT and aPTT with increase in the severity. Although CT and PT increase with the severity of PIH, it was not found to be statistically significant. Platelet count decreases significantly with increase in the severity.

**Conclusion:** The abnormalities pertaining to coagulation parameters in PIH indicate the impending intravascular coagulation.

**Keywords:** Coagulation parameters, Eclampsia, PIH, Pre-eclampsia

## INTRODUCTION

Pregnancy Induced Hypertension (PIH) is one of the most common disorders seen in human pregnancies.<sup>1</sup> Though relatively benign on its own, in roughly half of the cases the disorder progresses into pre-eclampsia, a dangerous condition that can prove fatal to expectant mothers.<sup>2</sup>

PIH is defined as hypertension that occurs in pregnancy for the first time after 20 weeks of gestation and disappears following delivery. It remains a disease of theories as its exact cause is not yet fully established.<sup>3</sup> Approximately 1, 00, 000 women die worldwide per annum because of eclampsia.<sup>4</sup> It is said that pre-eclampsia and eclampsia contribute to death of a woman every 3 minute worldwide.<sup>5</sup> In India the incidence of pre-eclampsia is reported to be 8-10% of the pregnancy.<sup>6</sup> It is the third leading cause of maternal mortality responsible for 17% of maternal deaths.<sup>6,7</sup>

There are many terms used to classify the hypertensive disorders of pregnancy, the classifications recommended by the American College of Obstetrics and Gynaecology in 1986 is listed below: American College of Obstetrics and Gynaecology Classifications for Hypertensive Disorders of Pregnancy.<sup>8</sup>

- Pregnancy-Induced Hypertension
- (a) Pre-eclampsia:      Mild  
                                  Severe

## (b) Eclampsia

- Chronic Hypertension Preceding Pregnancy (Any Etiology)
- Chronic Hypertension (Any Etiology) With
  - (a) Superimposed Pregnancy Induced Hypertension
  - (b) Superimposed Pre-eclampsia
  - (c) Superimposed Eclampsia

Profound changes in the coagulation and fibrinolytic system occurs during normal pregnancy causing a hypercoagulable state.<sup>9</sup> There is a distinct possibility of accentuation of this hypercoagulable state of pregnancy during eclampsia and pre-eclampsia. The prothrombotic state may culminate in a process of chronic disseminated intravascular coagulation (DIC) leading to changes in kidney and placenta.<sup>10</sup>

Early assessment of severity of pre-eclampsia and eclampsia is necessary to prevent complications like HELLP syndrome and increased maternal and fetal morbidity and mortality. Hence, this study was undertaken with the aim to compare the coagulation parameters of women with pre-eclampsia and eclampsia.

## MATERIAL AND METHODS

A hospital based cross-sectional study was conducted for a period of one year from July 2014 to June 2015. Total 90 PIH cases in their third trimester of pregnancy comprising of 30 Mild Pre-eclampsia, 30 Severe Pre-eclampsia and 30 Eclampsia patients from the Department of Obstetrics and Gynaecology, in a tertiary care centre of North-Eastern India, were enrolled for the study.

Ethical clearance was obtained from the Institutional Ethics Committee for conducting the study. Details of the study were explained to the subjects and written informed consent was taken from all the study subjects.

The coagulation parameters such as BT, CT, PT, aPTT, platelet count of the patients required for the study were carried out in the Advanced Hematology, Service Laboratory under Department of Pathology, in a tertiary care centre of North-Eastern India, by using SYSMEX XS-800i 5 part haematology analyzer and SYSMEX CA-500 series Coagulometer.

## Criteria for selection of cases

Pregnant females in their third trimester with signs and

<sup>1</sup>Post graduate trainee, <sup>2</sup>Associate Professor, <sup>3</sup>Associate Professor, Department of Obstetrics and Gynaecology, <sup>4</sup>Professor and Head of the Department of Pathology, Assam Medical College and Hospital, Dibrugarh, Assam, India

**Corresponding author:** Dr. Upam Kr. Sharma, Department of Pathology, Assam Medical College and Hospital, Dibrugarh, PIN-786002, Assam, India.

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symptoms of PIH were included in the study. Criteria for selection is elevation of systolic blood pressure above 140 mm of Hg and/or diastolic blood pressure above 90mm of Hg or a rise in former of at least 15 mm of Hg above baseline value on at least two occasions and at least 6 hours apart. All the patients fulfilling these criteria with or without edema or proteinuria after 20 weeks of pregnancy were included in the study. These patients were further categorized into three different categories: Mild Pre-eclampsia, Severe Pre-eclampsia and Eclampsia. Pre-eclampsia was diagnosed according to American College of Obstetrics and Gynaecology (ACOG) criteria;<sup>8</sup> a blood pressure higher than 140/90 mm of Hg, edema and proteinuria >300mg/24 hours or  $\geq 1+$  dipstick method after 20<sup>th</sup> week of gestation. Patient with blood pressure  $> 140/90$  mm of Hg but  $<160/110$  mm of Hg without proteinuria were included in the mild cases. And patient with blood pressure  $\geq 160/110$  mm of Hg, proteinuria and presence of headache, visual disturbances, upper abdominal pain, oliguria and thrombocytopenia were included in severe cases. Eclampsia is defined as pre-eclampsia associated with seizures.

#### Exclusion criteria

- (1) All cases with pre-existing hypertension other than PIH.
- (2) Patients having co morbid conditions such as
  - Severe anaemia
  - Diabetes mellitus
  - H/o auto immune disorder.
  - H/o I.T.P. (Idiopathic Thrombocytopenic Purpura)
  - H/o receiving drugs like aspirin, anti-coagulants etc
- (3) Patients who didn't give consent for the study.

#### STATISTICAL ANALYSIS

Data were presented with percentages and mean with standard deviation. Statistical significance among the groups were assessed using ANOVA (Analysis of Variance) followed by Bonferroni. Data were analyzed using MS Excel 2007 and GraphPad Prism 7.

#### RESULTS

The mean bleeding time (BT) among the mild pre-eclampsia, severe pre-eclampsia and eclampsia cases were  $87.87 \pm 7.48$  sec,  $102.50 \pm 10.15$  sec and  $103.27 \pm 16.78$  sec respectively (Figure-1). There was statistically significant increase in the BT between mild and severe pre-eclampsia and mild pre-eclampsia and eclampsia cases (Table-1).

The mean clotting time (CT) was  $144.50 \pm 8.44$  sec among the mild pre-eclampsia cases and  $156.17 \pm 11.57$  sec among the eclampsia cases. Among the severe pre-eclampsia cases the mean CT was  $152.83 \pm 9.53$  sec. Although the CT increased with the severity of PIH it was not found to be statistically

significant.

The mean prothrombin time (PT) was  $9.20 \pm 1.14$  sec among the mild pre-eclampsia cases and  $9.68 \pm 1.24$  sec among the eclampsia cases. The increase in PT with the severity of PIH was not found to be statistically significant.

Among the mild pre-eclampsia and eclampsia cases the mean aPTT levels were  $25.03 \pm 1.75$  sec and  $35.14 \pm 4.76$  sec respectively. The increase in aPTT level with the severity of PIH was found to be statistically significant.

The mean platelet count among the mild pre-eclampsia cases was

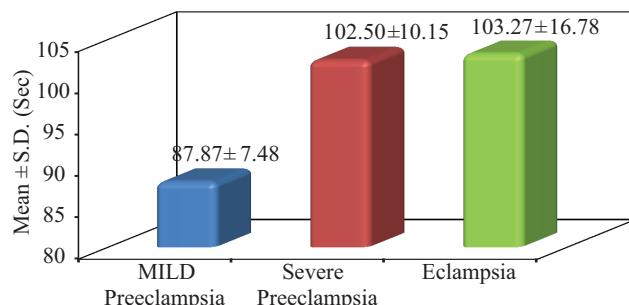


Figure-1: Coagulation profile of pih cases (bleeding time)

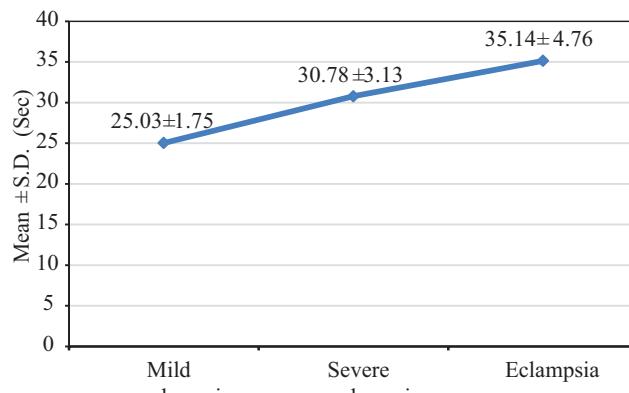


Figure-2: Coagulation profile of pih cases (apTT level)

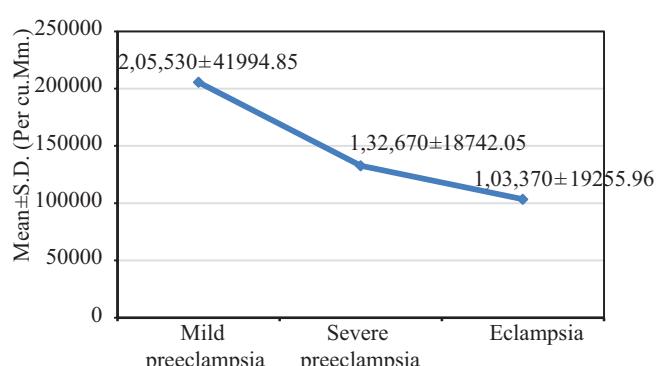


Figure-3: Coagulation profile of pih cases (platelet count)

	BT (sec)	CT (sec)	PT (sec)	aPTT (sec)	Platelet count (lacs per cu.mm.)
Mild pre-eclampsia (1)	$87.87 \pm 7.48$	$144.50 \pm 8.44$	$9.20 \pm 1.14$	$25.03 \pm 1.75$	$205530 \pm 41994.85$
Severe pre-eclampsia (2)	$102.50 \pm 10.15$	$152.83 \pm 9.53$	$9.27 \pm 0.98$	$30.78 \pm 3.13$	$132670 \pm 18742.05$
Eclampsia (3)	$103.27 \pm 16.78$	$156.17 \pm 11.57$	$9.68 \pm 1.24$	$35.14 \pm 4.76$	$103370 \pm 19255.96$
	P value	P value	P value	P value	P value
Group 1 vs 2	0.000	1.000	1.000	0.00	0.000
Group 1 vs 3	0.000	0.061	0.293	0.000	0.000
Group 2 vs 3	1.000	0.495	0.461	0.000	0.000

Table-1: Comparison of Coagulation parameter in patients with pre-eclampsia and eclampsia

2, 05, 530 ( $\pm 41994.85$ ) per mm<sup>3</sup> and 1, 03, 370 ( $\pm 19255.96$ ) per mm<sup>3</sup> among the eclampsia cases. The platelet count decreased significantly with the increase in severity.

## DISCUSSION

In the present study, there was statistically significant increase in the BT between mild and severe pre-eclampsia and mild pre-eclampsia and eclampsia cases. Chauhan P et al.<sup>11</sup>, found that BT was  $294.0 \pm 43.20$  (sec) in mild pre-eclampsia,  $324.79 \pm 59.00$  (sec) in severe pre-eclampsia and  $470.08 \pm 189.00$  (sec) in eclamptic patients and observed that the bleeding time increased significantly with the severity of PIH. The findings of the present study are in accordance with the study conducted by Chauhan P et al.<sup>11</sup>

In the present study, although the CT increased with the severity of PIH it was not found to be statistically significant. Joshi SR et al.<sup>12</sup> in their study of coagulation profile in pregnancy induced hypertension at MIMER Medical College, Talegaon, Dabhade found that CT was 4.24 min in mild pre-eclampsia, 4.17 min in severe pre-eclampsia, 4.27 min in eclampsia patients and didn't find any significant prolongation of CT. Chauhan P et al.<sup>11</sup> in their comparative study of coagulation profile in pre-eclamptic and eclamptic patients with normotensive patients found that the clotting time was  $368.40 \pm 146.20$  sec,  $374.20 \pm 124.80$  sec,  $376.64 \pm 130.40$  sec in mild pre-eclamptic, severe pre-eclamptic and eclamptic patients accordingly. However this increase in clotting time was not statistically significant. Shete AN et al.<sup>13</sup> in their study found that the clotting time increased in eclampsia patients compared to normal pregnant women. The increase was however not statistically significant. Jambhulkar S et al.<sup>14</sup> in their study in Govt. Medical College, Nagpur on coagulation profile in PIH patients didn't find any significant prolongation in the CT.

In the current study, although the PT increased with the severity of PIH it was not found to be statistically significant. Joshi SR et al.<sup>12</sup> in their study of coagulation profile in pregnancy induced hypertension at MIMER Medical College, Talegaon, Dabhade found that PT was 13.78 sec in mild pre-eclampsia, 13.93 sec in severe pre-eclampsia, 13.98 sec in eclampsia patients. Chauhan P et al.<sup>11</sup> in their comparative study of coagulation profile in pre-eclamptic and eclamptic patients with normotensive patients found that PT was  $13.78 \pm 1.82$  sec in mild pre-eclampsia,  $13.83 \pm 1.82$  sec in severe pre-eclampsia,  $14.14 \pm 1.50$  sec in eclampsia patients. However this increase in prothrombin time was not statistically significant. Jambhulkar S et al.<sup>14</sup> in their study in Govt. Medical College, Nagpur on coagulation profile in PIH patients didn't find any significant prolongation in the PT. Osmanağaoğlu MA et al.<sup>15</sup> in their study on coagulation inhibitors in pre-eclamptic pregnant women didn't observe any significant difference in the prothrombin time value between severe pre-eclamptic and the control group. The findings of the present study are almost similar to the study conducted by Joshi SR et al.<sup>12</sup>, Chauhan P et al.<sup>11</sup>, Shete AN et al.<sup>13</sup>, Jambhulkar S et al.<sup>14</sup> and Osmanağaoğlu MA et al.<sup>15</sup>

In the present study, the increase in aPTT level with the severity of PIH was statistically significant. Joshi SR et al.<sup>12</sup> found that aPTT was 28.44 (sec) in mild pre-eclamptic patients, 30.32 (sec) in severe pre-eclamptic patients and 31.62 (sec) in eclamptic patients and observed that the aPTT level in PIH patients was

significantly prolonged. Osmanağaoğlu MA et al.<sup>15</sup> in their study on coagulation inhibitors in pre-eclamptic pregnant women observed a significant difference with regard to partial thromboplastin time between severe pre-eclamptic and the control group ( $p < 0.0001$ ). Jambhulkar S et al.<sup>14</sup> in their study in Govt. Medical College, Nagpur on coagulation profile in PIH patients found that PTTK (aPTT) was significantly prolonged. The present study is in accordance with the study conducted by Joshi SR et al.<sup>12</sup>, Osmanağaoğlu MA et al.<sup>15</sup> and Jambhulkar S et al.<sup>14</sup>

In the current study, the platelet count decreased significantly with the increase in severity. Chauhan P et al.<sup>11</sup> in their study found platelet count  $173.33 \pm 25.91$  in mild pre-eclampsia,  $145.04 \pm 23.76$  in severe pre-eclampsia,  $121.05 \pm 22.44$  in eclampsia and observed a statistically significant decrease in platelet count with an increase in severity of PIH. Sarkar PD et al.<sup>16</sup> in their study found that platelet count was  $1.98 \pm 0.41$  lacs/cumm in mild pre-eclamptic women and  $1.47 \pm 0.32$  lacs/cumm in severe pre-eclamptic patients and this difference in the platelet count was statistically significant. Mohapatra S et al.<sup>3</sup> in their study found that platelet count was  $2.23 \pm 0.19$  lacs/cumm in mild pre-eclamptic,  $1.82 \pm 0.45$  lacs/cumm in severe pre-eclamptic,  $1.21 \pm 0.49$  lacs/cumm in eclamptic patients and observed that there is an inverse relationship between the severity of PIH and platelet numbers. Vrunda JK et al.<sup>17</sup> in their study found platelet count was 2.00 (lacs/cumm) in mild pre-eclamptic patient, 1.40 (lacs/cumm) in severe pre-eclamptic patients and 1.30 (lacs/cumm) in eclamptic patients and observed that thrombocytopenia is directly proportional to the severity of PIH. Shete AN et al.<sup>13</sup>, Government Medical College, Aurangabad, conducted a study to assess the physiological stress during Pregnancy Induced Hypertension and observed a significant decrease in platelet count. In a study conducted by Sultana R et al.<sup>18</sup> on platelet count in pre-eclampsia, it was observed that the mean platelet count in cases and controls were 1, 44,  $260 \pm 96$ , 472 and 1, 98,  $100 \pm 51$ , 219 respectively. The study revealed that low platelets count is associated with pre-eclampsia. The findings of the present study therefore correlates with the study conducted by Chauhan P et al.<sup>11</sup> (2014), Sarkar PD et al.<sup>16</sup>, Mohapatra S et al.<sup>3</sup>, Vrunda JK et al.<sup>17</sup>, Shete AN et al.<sup>13</sup> and Sultana R et al.<sup>18</sup>

## CONCLUSION

In the light of the results and observations of the present study, we can say that certain coagulation parameters such as BT, aPTT, platelet count were associated with the severity of the disease, although certain coagulation parameters such as CT, PT did not show a significant change with the severity of PIH. These abnormalities pertaining to coagulation parameters in PIH indicate the impending intravascular coagulation. Timely measurement of these parameters and prompt treatment might reduce systemic complications and maternal death due to Pregnancy Induced Hypertension.

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# Effect of Dexmedetomidine on Post Operative Analgesia and Haemodynamics when added to Bupivacaine 0.5% in Epidural Block for Pelvic and Lower Limb Orthopedic Surgeries

Vivek Chakole<sup>1</sup>, Praveen Kumar<sup>2</sup>, Meera Sharma<sup>3</sup>

## ABSTRACT

**Introduction:** Epidural blockade is one of the best procedures, providing better intra operative hemodynamic control, post operative pain relief and rapid recovery from surgery specially pelvic surgeries and orthopedic surgeries. Selective alpha 2 adrenergic agonist used as adjuvant in epidural blockade. Dexmedetomidine a more powerful and highly selective alpha 2 adrenoceptor agonist than clonidine. This study was designed to investigate appropriate doses 1.0, 1.5, 2.0 mcg/kg of dexmedetomidine added to bupivacaine for epidural block to prolong postoperative pain relief and reduce the requirement of rescue analgesia in pelvic and lower limb orthopedic surgeries with least side effects.

**Material and methods:** In our randomized control trial study, total 100 ASA class I and II patients of age between 15 to 65 years undergoing lower limb orthopedic and pelvic surgeries were given epidural block and studied for addition of dexmedetomidine on intra operative hemodynamic and post operative analgesia. Patients received 0.5% bupivacaine 20 ml alone in one group and with added Dexmedetomidine 1.0, 1.5, 2.0 mcg/kg in the other 3 groups respectively. All the patients were monitored for onset of sensory and motor blockade, intra operative hemodynamic, post operative analgesia, adverse effect and complications.

**Result:** Onset of sensory and motor blockade was same in all four groups. Addition of Dexmedetomidine increases the post operative pain free period significantly with all doses of dexmedetomidine. An increase of dose beyond 1.5 mcg/Kg did not further improved pain free period and in fact lowered by 1.24 hours and the incidences of complications started appearing which were absent up to 1.5 mcg/Kg dose. The incidence of side effects like hypotension, Bradycardia and shivering were not seen in patients receiving 1.0 and 1.5 mcg/Kg of Dexmedetomidine with bupivacaine. In patients receiving 2.0 mcg/Kg dexmedetomidine with bupivacaine 24 % of the patients had hypotension and Bradycardia and 4 % had shivering.

**Conclusion:** Addition of Dexmedetomidine in dose range of 1.0 to 1.5 mcg/Kg substantially prolongs postoperative analgesia without altering block characteristics offered by Bupivacaine for epidural blockade with no side effects and appears to be safe and reliable adjuvants.

**Keywords:** Epidural Anaesthesia, Bupivacaine, Dexmedetomidine, Post operative analgesia

## INTRODUCTION

Regional anaesthesia is supposed to be excellent anaesthesia in terms of safety and prolong post operative pain relief. In modern regional anaesthesia epidural blockade is one of the best procedures, providing better intra operative hemodynamic control, post operative pain relief and rapid recovery from surgery specially pelvic surgeries and orthopedic surgeries. Many adjuvants have been used with bupivacaine to increase

the post operative analgesia such as epinephrine, neostigmine, opioids with associated side effects like respiratory depression, pruritus, sedation, nausea, vomiting. Selective alpha 2 adrenergic agonist used as adjuvant in epidural blockade. Clonidine hydrochloride was the first drug from the group and was found clinically useful in peri operative period.<sup>1</sup> Dexmedetomidine a more powerful and highly selective alpha 2 adrenoceptor agonist than clonidine was introduced in clinical practice in 1999 and soon became popular for variety of indications in Anesthesiology.<sup>2-5</sup>

The current prospective randomized double blind study was undertaken in orthopedic and pelvic surgical patients to evaluate the comparative hemodynamic, analgesic, sedative and respiratory effects of different doses of dexmedetomidine in patients receiving bupivacaine epidural anaesthesia.

## MATERIAL AND METHODS

A study of effect of dexmedetomidine on post operative analgesia when added to bupivacaine 0.5% in epidural block was carried out in 100 patients undergoing lower limb orthopedic and pelvic surgeries. Sample size was based on inclusion and exclusion criteria.

Ethical approval was taken from Hospital Ethical Committee. Patients of ASA Grade I or II, aged 15-65 years, weighing 40-70 Kg were included in the study. Patients with hematological diseases, abnormal bleeding and clotting time, psychiatric disease, diabetes, sepsis at the site of injection, spinal deformities, non consenting patients and patient with allergy to local anaesthetic agent were excluded from the study. After detailed examination and informed consent, patients were randomly assigned in four groups of 25 patients each.

In the operation theatre, a good intravenous access was secured and monitoring devices were attached. Base line heart rate, electrocardiogram (ECG), pulse oximetry ( $SpO_2$ ), non invasive blood pressure (NIBP), respiratory rate recorded. The drug syringes were prepared with all aseptic technique. After antiseptic preparation of back and sterile draping the selected

<sup>1</sup>Associate Professor, Department of Anaesthesiology, C.M.M. Memorial Medical College, Kachandur, Durg (CG), <sup>2</sup>Assistant Professor, Department of Anaesthesiology, Rama Medical College and Hospital and Research Centre Hapur, UP, <sup>3</sup>Professor, Department of Anaesthesiology, R. D. Gardi Medical College, Ujjain (MP), India

**Corresponding author:** Dr. Vivek Chakole, Quarter A/3 C M Medical College Campus, Kachandur, Durg, Chhattisgarh, India

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space for epidural puncture was infiltrated with 1 ml of 2% Xylocaine solution, epidural puncture was done in the midline by using 18 gauge Touhy needle (Romsons) in sitting position and epidural space was identified by the loss of resistance to air injection technique. Procedure was conducted by same anesthesiologist every time.

After identifying the space a test dose of 2 ml lignocaine hydrochloride solution containing adrenaline 1:200000 was injected to avoid accidental intra vascular injection or massive intrathecal dose. After 2-3 minute of administering the test dose, Group A patients received local anaesthetic solution 0.5% preservative free Bupivacaine 20 ml as a single shot injection, Group B, C, and D received local anaesthetic solution 0.5% preservative free Bupivacaine 20 ml with 1.0, 1.5, 2.0 mcg/kg of Dexmedetomidine as a single dose respectively.

After injection of drug/s (as per the group assigned), patient was made to lie down supine with 10 degree head low tilt and each patient was observed for -

- A. Time of onset for sensory block
- B. Time of onset of motor block
- C. Highest Level of sensory block achieved (by pin prick method)
- D. Duration of sensory block
- E. Duration of motor block
- F. Intraoperative muscle relaxation (on Bromage scale)
- G. Degree of sedation on Ramsay sedation scale
- H. Duration of pain free period
- I. Any adverse drug effect and
- J. Any complication like bradycardia, hypotension, respiratory depression and sedation.

Continuous Intra operative monitoring of vital signs (Pulse rate, NIBP, SpO<sub>2</sub>, RR) was done by using multi parameters.

An independent observer who was totally unaware of the nature

of the study, recorded blood pressure and heart rate just before and after surgical incision and then every five minutes interval till the end of surgery using multi parameters. Postoperatively patient was monitored for offset time of epidural block (motor and sensory regression).

## STATISTICAL ANALYSIS

Descriptive statistics were used and mean and percentage were calculated. Paired t test applied using SPSS software for analysis between four groups. P value less than 0.5 percent was considered statistically significant.

## RESULT

Demographic data of patient included in the study was comparable with respect to height, weight and mean age of patient in each group (Table-1). The time for onset of sensory and motor block was similar in all groups and no statistical significant difference noted ( $p > 0.05$ ) (Table-2).

Two level decrease in sensory block (duration of sensory block) and offset of motor block (duration of motor block) was similar in all four groups and no statistical significant difference noted ( $p > 0.05$ ). Post operative analgesia increased significantly in B,C and D group when compared with A group ( $p < 0.005$ ). Side effect like hypotension, bradycardia and shivering was seen in Group D only (Table-2). Highest sensory level achieved in all four groups were comparable (Table-3). All patients in control group and study group were co-operative, oriented, calm and responsive to commands and mostly remained sleepy during entire surgery (Table-4).

In majority of the patient degree of muscle relaxation in study and control group was acceptable and provide smooth intra operative period (Table-5). Incidence of decrease in heart rate (35.2%) was seen in group D only (Table-6). Incidence of

Group	Group A	Group B	Group C	Group D
Age in years	41.4 ± 13.3	45.9 ± 11.1	33.76 ± 9.1	33.9 ± 8.8
Sex				
Male	9	20	23	16
Female	16	5	2	9
Weight in kg	51.6 ± 3.9	51.04 ± 2.07	52.08 ± 4.64	49.2 ± 4.8
Height in cm	153.2 ± 3.8	153.1 ± 3.6	152.8 ± 2.3	± 4.7

Table-1: Showing demographic data

Group	Group A	Group B	Group C	Group D
Mean time onset of sensory block (seconds)	715.20	686.40	688.80	696.80
Mean time onset of motor block (seconds)	919.20	890.40	864.00	854.40
Duration of sensory block (Minutes)	259.20	251.20	257.60	250.00
Duration of motor block(Minutes)	180.40	182.40	186.40	182.00
Post operative analgesia hrs	4.47	10.71	10.89	10.85
Hypotension	-	-	-	6
Bradycardia	-	-	-	6
Shivering	-	-	-	1
Vomiting(	-	-	-	-

Table-2: Showing duration and Adverse Effect

Dermatome Height	Group A (n=25)	Group B (n=25)	Group C (n=25)	Group D (n=25)
T4-T8	8	7	9	9
>T9	17	18	16	16

Table-3: Highest sensory level achieved

decrease in blood pressure was seen in group B, C and D over group A but were not statistically significant (Table-7).

## DISCUSSION

It is well established that Bupivacaine offer good anaesthesia in Epidural Block. However anesthesiologists persistently attempted to improve the quality of block by adding adjuvant drugs to local anesthetics. Adjuvants enhance the effectiveness and quality of analgesia offered by local anesthetics alone and also prolongs the post operative pain free period and decrease the requirement of systemic analgesics with minimum and no side effects and least possible effect on hemodynamic.

Dexmedetomidine is alpha two adrenoceptor agonist and has been introduced for clinical use in our country recently. Paracelsus very correctly stated that “There is no safe drug, only safe doses”. Dexmedetomidine being a new introduction in anesthesia armamentarium, it is important to find a dose of drug that would cause acceptable intra-operative sedation and enhancement of post-operative pain free period without significant side effects. Hence, the present study is aimed to determine an optimum dose.

Patients included in the study had a mean age of 38.7 years (20–60 years). Male / female ratio was 68/32. The patients included

in the study were adults and had vital signs within normal limits with no co morbid condition and thus belonged to grade I/II as per ASA classification.

The time for onset of sensory block was similar in all group and clinically insignificant changes were noticed. Mean time for onset of sensory block was found to be  $715.2 \pm 119.9$  seconds in control group. After addition of dexmedetomidine the mean time for onset of sensory block was not altered significantly in dose range of 1.0 and 2 mcg/kg. Salgado PF and colleagues<sup>6</sup> administered dexmedetomidine with 20 ml 0.75% ropivacaine and found that addition of dexmedetomidine in dose of 1 mcg/Kg did not alter onset time for sensory block. Experimental study of epidural dexmedetomidine in rabbits was shown to have no effect sensory and motor effects by Konakci S et al.<sup>7</sup>

Mean time for onset of motor block in patients receiving bupivacaine without dexmedetomidine was found to be  $919.2 \pm 139.3$  seconds and in other group marginal early onset occurred. In group B, C and D mean time of onset of motor block is 890.40 seconds, 864 seconds and 854.40seconds respectively which is statistically insignificant ( $p > 0.005$ ). Similar findings were observed by Salgado PF et al<sup>6</sup> and by Konakci S<sup>7</sup> in experimental study on rabbits.

Sedation score	Group A (n=25)	Group B (n=25)	Group C (n=25)	Group D (n=25)
1	0	0	0	0
2	0	7 (28%)	8 (32%)	13 (52%)
3	25 (100%)	18 (72%)	17 (68%)	12 (48%)
4	0	0	0	0
5	0	0	0	0
6	0	0	0	0

Table-4: Sedation Score

Muscle power grading	Group A (n=25)	Group B (n=25)	Group C (n=25)	Group D (n=25)
1	19	19	16	18
2	6	6	9	7
3-6	0	0	0	0

Table-5: Showing degree of muscle relaxation.

Groups	Preoperative HR/ bpm	Minimum HR/ bpm	RR / min
Group A (n=25)	$83.1 \pm 5.4$	$67.0 \pm 9.4$	$16.8 \pm 1.0$
Group B (n=25)	$82.2 \pm 8.7$	$64.0 \pm 9.3$	$17.0 \pm 1.1$
Group C (n=25)	$88.2 \pm 6.3$	$60.7 \pm 6.5$	$16.2 \pm 0.7$
Group D (n=25)	$84.0 \pm 9.3$	$54.4 \pm 10.4$	$16.6 \pm 0.9$

Table-6: Showing Changes in Heart rate and Respiratory Rate

Groups	Pre-block SBP (mmHg)	Pre-block DBP (mmHg)	SBP minimum (mmHg)	DBP minimum (mmHg)
Group A (n=25)	$135.2 \pm 11.1$	$78.0 \pm 7.9$	$99.3 \pm 10.9$ 35.9 (-26.5%)	$62.6 \pm 8.3$ 15.4 (-19.7 %)
Group B (n=25)	$137.6 \pm 11.6$	$79.9 \pm 8.4$	$92.0 \pm 18.6$ 45.6 (-33.1%)	$63.5 \pm 9.2$ 12.4 (-24.6 %)
Group C (n=25)	$139.4 \pm 8.4$	$81.0 \pm 8.2$	$98.4 \pm 6.5$ 41.0 (-29.4 %)	$65.2 \pm 9.9$ 15.8 (-24.2%)
Group D (n=25)	$132.4 \pm 11.5$	$74.3 \pm 7.4$	$91.2 \pm 9.9$ 41.2 (-31.2%)	$56.1 \pm 11.4$ 18.5 (-24.4 %)

Table-7: Showing Changes in Systolic and diastolic Blood Pressure

In our study offset time for sensory block 2 segments below the highest level of dermatome block in control group was found to be  $259.2 \pm 22.3$  minutes. In group B, C, D offset of sensory block time was 251.20, 257.60, 250.00 minutes respectively which was statistically insignificant. ( $p > 0.05$ ). Salgado PF et al<sup>6</sup> observed in his study that duration of sensory block is prolonged when Dexmedetomidine was added with 20 ml of 0.75% ropivacaine in epidural anaesthesia for hernia repair. Mean time for offset of motor block in control group was  $180.4 \pm 18.9$  minutes. In study group B, C and D patients the offset of motor block was 182.4, 186.40 and 182 minutes respectively which was not statistically significant ( $p > 0.05$ ), this observation is not supported by findings of Sabbage et al<sup>8</sup> and Kanazi et al<sup>9</sup>. In their study it was found that addition of dexmedetomidine prolonged the duration of motor block in epidural anaesthesia. Highest time for pain free period was recorded in group C patients and it was found to be  $10.89 \pm 2.39$  hours which was followed by group B patients who had pain relief for  $10.71 \pm 1.75$  hours. In control group patients shortest pain free period was seen and it was  $4.47 \pm 1.27$  hours in group D ( $10.85 \pm 2.31$ ). From the finding of our study it can be observed that dose beyond 1.5 mcg/Kg did not enhance the post operative analgesia. The results observed in our study are comparable with the findings of several studies which show that addition of Dexmedetomidine increased post operative pain free period and also the time for demand of first rescue dose of systemic analgesic. Sukhminderjit singh<sup>13</sup> 2011, Vijay G Anand<sup>10</sup>, Harsoor SS et al<sup>11</sup>, A.M.El- Hennawy et al<sup>12</sup>, Salgado PF et al.<sup>6</sup> In none of the patients from control and study group (B and C) complication like hypotension, bradycardia, vomiting and shivering were seen whereas Group D patients who received 2 mcg/Kg of Dexmedetomidine showed occurrence of hypotension, bradycardia. Sukhminderjit singh<sup>13</sup> et al used the mephenetermine and atropine in their study for treating low HR and blood pressure. Salgado et al<sup>6</sup> noticed low incidence of shivering in their study with 1 mcg/kg of Dexmedetomidine. In one study by Michael Smith and Marrof<sup>14</sup> used Dexmedetomidine successfully to prevent shivering associated with anaesthesia. Highest Level of block achieved in these patients was up to T 9 dermatome in most of the cases, in all groups. Addition of dexmedetomidine did not affect the height of block in majority of patients. Similar observation was made by Salgado PF et al.<sup>6</sup> Whereas SukhminderJit Singh Bajwa et al<sup>13</sup> 2011 found that dexmedetomidine not only provided a higher dermatomal spread but also helped in achieving the maximum sensory anesthetic level in shorter period in comparison to clonidine. No patient in control and study group had clinically significant respiratory depression. Oxygen saturation was maintained during entire surgery and post operative period. None of the patient from any group had sedation score 1, 4, 5 and 6. All 25 patients in control had Ramsey score of 3. In group B 72% of cases had score of 3 and rest of the patient means 28% had score 2. In group C patients 32% and 68% of the cases had score of 2 and 3 respectively. For group D sedation score of 2 and 3 was observed in 52% and 48%. The same sedation scoring was seen in studies of Sukhminderjit singh et al<sup>13</sup>, Vijay G Anand<sup>10</sup> and Saadawy et al<sup>6</sup> when they used the Dexmedetomidine as a adjuvant with local anaesthetic for epidural anaesthesia. Elhakim et al<sup>12</sup> 2010, noted a decrease

in narcotic requirements after epidural dexmedetomidine during combined epidural and general anesthesia for thoracic surgery employing one lung ventilation.

In majority of the patient degree of muscle relaxation in study and control group was acceptable and provide smooth intra operative period. Total time taken by group D patients to achieve bromage scale 1 ( $33.3 \pm 5.5$ ) minutes whereas in control group it took more time ( $36.7 \pm 5.5$  minutes) and similar results found by Sukhminderjit Singh et al<sup>13</sup>, in his study of epidural block by using 17 ml of 0.75 % ropivacaine with 1.5 mgm/kg of Dexmedetomidine.

decrease of mean heart rate by 35.2% of preoperative mean pulse rate was seen in Group D patients. In groups B, and C, fall in mean heart rate was 22.1% and 29.9% of the mean preoperative heart rate. Bradycardia was responsive to injection Atropine 0.6 mg given intra operatively. No patient in group A, B, and C, had pulse rate 30 % lower than his own pre-operative value. Sukhminder jit singh<sup>13</sup>, Taylor Brandao Schnaider et al<sup>15</sup> showed a drop in pulse rate by 20% to 30% in their studies. Changes noticed in respiratory rate were not clinically significant in any group when compared with their base line preoperative respiratory rate. During the whole period of observation SpO<sub>2</sub> remained more than 98 %.

In all group patients mean preoperative systolic and diastolic pressure was between 132.4 and 139.4 and 74.3 and 79.9 mm of Hg. Maximum lowering of 33.1% in systolic pressure and 19.7% in diastolic pressure was seen in Group B patients. Greater than 30% fall from preoperative mean systolic pressure was noticed in group D patients as 31.2%. Hypotension well responded to mephentermine 3- 6 mg IV bolus. In other groups A, and C, fall in blood pressure remained below 30%. Sukhminder jit singh et al<sup>13</sup>, Taylor Brandao Schnaider et al<sup>15</sup> also observed fall in systolic blood pressure more than 20% when they used Dexmedetomidine in a dose of 1.0 to 2.0 mcg/kg in their studies.

## CONCLUSION

Addition of Dexmedetomidine, an alpha 2 agonist to local anaesthetic solution for conduct of lumbar epidural block in the dose range of 1.0 to 1.5 mcg/Kg substantially prolongs postoperative analgesia without altering block characteristics offered by Bupivacaine without any significant side effects and appears to be safe and reliable adjuvant.

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# Correlation of HbA1c with Mortality and severity in Acute Coronary Syndrome

T. N. Dubey<sup>1</sup>, Kaustubh Mundada<sup>2</sup>, A Arya<sup>3</sup>

## ABSTRACT

**Introduction:** Coronary Artery Disease (CAD) has emerged as the single most important cause of death worldwide and as well as in India. Diabetes Mellitus (DM) is a major risk factor for CAD and there appears to be a **graded** rise in cardiovascular risk with increasing degrees of glucose intolerance well below the definition of overt diabetes. The aim of the study was to define the relationship between HbA1c levels with mortality, morbidity and severity in patients with Acute Coronary Syndrome (ACS).

**Material and Methods:** This was an observational prospective study. The sample size was 110 patients with ACS. Detailed history, examination and investigations were done as per preformed proforma. ECG, CPK-MB, echocardiography was done in all patients and coronary angiography (CAG) was done in half of the patients.

**Results:** The mean age was  $58.17 \pm 9.87$ . Out of 110 patients, 64 (57.2%) were non-diabetic, 27 (24.5%) were diabetic and 20 (18.2%) had impaired glucose tolerance. 46 patients (41.8% of patients) had hypertension. The most common complications were left ventricular dysfunction (LVD) and Heart Failure (HF) and this were significantly more present in diabetics compared to nondiabetics ( $p$  value 0.009). The mean HbA1c level was higher in patients with complications ( $6.61 \pm 2.13$ ) than in patients with complications as compared ( $5.90 \pm 1.27$ ) in patients without complications.

**Conclusion:** ACS can be presenting manifestation of DM thus each patient of ACS should be screened for diabetes and glucose intolerance. Patients with DM when compared to nondiabetics have increased morbidity and severity after an ACS.

**Keywords:** Coronary Artery Disease, Diabetes Mellitus, Stress Hyperglycemia, Coronary Angiography.

## INTRODUCTION

Coronary Artery Disease (CAD) has emerged as the single most important cause of death worldwide and as well as in India. In 2013 CAD caused an estimated 7.5 million deaths worldwide accounting for 13.3% of all deaths.<sup>1</sup> Diabetes mellitus (DM) is a major risk factor for CAD and among the most common chronic diseases in the world. According to seventh edition of International Diabetes Federation Diabetes Atlas 2015, worldwide around 415 million people are suffering from DM and nearly half of these are undiagnosed. This number is expected to rise to 640 million in 2040. At the same time, another 318 million people have impaired glucose tolerance and this number expected to increase to 482 million in 2040. Compared to nondiabetics, persons having diabetes have a two to fourfold increased risk of development of and death from CAD.<sup>2</sup> In patients having Acute Coronary Syndrome (ACS), more than one in three may be affected by diabetes and those with diabetes have worse outcomes after ACS.<sup>3-5</sup> Also this graded association of increased risk observed in diabetics in the setting of ACS extends to glucose values in the range way below threshold for

diabetes.<sup>6</sup> In addition, diabetes is also associated with increased HF risk in the setting of ACS.<sup>7</sup> The primary aim of the study was to define the relationship between HbA1c levels with mortality, morbidity and severity in patients with ACS in both diabetics as well as patients having impaired glucose tolerance.

## MATERIAL AND METHODS

This was an observational prospective study done at tertiary centre from December 2014 to December 2015 after obtaining ethical clearance from the institutional ethical board. 110 consecutive cases of acute coronary syndrome were included in the study based on inclusion exclusion criteria. The inclusion criteria were all patients with acute coronary syndrome presenting within 24 hours. Patients who were K/C of Diabetes Mellitus or Coronary Artery Disease or having co-morbidities like sepsis, hemoglobinopathy or chronic kidney disease were excluded from the study. Informed consent was taken from the study participants before the start of the study. These patients were subjected to detailed history, examination and baseline investigations. Anthropometric measurements like Body mass index, waist circumference and Waist to Hip ratio were calculated. Patients were evaluated for dyslipidemia and HbA1c was done in all patients by HPLC method. ECG, cardiac echocardiography and cardiac enzymes like CPK-MB were done in all patients and coronary angiography was done in half of patients.

The subjects were divided into three groups – nondiabetic, impaired glucose tolerance and diabetic.

## STATISTICAL ANALYSIS

Data was analysed using a computer based statistical analysis programme, SPSS (Statistical Program for Social Sciences) version 22.0. The Chi-square test was used wherever comparisons were needed between the two groups for categorical variables and Student's T test was used for continuous variables. A  $p$  value  $< 0.05$  was considered significant.

## RESULTS

Out of 110 subjects, 81 were males and 29 females. The mean age was  $58.17 \pm 9.87$ . Out of 110 patients, 64 (57.2%) were non-diabetic, 27 (24.5%) were diabetic and 20 (18.2%) had impaired glucose tolerance. 46 patients (41.8% of patients) had

<sup>1</sup>Professor and Head of Department, <sup>2</sup>Resident, <sup>3</sup>Associate Professor, Department of Medicine, Gandhi Medical College, Bhopal, India

**Corresponding author:** Dr. Kaustubh Mundada, Room No. 78,F Block, Gandhi Medical College Hostel, Hamidia Hospital Campus, Bhopal 462001, India

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hypertension. 62 patients out of 110 had increased weight (BMI >23) out of which 21 (77.7% of diabetics) were diabetic, 29 (46% of nondiabetic) were non diabetic and 12 (60% of prediabetic) had impaired glucose tolerance. When BMI was correlated with HbA1c, increased BMI was significantly associated with diabetics compared to nondiabetic ( $p$  value 0.005).

Dyslipidemia was present in 50 % of the patients (55 patients). 70% of patients with diabetic had dyslipidemia as compared to 50% of prediabetic and 41% of nondiabetic patients. Dyslipidemia was significantly more prevalent in diabetic patients as compared to nondiabetic ( $p$  value 0.001.). Similarly low serum high density lipoprotein (HDL) was present in 43 (i.e. 39%) patients and this was also found to be significantly more low in diabetic patients (17 patients i.e. 62.7%) compared to nondiabetics (19 patients i.e. 30.2%) ( $p$  value 0.003).

Out of 110 patients in our study, 27 patients had complications (LVD, shock, HF, Arrhythmia) during the course of hospitalization. Out of these 27, 13 were nondiabetic (20.6% of total nondiabetics), 9 were diabetic (37% of total diabetics) and 5 had impaired glucose tolerance (25%) (Table-1). The most common complications were left ventricular dysfunction and heart failure and this were significantly more present in diabetics compared to nondiabetics ( $p$  value 0.009). LVD (EF < 40%) was present in 8 out of 27 diabetic patients (i.e. 29.6%) whereas HF was seen in 7 patients (22.2%). The mean HbA1c level was higher in patients with complications ( $6.61 \pm 2.13$  in patients with complications as compared  $5.90 \pm 1.27$  in patients without complications, Table-2) and this was statistically significant ( $p$  value 0.038).

Severity of CAD was assessed in 58 patients who underwent CAG. Multivessel disease involvement was seen significantly more in diabetics as compared to nondiabetic. The mean HbA1c was found to be significantly more in patients with multivessel disease compared to those without multivessel disease (6.74 vs. 5.86  $p$  value 0.048.) (Figure-1).

## DISCUSSION

Though major advances in cardiovascular disease, and specifically the treatment of acute coronary syndrome (ACS), have had a significant impact on the morbidity and mortality of patients with acute myocardial infarctions (AMI), diabetes mellitus (DM) continues to put patients with and without a prior history of myocardial infarction at significant cardiovascular risk.

The presence of DM doubled the age-adjusted risk for cardiovascular disease in men and tripled it in women in the Framingham Heart Study, and it remained an independent risk factor even after adjusting for age, hypertension, smoking, hyperlipidemia, and left ventricular hypertrophy.<sup>8</sup> In a meta-analysis of 13 prospective cohort studies, for every one-percentage point increase in glycosylated hemoglobin (HbA1c), the relative risk for any cardiovascular event was 1.18 (95% CI 1.10–1.26).<sup>9</sup> Also even with all other factors similar, diabetic patients when compared to those without diabetes, have worse long-term outcomes after an acute coronary syndrome.<sup>10,11</sup> Sustained chronic hyperglycemia has been shown to be an important cause for complications and poor outcomes in ACS. Studies have shown that there is a persistent progression of diabetic vascular disease despite reversal of hyperglycemia

Category	All complications		Total
	Present	Absent	
Diabetics	10	17	27
	37.0%	63.0%	100.0%
Impaired glucose tolerance	5	15	20
	25.0%	75.0%	100.0%
Non Diabetics	13	50	63
	20.6%	79.4%	100.0%
Total	28	82	110
	25.5%	74.5%	100.0%

Table-1: Correlation of HbA1c with Complications

All complications	Mean hba1c	Std. Deviation	No of Patients
Present	6.61	2.13	28
Absent	5.90	1.27	82

P=0.038 [The HbA1c level was significantly higher in patients with complications]

Table-2: Correlation of mean HbA1c with Complications

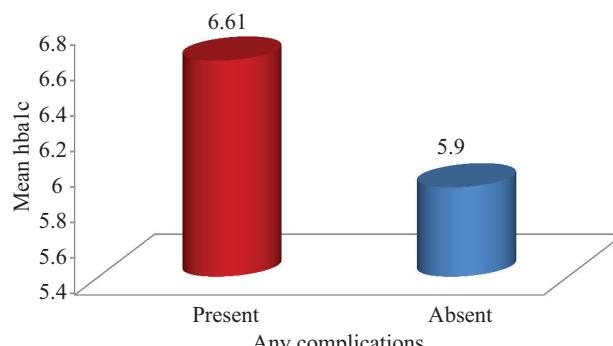


Figure-1: Correlation of HbA1c with complications

and this effect of prior hyperglycemia on the initiation and progression of diabetic vascular disease is defined as “metabolic memory”.

In our study we found that 27 patients (i.e. 24.5%) with no past history of DM had HbA1c more than 6.4% i.e. they were found to be diabetic. Thus these patients presented to the hospital directly with acute coronary syndrome. Similarly 20 patients (i.e. 18.2%) had HbA1c in the impaired glucose tolerance range (5.7 to 6.4%). Thus patients of DM can have macrovascular complications of diabetes without having the usual symptoms of DM and can directly present with them. This is partly because majority of patients of type 2 DM are asymptomatic and can directly present with chronic complications unlike type 1DM. The classic symptoms of hyperglycemia like polyuria, polydipsia, polyphagia, nocturia, weight loss are often noted only in retrospect when hyperglycemia is noted on laboratory evaluation done either routinely or due to some complication. This findings are similar to other studies like Khaw KT et al<sup>12</sup> which also reported that myocardial infarction may be the initial presentation of diabetes and that there appears to be a graded rise in cardiovascular risk with increasing degrees of glucose intolerance below the definition of overt diabetes. Norhammar A et al<sup>13</sup> reported that previously undiagnosed diabetes and impaired glucose tolerance are common in patients with an acute myocardial infarction. In a meta-analysis of 20 studies that included almost 100,000 people, Coutinho M et al<sup>14</sup> showed that

there was a curvilinear increase in the risk for a cardiovascular event with increasing glucose intolerance. Similarly Haffner AM et al<sup>15</sup> and Juutilainen A et al<sup>16</sup> also showed that diabetic patients without previous myocardial infarction have as high a risk of myocardial infarction as nondiabetic patients with previous myocardial infarction.

Increased blood sugar levels performed during the hospitalization in patients could reflect either previously unrecognized diabetes or that the stress of MI unmasks or worsens the tendency toward hyperglycemia. Therefore in our study we used HbA1c levels to categorize patients as diabetic, impaired glucose tolerance and nondiabetics (as per the American Diabetes Association 2003 criteria of HbA1c <5.7% normal; 5.7% to 6.4% impaired glucose tolerance; ≥6.5% diabetes)

In our study we found positive correlation between HbA1c levels and complications. Complications were present in 25% of patients (28 patients) the most common being LVD. Both LVD and HF were more common in diabetics as compared to nondiabetic patients. These findings are in agreement in earlier reports of Mouhamad H et al and Stone P H et al<sup>17</sup> who found that diabetic patients presenting with acute coronary syndrome (ACS) have a worse prognosis. Iribarren C et al<sup>18</sup> in a prospective study of 48,858 adults with DM showed that each 1% increase in HbA1c was associated with an 8% increased relative risk of HF. The clinical manifestations of an acute myocardial infarction are more severe in diabetics than in nondiabetics. Both acute pulmonary edema and heart failure occurs significantly more in diabetics compared to nondiabetics despite similar infarct sizes and left ventricular ejection fractions suggesting that the left ventricle in diabetes tolerates infarction poorly. Diabetic patients have higher LV mass, wall thickness, and arterial stiffness, reduced resting LV ejection fraction (LVEF) and diminished systolic function and reduced cardiac reserve as compared to individuals without diabetes. They also have increased impairment in coronary flow than nondiabetics which might reflect a prothrombotic state or endothelial dysfunction associated with hyperglycemia.

In our study we didn't find any correlation between admission HbA1c levels and outcome. This is in agreement with earlier finding of Corpus RA et al<sup>19</sup>, Timmer JR et al<sup>20</sup> and Cakmak M et al<sup>21</sup> who showed that although crude mortality data was higher in patients with elevated HbA1c following adjustment for many cardiovascular risk factors, HbA1c values failed to predict in-hospital mortality. Similarly Hadjadj S, Coisne D et al found no correlation between HbA1c levels and short term outcome of patients. Whereas Chowdhury TA et al<sup>22</sup>, Rasoul S et al<sup>23</sup> and Cicek G et al<sup>24</sup> suggested that HbA1c level was also a potent predictor of both in-hospital and long-term mortality. A meta-analysis done by Yao Liu et al found that elevated HbA1c level is an independent risk factor for mortality in CAD patients without diabetes, but not in patients with established diabetes. The negative correlation with outcome in our study may be due to less number of patients and thereby less mortality in our study. It may be also because in our study we followed up and compared mortality of patients for only seven days and didn't compare long term outcome. It may also be due to the fact that in our study we didn't include known diabetic patients but those patients who presented with ACS and then were found to have DM. Another reason might be that short term outcome in ACS

is more affected by acute hyperglycemia rather than chronic hyperglycemia of which HbA1c is a marker.

## CONCLUSION

As shown in our as well as previous studies, ACS can be the initial presentation of DM and there appears to be a graded rise in cardiovascular risk with increasing degrees of glucose intolerance well below the definition of overt diabetes. Also our study showed that patients with DM when compared to nondiabetics have increased morbidity and severity after an ACS. We conclude that every patient of ACS should be screened for glucose intolerance and diabetes by testing for HbA1c levels and more importantly every person above 35 years of age should be routinely screened for diabetes mellitus and impaired glucose tolerance especially if they have risk factor for insulin resistance like obesity.

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# A Prospective Study to Predict difficult intubation using Simple Non-Invasive Tests

Amit Dalvi<sup>1</sup>, Sarita Fernandes<sup>2</sup>, Swapnil Aswar<sup>3</sup>

## ABSTRACT

**Introduction:** Failure to achieve endotracheal intubation causes considerable morbidity and mortality in anaesthetised patients. Preoperative identification of such patients would help the Anesthesiologist to be prepared for such a difficult situation. The purpose of our study was to determine the ability to predict difficult visualization of larynx using the Upper Lip Bite Test (ULBT), Hyomental distance (HMD), Thyrosternal distance (TSD), and the Mandibular length (ML).

**Material and methods:** Study group included 100 patients undergoing elective surgical procedures under general anaesthesia with endotracheal intubation. ULBT, HMD, TSD and ML measurements were performed on all patients preoperatively. ULBT class III, HMD <3.5cm, TSD < 6.5cm and ML < 9cm were considered potentially difficult intubation. An experienced anesthesiologist, unaware of preoperative airway evaluation, performed the laryngoscopy and graded the glottic view (as per Cormack and Lehane's (CL) classification). CL Grade III and IV were considered as difficult intubation. We calculated the Sensitivity, specificity, accuracy, positive and negative predictive values of upper lip bite test and Modified Mallampati test.

**Results:** ULBT had a sensitivity, specificity, PPV and NPV of 45.45%, 100%, 100% and 93.68%, respectively. HMD showed a Sensitivity, Specificity, PPV and NPV of 9.09%, 97.75%, 33.33% and 89.69%, respectively. TSD showed a Sensitivity and PPV came of 0% while the Specificity and NPV of the test to be 97.75% and 88.78%, respectively. ML showed Sensitivity, Specificity, PPV and NPV and found of 18.18%, 98.88%, 66.67% and 90.72%, respectively.

**Conclusion.** ULBT comes out to be a better predictor of Difficult Intubation over HMD, TSD and ML. Though, ULBT appears to be better amongst the four tests, none of them is a foolproof test. None of them can be used as a reliable screening test as no one had a sensitivity even more than 50%. But, ULBT is better predictor amongst above parameters.

**Keywords:** Difficult Intubation, Cormack Lehane Grading, Upper lip Bite Test, Hyomental Distance, Thyrosternal Distance, Mandibular Length

## INTRODUCTION

Failure to achieve endotracheal intubation causes considerable morbidity and mortality in anaesthetised patients. Of all the anaesthetic deaths, 30% to 40% are attributed to the inability to manage a difficult airway.<sup>1</sup> Preoperative identification of such patients would help the Anesthesiologist to be prepared for such a difficult situation. Various techniques like Radiographs and Airway Imaging have been advocated to predict difficult intubation but are too expensive and inconvenient for patients to undergo as screening tests.<sup>2</sup> Highly specialized techniques such as Acoustic Reflectometry are of dubious reliability.<sup>3</sup> More quantitative, non-invasive measurements such as those with the laryngeal indices calliper<sup>4</sup> and bubble inclinometer<sup>5</sup>

offer the potential for accurate measurements but have never found their way into clinical practice. In contrast, the various simple bedside predictors of difficult airway like Mallampati class, Atlanto-occipital extension, Upper Lip Bite Test, Thyromental, Hyomental, Thyrosternal and Sternomental distances, Mandibular length, Neck Circumference, etc. are easy to perform, with no extra cost or inconvenience to patient. However, no single test alone has been found to be a foolproof predictor of difficult visualization of larynx.

The purpose of our study was to determine the ability to predict difficulty in visualization of larynx using the Upper Lip Bite Test (ULBT), Hyomental distance (HMD), Thyrosternal distance (TSD), and the Mandibular length (ML). We wished to determine whether there was a direct correlation between each of these parameters and the laryngoscopic view i.e. Cormack Lehane grading and difficult intubation and the diagnostic value i.e. which test predicts the difficult visualization better than others with the help of sensitivity, specificity, positive predictive value and negative predictive value of each test.

## MATERIAL AND METHODS

After obtaining institutional ethics committee clearance and taking written informed consent, this prospective study was conducted in 100 patients of either sex, aged between 25 years and to 60 years, ASA physical status I/II and BMI 18.5 to 24.9, undergoing elective surgical procedures under general anaesthesia with endotracheal intubation at a tertiary care hospital (NAIR Hospital, Mumbai). All patients included in this study underwent a routine pre anesthetic check up. Apart from Mouth Opening and Modified Mallampati Test (MMT), which are routinely done, airway assessment included Upper Lip Bite Test (ULBT), Hyomental distance (HMD), Thyrosternal distance (TSD) and Mandibular length (ML). Edentulous patients, patients with BMI > 30, uncooperative and patients with altered consciousness, patients unable to open the mouth, patients requiring Rapid sequence induction of anaesthesia, patients with cervical spine fractures and deformities, those with restricted mobility of neck and mandible, any oropharyngeal, airway abnormality or obvious neck pathology, pregnancy, temporomandibular joint and atlanto-axial joint dislocation were excluded from the study. A power analysis was conducted

<sup>1</sup>Assistant Professor, <sup>2</sup>Additional Professor, NAIR Hospital, <sup>3</sup>Senior Resident, Tata Memorial Hospital, Mumbai, India

**Corresponding author:** Dr. Amit Dalvi, flat no. 15, A-Wing, Anandbhavan, Nair Hospital Campus, Mumbai Central, Mumbai-400011, India

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assuming a moderate effect, a power of 80% and type I error of 5% and using two sided alternative hypothesis, a sample size of 100 was determined to be appropriate for the study. All the patients were explained about the procedure in detail preoperatively and all the patient's airway was evaluated using ULBT.

Description of the airway assessment tests is as follows:

**Upper Lip Bite Test (ULBT):** It is a scale indicating range of motion of bite of lower teeth onto upper lip. ULBT was assessed with the participant in sitting position at the eye level and graded as follows.

Class 1: Lower incisors can bite the upper lip above the vermillion border.

Class 2: Lower incisors can bite the upper lip below the vermillion border.

Class 3: Lower incisors cannot bite the upper lip (potentially difficult intubation).

**Hyomental distance (HMD) Test:** HMD was measured in supine position with head in full extension and mouth closed. The straight distance from the lower border of the mandibular mentum to the superior border of hyoid bone was measured in centimeters.

HMD is graded as:

≥3.5 cm- expected easy intubation

<3.5 cm-potentially difficult intubation

**Thyrosternal distance (TSD) Test:** TSD was measured in supine position with head in full extension and mouth closed. The straight distance between the prominent laryngeal cartilage of the thyroid cartilage and incisura jugularis of the sternal bone was measured in centimeters.

TSD is graded as:

≥6.5 cm- expected easy intubation

<6.5 cm- potentially difficult intubation

**Mandibular length (ML):** ML was measured from the angle of mandible to the tip of the chin with the patient in sitting position. ML is graded as:

≥9 cm- expected easy intubation

<9 cm- potentially difficult intubation

All the distances were measured with the help of a flexible plastic material scale so as to measure the distances accurately. Consent and NBM status were confirmed. Monitoring included the Non Invasive Blood Pressure (NIBP), Electrocardiography, Pulseoximetry and Capnography, Baseline heart rate, SpO<sub>2</sub>, Systolic and Diastolic Blood Pressure, Mean arterial Blood Pressure were recorded. Peripheral line was taken with 18G IV cannula (standard protocol). Patient was preoxygenated and pre Medication was given as per routine protocol.

Propofol 2mg/kg was used as intravenous induction agent. Ventilation was confirmed. Intravenous Vecuronium 0.1mg/kg was given as muscle relaxant and patient was ventilated for 3 minutes. Laryngoscopy was performed with No.3 or No.4 Macintosh blade by an experienced anesthesiologist (who has completed atleast 3 years of postgraduate training in Anesthesia).

CORMACK and LEHANE'S grading system is the gold standard parameter in diagnosing level of difficulty in INTUBATION.

Laryngoscopy view was graded according to Cormack and Lehane scale as follows:

Grade 1: Full view of glottis seen.

Grade 2: Anterior commissure not visible, Glottis seen partially.

Grade 3: Only epiglottis is seen.

Grade 4: Epiglottis is not seen.

Grade 3 and 4 are considered as potentially difficult intubations. Intubation was declared difficult if a second experienced anaesthesiologist failed to visualize the larynx even after using conventional measures of changing the head position, blade and application of external laryngeal pressure.

### Outcome measures

*Predicted easy intubation:*

a) Thyrosternal distance ≥6.5cm

b) ULBT: class 1 and 2

c) Hyomental distance ≥3.5cm

d) Mandibular length ≥9cm

### Predicted difficult intubation

a) Thyrosternal distance <6.5cm

b) ULBT: class 3

c) Hyomental distance <3.5cm

d) Mandibular length <9cm

### Actual easy intubation

Cormack Lehane grade 1 and 2

### Actual difficult intubation

Cormack Lehane grade 3 and 4

## STATISTICAL ANALYSIS

The completed data sheets were analysed by SPSS version 17 software (SPSS Inc.). The preoperative assessment data and the laryngoscope findings were used to evaluate the predictive value of each test for difficult laryngoscopy. As ULBT class, HMD, TSD, ML are categorical variable, we used a 2 × 2 table to assess the validity parameters i.e sensitivity, specificity, positive and negative predictive values, and accuracy. Calculations were performed using Excel 2013 for Windows. Qualitative data is represented in form of frequency and percentage. Quantitative data is represented using mean±sd and Median and IQR (Interquartile range). Predictiveness of various variables towards CL was assessed using Linear Regression analysis. Results were graphically represented wherever required. Diagnostic efficacy was calculated through Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value.

## RESULTS

Our study included 100 patients, 51 males and 49 females. 75 patients came under ASA status I and 25 under ASA II. Mean age was 34.27 years and mean BMI was 22.23. Difficult intubation was seen in 11 (11%) patients. Cormack Lehane (CL) Grades I and II were included in Easy Cormack Lehane grading, whereas Grades III and IV were included in Difficult Cormack Lehane. All of our patients with difficult intubation had CL grading III and none had CL grade IV. There was no failure to intubate the trachea in any of the patients in our study. External Laryngeal pressure or Gum elastic Bougie was used to intubate patients with CL grade III patients. Remaining patients were intubated at the first attempt.

We studied the validity of ULBT, HMD, TSD and ML on the basis of sensitivity, specificity, positive predictive value and negative predictive value. In our study we found Sensitivity of

Upper Lip Bite Test (ULBT) to be 45.45%, specificity of 100%, positive predictive value of 100% and negative predictive value of 93.68% (Table-1). This means ULBT is less sensitive but highly specific and has very good positive predictive value with good negative predictive value. Hyomental distance (HMD) showed a Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of 9.09%, 97.75%, 33.33% and 89.69%, respectively (Table-2). ThyrosternalI distance showed a Sensitivity and Positive Predictive Value came of 0% while the Specificity and Negative Predictive value of the test to be 97.75% and 88.78%, respectively (Table-3). Mandibular length. showed Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value and found of 18.18%, 98.88%, 66.67% and 90.72%, respectively (Table-4).

## DISCUSSION

Securing an airway is the most important part of general anaesthesia. Difficult Intubation is a nightmare for every anaesthesiologist. Being prepared for a difficult intubation reduces the adverse events due to difficulty in or failure to intubate. To be prepared for Difficult Intubation, it is vital to predict the difficult airway correctly before induction of anaesthesia. There has been an extensive research on the predictors for difficulty in intubation, right from radiological imaging to external anatomical factors, but there's no single test which is easy to perform, highly sensitive, highly specific and which possess high positive predictive value with few false negative predictions, i.e. an ideal test.

ULBT		Cormack Lehane Grading		Total
		Difficult	Easy	
Predicted Difficult	No.	5	0	5
Predicted Easy	No.	6	89	95
Total	No.	11	89	100

Diagnostic tests	Estimate	Lower 95% CI	Upper 95% CI	Total
Sensitivity	45.45%	16.75%	76.62%	
Specificity	100.00%	95.94%	100.00%	
Predictive value of positive test	100.00%	47.82%	100.00%	
Predictive value of negative test	93.68%	86.76%	97.65%	

**Table-1:** Association between ULBT and Cormack Lehane Grading among the cases

HMD (cm)		Cormack Lehane Grading		Total
		Difficult	Easy	
Predicted Difficult	No.	1	2	3
Predicted Easy	No.	10	87	97
Total	No.	11	89	100

Diagnostic tests	Estimate	Lower 95% CI	Upper 95% CI	Total
Sensitivity	9.09%	0.23%	41.28%	
Specificity	97.75%	92.12%	99.73%	
Predictive value of positive test	33.33%	0.84%	90.57%	
Predictive value of negative test	89.69%	81.86%	94.94%	

**Table-2:** Association of HMD and Cormack Lehane among the study population

A test to predict difficult intubation should have high sensitivity, so that it identifies most patients in whom intubation will truly be difficult. It should also have a high Positive Predictive Value, so that only few patients with airways actually easy to intubate are subjected to the protocol for management of a difficult airway. Similarly, a test should have a high specificity and Negative Predictive Value to correctly predict the ease of laryngoscopy and intubation.

This study was designed to evaluate the efficacy of Upper Lip Bite Test, Hyomental distance, Thyrosternal distance and Mandibular length in terms of Sensitivity, Specificity, positive Predictive Value and Negative Predictive Value in forecasting a difficult intubation, and to draw a possible relation between the Tests/ Parameters and Cormack–Lehane grades which was used as the gold standard in our study.

Upper Lip Bite Test proposed by Khan et al in 2002<sup>6</sup> is a simple assessment method in predicting difficulty in intubation. It tests the range and freedom of mandibular movement and the architecture of the teeth. ULBT is easy to demonstrate to patients and very convenient to perform as a bedside test.

We have studied ULBT along with Hyomental distance(HMD), Sternothyroid distance (STD) and Mandible length (ML).

In our study, the sensitivity of ULBT was found out to be 45.45%. The sensitivity we found is in contrast with the findings of Zahid khan, et al<sup>6</sup>, 2003, who found the sensitivity of 76.5% and Eberhart et al<sup>8</sup> who got sensitivity to be 28%. Lower sensitivity of ULBT in Eberhart, et al study can be explained due to higher incidence of difficult intubation in the study with

TSD (cm)		Cormack Lehane Grading		Total
		Difficult	Easy	
Predicted Difficult	No.	0	2	2
Predicted Easy	No.	11	87	98
Total	No.	11	89	100

Diagnostic tests	Estimate	Lower 95% CI	Upper 95% CI	Total
Sensitivity	0.00%	0.00%	28.49%	
Specificity	97.75%	92.12%	99.73%	
Predictive value of positive test	0.00%	0.00%	84.19%	
Predictive value of negative test	88.78%	80.80%	94.26%	

**Table-3:** Association between TSD and Cormack Lehane among the cases

ML (cm)		Cormack Lehane Grading		Total
		Difficult	Easy	
Predicted Difficult	No.	2	1	3
Predicted Easy	No.	9	88	97
Total	No.	11	89	100

Diagnostic tests	Estimate	Lower 95% CI	Upper 95% CI	Total
Sensitivity	18.18%	2.28%	51.78%	
Specificity	98.88%	93.90%	99.97%	
Predictive value of positive test	66.67%	9.43%	99.16%	
Predictive value of negative test	90.72%	83.12%	95.67%	

**Table-4:** Association between ML and Cormack Lehane among the cases

large proportion of false negative results (6%).

Zahid Khan et al<sup>6</sup> in 2003 found the specificity of 88.7% against 100% what we found which can be explained by no false positive obtained in our study with ULBT as compared to Khan's study (10.6%). E Allahyary et al<sup>9</sup> and Khan ZH et al<sup>7</sup>, found the specificity for ULBT to be 97.6% and 91.69%, respectively, which were close to what was found in present study.

The positive predictive value and negative predictive value of ULBT were found to be 100% and 93.68%, respectively. E Allahyary et al<sup>9</sup>, found the positive predictive value of 89.7% which is quite close to present study findings.

We also studied Hyomental distance and found its sensitivity to be very low as 9.09% which was in accordance with study of Khan et al in 2011,<sup>7</sup> who found the sensitivity of HMD to be 8.8%. Huh J et al<sup>10</sup> in 2009 assessed Modified Mallampati Test, HMD, HMD ratio and Thyromental distance and found the sensitivity of HMD to be 23% which was again not a very good predictor in terms of screening test which requires a good sensitivity. The Specificity, Positive Predictive Value and Negative Predictive Value in our study for HMD were 97.75%, 33.33% and 89.69%, respectively. Khan et al<sup>2</sup> found the Specificity, Positive Predictive Value and Negative Predictive Value of HMD to be 98.9%, 50% and 89.5%, respectively which were almost similar to what we found in our study. Huh J et al<sup>10</sup> found the Specificity, Positive Predictive Value and Negative Predictive Value of HMD to be 95%, 40% and 90%, respectively which were also similar to what we found in our study

Cattano et al<sup>11</sup> studied Hyomental distance and found its sensitivity to be 16%, specificity of 91%, Positive Predictive Value of 4% and Negative Predictive Value of 98%. All other results were comparable to our study except the very low positive predictive value they found which might be due to not calculating the Hyomental distance in full extension of neck and taking the cut off point for predicting difficult intubation by Hyomental distance as 4.5cm against our study and also the other studies conducted by Khan et al<sup>2</sup> and Huh J et al.<sup>10</sup>

We also studied Thyrosternal distance (TSD) and found its Sensitivity and Positive Predictive Value came to be 0%. We found the specificity and Negative Predictive value of the test to be 97.75% and 88.78%, respectively. So it appears that TSD has a poor sensitivity and Positive Predictive value and hence a bad predictor of difficult intubation as a screening test.

Mandibular length had the Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of 18.18%, 98.88%, 66.67% and 90.72%, respectively. E Allahyary et al<sup>9</sup> also studied Mandibular length along with other five parameters and found the sensitivity to be 62.2% which was comparatively higher as compared to our study result. Specificity of their study was 43.14% which was quite low as compared to our study. The positive predictive value and negative predictive value of were 19.7% and 83.7%. The difference in the finding might be due to difference in the population composition.

In our study, we found the sensitivity of ULBT to be higher compared to HMD, STD and ML. Sensitivities of ULBT, HMD, TSD and ML were 45.45%, 9.09%, 0% and 18.18%, respectively. Thus the overall sensitivity of ULBT is low but it is better than other tests compared in our study. The specificity

of ULBT, HMD, TSD and ML were 100%, 97.75%, 97.75% and 98.88%. Thus we found a very a specificity of all the tests but even in them ULBT had the highest specificity of 100%, which means the predictions on the basis of ULBT were every time correct. The high specificity of ULBT means it is a good test to predict easy intubations. So, comparing the above parameters, ULBT comes out to be a better predictor of Difficult Intubation over HMD, TSD and ML. Also we found out that ULBT is easy to perform and very convenient to use as a bedside test. The classes are clearly demarcated making inter observer variability highly unlikely while using this test. But, during the study, we found that repeated demonstrations were required for patients to perform ULBT and a few failed to understand the procedure inspite of our repeated efforts. Another interesting observation was the reflex movement of the upper lip in the reverse direction over the upper teeth. This movement may alter the point of meeting of vermillion line with the lower incisors. So, proper explanation and comfortable environment are required for the patients to be cooperative to do the test. However, ULBT on its own fails to take into account relative tongue and pharyngeal size, mandibular space and a narrow high arched palate. Also, ULBT requires patient's cooperation, ability to move the teeth and the presence of teeth.

## CONCLUSION

Though, ULBT appears to be better amongst the four tests, none of them is a foolproof test. None of them can be used as a reliable screening test as no one had a sensitivity even more than 50%. So, negative test doesn't rule out a difficult intubation and we need to be prepared with the Difficult Intubation cart all the time.

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# TMJ Imaging: A Review

Irfan Ashraf Baba<sup>1</sup>, Mohd Najmuddin<sup>2</sup>, Aasim Farooq Shah<sup>3</sup>, Asif Yousuf<sup>3</sup>

## ABSTRACT

**Background:** Our understanding and interest in the diagnosis and management of patients with various types of temporomandibular joint disorders has increased as research has identified structural abnormalities and disease mechanisms associated with some of these disorders. Clinical examination only cannot lead to the correct diagnosis of TMJ dysfunctions. Among the basic examinations used are: X-ray examination (RTG), computer tomography (CT) and magnetic resonance imaging (MRI). Radionuclide examination (scintigraphy), ultrasonography and arthroscopy are less used secondary methods of imaging. Arthroscopy is classed as a therapeutic method. The present paper attempts to highlight the various imaging modalities for TMJ diagnosis.

**Conclusion:** Conventional radiography helps identify gross bone abnormalities. CT, especially multisection CT, is the modality of choice for assessing the hard tissue of the TMJ. Magnetic resonant imaging is a standardized imaging protocol for depicting the soft-tissue anatomy. Because of the operator dependence of sonography and the invasiveness and propensity for severe complications of arthrography, these modalities are not a part of routine work-up of the TMJ.

**Keywords:** TMJ, TMJ Imaging, MRI of TMJ

## INTRODUCTION

A multitude of terms have been used to describe patients presenting with pain and dysfunction of the temporomandibular joint (TMJ) and related masticatory muscles: such as Costen's syndrome, dysfunctional temporomandibular joint and muscle pain, myofascial pain dysfunction (MPD), temporomandibular joint syndrome, mandibular dysfunction and craniomandibular disorders. These terms include several entities that have different etiology, but present with similar signs and symptoms.<sup>1</sup>

Temporomandibular disorders (TMD) are one subgroup of any of these terms, and they embrace a number of clinical problems that involve the masticatory muscles and/or the temporomandibular joint. This term is most frequently used in clinical practice.<sup>1</sup>

Most studies agree that TMD cannot be diagnosed only on the basis of findings by clinical examinations. The purpose of an imaging assessment of the temporomandibular joint (TMJ) is to graphically depict clinically suspected disorders of the joint. Diagnostic imaging has been helpful in substantiating temporomandibular joint (TMJ) disorders such as internal disk derangements.<sup>1-3</sup>

There seems to be growing confusion among dentists, both specialists and general practitioners, as to when imaging should be used, if at all and when each modality can be expected to be most useful. The need for imaging of the TMJ should be established on the basis of selection criteria. Selection criteria represent those clinical signs and symptoms that suggest that a radiographic examination would contribute to the proper diagnosis and care of the patient.<sup>4</sup> It provides a rationale for

selecting among the various imaging modalities, with the purpose of obtaining the important diagnostic information with less radiation exposure. The most accurate diagnostic techniques are those that provide new information that will influence the patient care. The decision on selecting an examination should be made after considering the history, clinical findings, diagnosis, cost of the examination and radiation exposure.<sup>2</sup> This review paper describes the alternative imaging methods for TMJ Disorders and makes recommendations for their appropriate use.

## PLAIN RADIOGRAPHY

The most common and most well-established plain film technique for examination of the TMJ is the transcranial projection of both the right and left sides with the jaw closed and opened. The lateral aspect of the joint is well visualized, but the central and medial parts of the joint are not clearly seen because the X-ray beam is not tangent to these articular surfaces. This disadvantage is partly compensated for by the fact that most of the early osseous changes occur laterally in the joint. It is recommended that, in addition to the transcranial projection, an anteroposterior projection should be used to depict the central and medial parts of the condyle. A transorbital and a transpharyngeal projection is also suggested. These images are acquired as a screening evaluation but are not useful in depicting the soft-tissue elements of the articulation. Positive findings observed on transcranial radiographs are those of degenerative joint disease of TMJ in the range of 5%-10%.<sup>2</sup>

## PANORAMIC RADIOGRAPHY

Previously, orthopantomograph was considered a gold standard for imaging TMJ since teeth and other structures of the jaws were also seen on the image. However, the superimposition of the base of the skull and zygomatic arch restricted the evaluation of the condyle and glenoid fossa in the panoramic film.<sup>1</sup>

## TOMOGRAPHY

Conventional tomography has been used extensively to evaluate the osseous components of the TMJ, generally in a lateral orientation but sometimes in combination with frontal views. When compared to oblique transcranial projection, computed tomography has been found to help in revealing a vast number

<sup>1</sup>Registrar, Department of Oral Medicine and Radiology, <sup>2</sup>Registrar, Department of Public Health Dentistry, Government Dental College and Hospital, Shreen Bagh, Srinagar, Jammu and Kashmir, <sup>3</sup>Assistant Professor, Department of Oral Medicine and Radiology, AME'S Dental College, Raichur, India

**Corresponding author:** Dr. Aasim Farooq Shah, Registrar, Department of Public Health Dentistry, Government Dental College and Hospital, Shreen Bagh, Srinagar, Kashmir, Jammu and Kashmir, India. 190010.

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of structural variations. In certain TMJ specimens evaluated for autopsy, computed tomography has been more specific in evaluating the anatomic structures better than transcranial radiography.<sup>2</sup> Some studies have indicated that tomography can provide unanticipated information that may lead to a change in treatment plan.<sup>4-6</sup> In contrast, however, other investigations have concluded that the presence or extent of radiographic signs of osseous pathoses are of little prognostic value in the outcome of treatment<sup>4,7</sup> and that tomography has little effect on the diagnosis or treatment plan of patients with TMJ disorders.<sup>2,8</sup>

## ARTHROGRAPHY

Early attempts at TMJ arthrography were undertaken by Nørgaard in the 1940s. Toward the end of the 1970s several articles appeared, describing the clinical and arthrographic characteristics of internal derangement related to displacement of the disk.<sup>1</sup> These arthrographic studies were actually the first to depict displacement of the disk, a pathologic entity that had been suspected earlier.<sup>2,9</sup> During the following years, considerable enthusiasm developed for TMJ arthrography, and a large number of publications describing the usefulness of the technique appeared. The changed attitude toward TMJ arthrography can be traced to the following factors: (1) use of an image intensifier to facilitate joint puncture and to study and document joint dynamics, (2) identification of disk displacement as a common cause of TMJ pain and dysfunction, and, probably most important, (3) introduction of new, conservative surgical methods for treating disk displacement. Arthrography is indicated for an evaluation of the soft-tissue components of the TMJ, especially disk position, function, and morphology in those patients presenting with a suspected internal derangement. There are two important imaging modalities for TMJ arthrography. In single-contrast arthrography, radiopaque material is injected into either the lower or upper joint space, or into both compartments. In double-contrast arthrography, a small amount of air is injected into the joint space after the injection of contrast materials.<sup>2,9</sup> Several studies have shown that arthrography is an accurate imaging method for evaluating anterior disc displacement. The accuracy for diagnosing the position of the disc ranged from 84% to 100% compared with the corresponding cryosectional morphology and surgical. Perforation and also adhesion of the disc can also be evaluated by such techniques.

## COMPUTED TOMOGRAPHY

In the 1980s, computed tomography (CT) began to be applied in the diagnosis of TMJ ankylosis, condyle fracture, disc displacement and osseous changes.<sup>3</sup> In an earlier report, the accuracy for disc displacement was high (81%) when comparing imaging observations of CT and surgical findings. Some reports considered that CT might replace the technically difficult and invasive arthrography in the diagnosis of disc displacement in TMD. However, the accuracy of the disc displacement was only 40%-67% in CT in studies of autopsy specimen materials. The accuracy of osseous changes of TMJ in CT compared with cadaver material was 66%-87%. Some reports pointed out that radiographic evidence of arthrosis may or may not be associated with clinical symptoms of pain dysfunction. Thus patients without osseous changes in TMJ may have pain, and those with clear signs of bony abnormalities may be pain-free.<sup>5-10</sup>

## MRI

Computed tomography (CT) has been replaced by Magnetic resonance imaging (MRI) and arthrography as the primary diagnostic tool in the evaluation of the temporomandibular joint (TMJ) disorders.<sup>11-12</sup> MRI evaluation of TMJ disk offers a distinct advantage over TMJ arthrography. Despite the superior resolution of CT and limited visualization of cortical bone by MRI, most osseous pathology is accurately depicted. Intrarticular abnormalities are readily visible on MRI images, providing further information not available with other imaging modalities.<sup>13-15</sup>

Magnetic resonance imaging (MRI) is unique in that there is no associated risk of ionizing x-ray. For MRI, the patient placed in a strong static magnetic field. The hydrogen nuclei, or protons, in the body align with the direction of the main magnetic field, a short radiofrequency (RF) pulse at the proper frequency and duration is then transmitted into the body.<sup>1</sup> The protons absorb RF energy and flip over into a plane that is at an angle with the direction of the main magnetic field, the protons reemit some of the absorbed energy, which induces an electric current in a specially designed RF receiver coil. The induced current, *so-called the magnetic resonance (MR) signal*, is then transformed into an image by computerized mathematical methods.<sup>1,7,9</sup>

An MR image is produced from signals coming from the hydrogen nuclei, or protons, in the body. The contrast of the image is provided by differences in signal intensity from protons in different tissues. Magnetic resonance imaging (MRI) is preferably appropriate to assess variations of the disk. Spin-echo pulse sequences typically are used for MR imaging of the TMJ. The most frequently used ones in TMJ images are *T<sub>1</sub>-weighted* image (short TR and TE), *T<sub>2</sub>-weighted* image (long TR and TE) and proton-density (PD) image (long TR and short TE). Typical values for T<sub>2</sub> in tissue range from 0.02 to 0.30 seconds. In general, the more water a tissue contains, the longer the T<sub>2</sub>. Thus, areas of long T<sub>2</sub> can be interpreted as areas of edema, effusion, or inflammation.<sup>4</sup> Typical T<sub>1</sub> values for tissue range from 0.2 to 3 seconds. Much of the power of MRI comes from the fact that various tissues have different values of T<sub>1</sub> and T<sub>2</sub> and contrast can be varied over a wide range by adjusting TE and TR. The intrinsic contrast of the anatomy in the region makes T1-weighted images satisfactory in majority of cases. When joint fluid, tumor, edema or infections are doubted, T2-weighted images are more useful. Sagittal and coronal images are attained with the patient's mouth opened and closed. Because of the small size of the structures of concern here, surface coils are essential for acceptable signal-to-noise (S/N) ratio. The significant landmarks for valuation of TMJ function comprise the articular fossa of the temporal bone, the mandibular condyle, the disk, and the bilaminar zone.<sup>11,14,15</sup> The closed-mouth scans are inspected first. Damage to the bilaminar zone permits the unopposed lateral pterygoid muscle to shift the disk anteriorly. This is perceived as displacement of the disk anteriorly in relation to the articular fossa.

Furthermore, the relationship of the disk and the mandibular condyle with the patient's mouth opened is assessed. Normally the disk and the condyle move as a unit anteriorly when the mouth opens.<sup>12</sup> If the disk gets displaced with mouth closed

position and retakes its physiological relationship with the condyle then anterior dislocation with reduction is present. While on the other hand if when the mouth is opened, the condyle and the disk do not come to physiological relationship, anterior displacement without reduction is present (Table-1).

#### Direct and Indirect Magnetic resonant imaging Signs of TMJ Dysfunction

##### Direct signs

###### 1. Abnormal disk morphologic features

- Crumpled
- Rounded
- Flat
- Perforated

###### 2. Abnormal disk displacement in closed-mouth position

- Anterior displacement
- More frequently observed
- Posterior band exceeds 10° or 30° from vertical
- Posterior displacement
- Rare
- Posterior band exceeds 10° or 30° from vertical
- Lateral or medial displacement

###### 3. Abnormal disk movement in open-mouth position

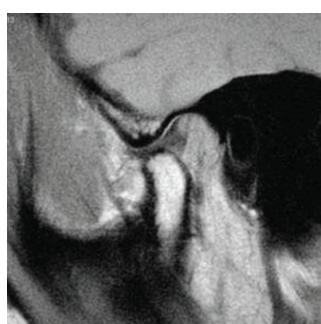
- Anterior disk displacement with reduction



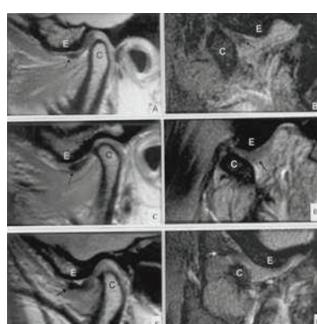
**Figure-1:** Coronal CT of TMJ;



**Figure-2:** Sagittal CT of TMJ



**Figure-3:** MRI of TMJ;



**Figure-4:** MRI of TMJ

- Anterior disk displacement without reduction
- Stuck disk (disk remains fixed)

#### 4. Osteoarthritic changes of the condyle

- Flattening
- Osteophytes
- Erosion
- Sclerosis

##### Indirect signs

- Large amount of joint fluid (joint effusion)
- Increased thickness of LPM attachments
- Rupture of retro-diskal layers<sup>5</sup>

Numerous studies have equated MRI of TMJ with arthrography and CT. The MRI findings were also compared with anatomical and histological observations. In studies on autopsy specimens, the accuracy of MRI in evaluating osseous changes in TMJ was 60% to 100% and the accuracy in evaluating disc displacement was 73% to 95%. All these studies showed that MRI was the best method of imaging both the hard and soft tissues of the TMJ.<sup>15</sup>

Although many studies agree that muscular pain is another major aspect of TMD, the evidence of pathological changes of the masticatory muscles may have been ignored in imaging diagnosis. The reports shown in few previous studies suggest that MRI is not only an accurate method to detect the position of the disk but also helps in evaluation of the pathological changes of the masticatory apparatus in Temporo mandibular joint disorders.<sup>10</sup>

#### ULTRASONOGRAPHY

TMJ ultrasonography is a non-invasive, readily available and relatively cheap dynamic “real time” examination, featuring soft joint tissues. It serves both for diagnosis and differential diagnosis and for the comparison of therapeutic results in treating internal joint defects. The first reports of TMJ sonography date back to 2000.<sup>3</sup> It uses presently available types of USG equipments with scanning transducer of 7.5–12 MHz frequency, which makes it easy to depict the narrow space of the jaw joint and the position of the joint disk and it reveals ligament adhesion. During the evaluation of the patient is in semi-reclining position, the transducer is placed over the joint parallel to the long axis of the mandible. The joint disk is scanned on the screen as a thin homogenous hypo, as far as the isoechogenic strip adjacent to the condylar border. The condylar borders and articular eminence are seen as hyperechogenic line. During the examination it is possible to directly observe the joint disk move when the mouth is opening and closing. A 70–85 % agreement was seen in studies comparing the results of MRI and USG. An ultrasonographic system using the high frequency

Diagnostic task	Panoramic	Transcranial	Skull views	Tomography	Arthrography	CT	MRI
Ankylosis Bony	0	0	0	++	0	+++	+
Ankylosis fibrous	0	0	0	0	0	++	+++
Arthritis	+	+	0	++	O	++	+++
Anomaly	+	+	+	++	0	+++	++
Disk position	0	0	0	0	++	+	+++
Fractures	++	+	++	++	0	+++	++
Inflammatory conditions	0	0	0	+	++	+	+++

**Table-1:** Radiographic appearances of TMJ anomalies in relation to various imaging techniques

and conveyors with a large diameter has been recently invented. The ultrasonograph waves, generated by this system, are able to penetrate easily through the small aperture between the glenoid fossa and the condyle. The new transducers invented have a high focus depth and narrow wave beam. The rebound potential of bone surface is as much as 2/3 waves and only 1/3<sup>rd</sup> propagate down to deeper anatomic structures. For this reason the transmitter must be placed on a specific place, with the aim to transmit waves through the soft tissues, situated between the condyle and the eminence.<sup>3,8</sup>

## RADIONUCLIDE IMAGING

This method of imaging provides the only means of assessing physiologic change that is direct result of biochemical alteration. It is based on radiotracer method, which assumes that radioactive atoms or molecules in an organism behave in a manner identical to that their stable counterparts because they are chemically indistinguishable. Scintigraphy aids in discovering the early changes in the TMJ apparatus which may also result in joint disc abnormalities. The temporomandibular joint is ideal for SPECT (single proton emission computed tomography), as TMJ is a small joint situated close to the skull base, which is ideal for evaluation by SPECT. In normal individual, the perfusion is symmetrical, TMJ being perfused at same rate as rest of facial structure. The radionuclide examination sensitivity is high, its specificity is however low. Any inflammation, trauma or tumors increase the local isotope concentration. For this reason many studies state that radionuclide examination is relevant only as a screening method.<sup>3</sup>

## TMJ Imaging in Orthodontics

The initial appreciation of problematic cases provides valuable hints:

- To shun treatment errors and functional disorders, (preventive reasons)
- To develop the treatment planning, and decrease relapse.
- To treat TMD during the orthodontic Restoration.

The TMJ remodeling and bite jumping during the mandible progression depends not just on age, sex, maturity, timing, duration of treatment, and the facial growth pattern, but also on the state of TMJ, which is evidently related to the efficiency and stability of occlusal rehabilitation.<sup>6</sup>

## CONCLUSION

The reliability of a complex joint such as that of the jaw is the result of a stable interaction of soft tissue and bony structures. In spite of its daily exposure to wear and tear, simple changes in the TMJ are rare. Trauma, internal derangement with conceivable sequel and inflammation are the most mutual forms of pathologic conditions.

The general radiologist is frequently challenged to manage the diagnostic pathway and to provide a good basis for planning the proper therapeutic strategy. A chart has been prepared to help the diagnostician in selecting proper imaging modality based on desired area of interest. (Table-1) Conventional radiography helps to identify major bone abnormalities. Multislice CT, is the modality of choice for assessing the hard tissue of the TMJ. Soft-tissue anatomy is best showed with MR imaging and a standardized imaging protocol. Since the operator dependence of ultra sonography and the intrusiveness and propensity for

severe complications of arthrography, these modalities are not part of a repetitive work-up of the TMJ.

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# A Study on Refractive Errors Among the School Children of Guwahati City

Kabindra Deva Sarma<sup>1</sup>, Mousumi Krishnatreya<sup>2</sup>

## ABSTRACT

**Introduction:** Refractive error is one of the commonest causes of visual impairment around the world. Undetected and uncorrected refractive errors are particularly a significant problem in school children. With these rationales this study has been undertaken in schools of Guwahati city with the objective to assess the magnitude of refractive error and assess the degree of myopia among school-going children of Guwahati city of Assam, India, **Materials and Methods:** This cross-sectional study was conducted in schools of Guwahati city from May 2014 to April 2015. Sample size was calculated to be 400. The 6 to 16 years children of selected schools of Guwahati City who were present on the day of the interview were interviewed and examined. Snellen chart, pinhole, a trial box, a trial frame, self illuminated vision box and streak Retinoscope were used to detect refractive error. MS excel package and SPSS11.5 software was used for analysis.

**Results:** Prevalence of refractive errors was 23.5%. Myopia was the major refractive error (81.92%) among total refractive errors, followed by astigmatism (14.89%) and hypermetropia (3.19%). Majority of the myopic children were of low degree myopia. (89.61%). Study reveals that only 24.47% students were already wearing spectacles where as remaining 75.53 % of students are unaware about their problems.

**Conclusion:** refractive error was a significant cause of visual impairment among school children and screening of school children plays a major role in detecting refractive errors.

**Keywords:** Refractive error, prevalence, myopia, school students

## INTRODUCTION

Uncorrected refractive error is one of the most common causes of blindness around the world. About 80% of blindness is treatable or preventable. Refractive errors are one of the common causes of this treatable blindness. Globally, the major causes of blindness are cataract, uncorrected refractive errors and glaucoma and their prevalence are 33%, 43% and 2% respectively.<sup>1</sup> An estimated 19 million children are visually impaired worldwide of which 12 million are due to refractive errors which could be easily corrected.<sup>1</sup>

Refractive error is one of the commonest causes of visual impairment around the world. Around 2.3 billion people worldwide is estimated to have refractive errors and of these 1.8 billion have access to adequate eye examination and affordable corrections.<sup>2</sup> In India refractive error is the second most major cause of patients to consult ophthalmologists<sup>3</sup>

Epidemiological study indicates that among the refractive errors, prevalence of myopia is increasing worldwide in economically developed societies.<sup>4</sup> This is mainly the case in East-Asian populations like China, Japan, and Singapore<sup>5</sup>

Different study reveals that refractive errors are usually present in the childhood and continue to the adult life.<sup>6</sup> Undetected and uncorrected refractive errors are particularly a significant

problem in school children. Children generally never complain of defective vision. Generally they are not aware of their problem or they may adjust to their poor vision. Even some time they used to avoid work which need visual concentration. Uncorrected refractive error can cause adverse impact on learning process and educational capacity.<sup>7</sup> Blindness due to refractive error can also have dramatic effect in personality development and career opportunities, along with causing an economic burden to the society.<sup>2</sup> Most of the children with such diseases are apparent and hence, screening helps in early detection and correction with spectacles.<sup>8</sup> Refractive error has been given high priority under the National Programme for Control of Blindness. It took central part in the global initiative Vision 2020, for the elimination of avoidable blindness.<sup>8</sup>

With these rationales this study was done to assess the magnitude of refractive error and to assess the degree of myopia among school-going children of Guwahati city of Assam, India,

## MATERIALS AND METHODS

Ethical clearance was taken from institutional ethical committee of Gauhati Medical College and hospital before doing this study.

**Study Design:** This cross sectional study was carried out in the schools of Guwahati city from May 2014 to April 2015

**Study population:** All the children in the age group of 6 to 16 years (i.e from class 1 to class 10) of selected schools of Guwahati City who were present on the day of the interview.

**Exclusion Criteria:** Children having defective vision because of other reasons like trachoma, corneal injuries or ulcers.

**Sample size and sampling technique:** The sample size was calculated by taking the prevalence rate of refractive error as 8.8 (from previous study done in the region)<sup>9</sup> at 5% significance level and 3% absolute error as follows:

$$n = 4pq/L^2$$

Where, p = 8.8% (prevalence of refractive error)<sup>3</sup>

$$q = 100 - p = 100 - 8.8 = 91.2$$

$$L = 3\% \text{ (absolute error)}$$

$$N = 4(8.8)(91.2)/9 = 357 \text{ which can be rounded off to 400.}$$

In this study, 5 schools were taken at random by lottery method from the total no of 21 schools present in Guwahati city.

<sup>1</sup>Assistant Professor, Department of Ophthalmology, RIO, <sup>2</sup>Associate Professor, Department of Community Medicine, Gauhati Medical College and Hospital, Guwahati, Assam, India

**Corresponding author:** Dr Mousumi Krishnatreya, Associate Professor, Department of Community Medicine, Gauhati Medical College, Guwahati, Assam, India

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Schools were visited until we got the desired sample size of 400 children. From each selected school all the students of 6 – 15 years were included in the study. The list of schools was taken from the Office of District Educational Office, Kamrup District. Prior information about the study was provided to the Principals of the selected schools and permission sought from them to conduct the study in their schools.

Refractive error was tested using the following instruments:

1. Snellen's chart
2. Opaque disc perforated by small central hole
3. Occluder-
4. A trial box, a trial frame, self illuminated vision box, streak Retinoscope

## STATISTICAL ANALYSIS

The Data collected was compiled, tabulated and subjected to descriptive analysis wherever applicable. The analysis was done in computer using MS excel package and SPSS 11.5 software.

## RESULTS

It was seen that out of 400 children 94 children had refractive errors (23.5%). Out of these 94 children with refractive errors, 86 were confirmed as myopia by the refractionist. The prevalence of Myopia, Hypermetropia, Astigmatism are shown in Table-1. It was observed that Myopia was the major refractive error (81.92%) among total refractive errors, followed by astigmatism (14.89%) and hypermetropia (3.19 %).

Among myopia detected cases majority complaint of difficulty in reading blackboard from back benches (46.35%) followed by headache (39.36%) and eye strain (11.70%). (Table-2).

Study reveals that the majority of the myopic children were of low degree myopia. (89.61%) followed by moderate degree of myopia (10.39%). No cases of high myopia was detected in this study (Table-3).

Table 4 shows that in 77.66% myopic children, both the eyes were involved. Only Right eye was involved in 12.77% cases and only 9.57% children showed left eye involvement.

It was observed from the study that out of 94 children having refractive error, 23 children (24.47%) were already wearing spectacles (old cases) where as rest 71 cases (75.53%) were detected during the study.

## DISCUSSION

This study shows that the prevalence of refractive errors were 23.5% among the school children which was more than the studies conducted by Rahman M, Devi B, Kuli JJ, Gogoi.<sup>9</sup> Pavithra MB, et al.<sup>10</sup> EL-Bayoumy BM, Saad A, Choudhury AH<sup>11</sup> and Kaushik Tripura, N. C. Luwang, Subrata Baidya, Phani Sarkar.<sup>12</sup> But study by Prema N found the prevalence similar to our study.<sup>13</sup> Similar observations were also found in the study done by Hussein A Bataineh, Ahmed E Khatatbeh.<sup>14</sup> where prevalence of refractive errors was 25.32%. These variations in prevalence could have been due to differences in demographic factors.

Our study showed that myopia was the most common refractive error (81.92%) followed by astigmatism (14.89%) and hypermetropia (3.91%). Similar observations were found in the study done by Rahman M, Devi B, Kuli JJ, Gogoi G.<sup>9</sup> Study by Nisha Dulani and Harish Dulani on Prevalence of Refractive Errors among School Children in Jaipur, Rajasthan also found

Type of Refractive Error	No	%
Myopia	77	81.92
Hypermetropia	3	3.19
Astigmatism	14	14.89
Total	94	100

**Table-1:** Distribution of children according to the type of refractive errors

Complaint	No	%
Difficulty in seeing blackboard from back benches	44	46.35
Headache	38	39.36
Eye Strain	11	11.70
Half shutting of the eye gives better vision	7	7.45

\*\* multiple response

**Table-2:** Common Complaints among children with refractive errors (N=96)

Degree of Myopia	No	%
Low (< -0.5D to -2.00D)	69	89.61
Moderate (-2.00D to -6.00D)	8	10.39
High (> -6.00D)	0	0
Total	77	100

**Table-3:** Classification of myopia based on degree of myopia (N=77)

Eye involved	No	%
Right eye	12	12.77
Left Eye	9	9.57
Both Eye	73	77.66
Total	94	100

**Table-4:** Distribution of children according to involvement of eye

similar observation where Myopia was 63.4%, Astigmatism was 25.8% and followed by Hypermetropia of 11.35%.<sup>15</sup>

It was evident from this study that among refractive error detected cases majority complaint of difficulty in reading blackboard from back benches (46.35%). EL-Bayoumy BM, Saad A, Choudhury AH reported a similar finding where the prevalence of refractive error was higher among those who had problem in seeing distant objects.<sup>11</sup> Similar finding were found in the study done by Kumar KS, Akojam BS.<sup>16</sup>

Our study revealed that the majority of the myopic children were having low myopia (89.61%), followed by moderate degree of myopia (10.39%). Study by Rahman M, Devi B, Kuli JJ, Gogoi G found that maximum students had low myopia (60.4%).<sup>9</sup> These finding are similar to our study.

This study revealed that 75.53 % cases of refractive errors were detected during the study where as only 24.47% were already wearing spectacles (old cases). Prema N in the study done in Kancheepuram Dist., Tamil Nadu, India found that Only 7% of students with poor vision who wore eyeglasses but 93% of student having poor vision did not have glasses.<sup>13</sup> Study done by Rahman M, Devi B, Kuli JJ, Gogoi G in Dibrugarh, Assam<sup>9</sup> and Kumar KS, Akojam BS in Imphal, Manipur<sup>16</sup> also found the high prevalence of uncorrected refractive errors. The possible reasons for students for not wearing glasses may be lack of awareness about refractive errors. These finding comply with the present study.

## CONCLUSION

From this study we can conclude that refractive error was a significant cause of visual impairment among school children and screening of school children can play an important part in detecting refractive errors. As prevalence of uncorrected refractive error was also found to be high, therefore students, parents, and teachers must be educated about signs and symptoms of refractive errors, so that they can get early detection and correction with spectacles to prevent progression of visual impairment. The existing school health services should be strengthened and implemented effectively so that it would be helpful to attain the global initiative for elimination of avoidable blindness by the year 2020.

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# A Clinical Study of Fundus Changes in Diabetic Patients

Vaggu. Sree Kumar<sup>1</sup>, Ramya. B<sup>2</sup>, Soujanya. T<sup>3</sup>

## ABSTRACT

**Introduction:** Usually a diabetic patient seeks the advice of ophthalmologist only when the ocular condition is in an advanced stage and it becomes a challenging task for an ophthalmologist to treat the condition and to give satisfactory results. It is therefore essential to examine the fundus of every diabetic patient periodically at a regular intervals to detect early changes. So the present study was done to know the incidence of retinopathy in type - 2 diabetic patients with its onset, severity, sex distribution, early diagnosis and visual prognosis and to analyse the fundus changes of diabetic patients with relation to the duration and other associated risk factor like hypertension, hyperlipidemia, smoking, alcohol.

**Material and methods:** This study was conducted in 100 patients who attended the OPD of Regional Eye Hospital, From February 2014 To July 2015 and were diagnosed with Diabetes mellitus. Fundus examination was done with indirect ophthalmoscope after dilatation of the pupil.

**Results:** Diabetic retinopathy changes seen in duration of diabetes about less than 10 years were 22.2%. In diabetics of duration about 11-15 years, the retinopathy changes were seen in 29.2%. In duration more than 16 years, in 64.2% of cases the retinopathy changes were seen. 20 cases were NPDR, 8 cases were PDR, 3 cases were advanced diabetic retinopathy. 20% cases of NPDR were with CSME, 37% cases of PDR were with CSME. The most common cause of diminution of vision were cataract and macular edema.

**Conclusion:** The risk factors for DR in Male gender are poor glycaemic control with long duration of diabetes, high blood pressure, sedentary life style and unhealthy food preferences.

**Keywords:** Diabetic Retinopathy, Clinically Significant Macular Edema

## INTRODUCTION

Diabetic retinopathy is main cause of vision loss in working age adults.<sup>1</sup> Diabetic macular edema is the vision threatening complication of diabetic retinopathy and represents a significant public health issues. Diabetic retinopathy is a micro angiopathy that exhibits features of both micro vascular occlusion and leakage with characteristic picture in the fundus.<sup>2</sup> In Diabetic retinopathy vision is decreased because of maculopathy or proliferative complications. It is essential to examine the fundus of every diabetic patient periodically at a regular intervals to detect early changes. The complications mainly intraocular hemorrhage and its sequel, tractional retinal detachment, vitreous hemorrhage, cystoid macular edema, optic neuritis are the causes for ocular and visual morbidity. Diabetic retinopathy remains the number one cause of new individuals who lose the vision, because of delay in detection of Diabetic retinopathy. In many developing countries, the incidence is dramatically increasing.<sup>3</sup> In view of this, incidence of retinopathy in type 2 diabetics, role of early diagnosis and treatment in patients who attended REH is studied and analysed.

Aim of the study was to know the incidence of retinopathy in type - 2 diabetic patients above 35 years of age with its onset, severity, sex distribution, early diagnosis and visual prognosis and to analyse the fundus changes of diabetic patients with relation to the duration and other associated risk factor like hypertension, hyperlipidemia, smoking, alcohol.

## MATERIAL AND METHODS

This study was conducted in 100 patients who attended the OPD of Regional Eye Hospital, From June 2014 To July 2015 and were diagnosed with Diabetes mellitus. Total of 100 Patients were examined and taken into the study. All the patients were above 35 years of age. Patients who fulfilled the inclusion exclusion criteria were taken into the study. All the patients were examined with dilated pupil and fundus examination was done with indirect ophthalmoscopy. Informed consent was taken from all the patients before the start of study.

### Inclusion Criteria

Patients above 35 years of age.  
Who gave consent for the study.  
Confirmed case of Diabetes mellitus.

### Exclusion criteria

Those with advanced cataracts or otherwise where the retina cannot be visualized.

## STATISTICAL ANALYSIS

Microsoft office 2007 was used to make tables. Results of the study are based on descriptive statistics. Mean and percentages were calculated to infer the data.

## RESULTS

The male to female ratio in this study was 1.6:1. Men were at higher risk having retinopathy changes. Majority of them fall in the middle age group (40-60years) (Table-1). 48% were without

S. No	Age	Number of cases examined	Percentagae
1.	35-40 years	12	12%
2.	41-50 years	26	26%
3.	51-60 years	30	30%
4.	61-70 years	24	24%
5.	70 and Above	08	08%

Table-1: Age distribution

<sup>1</sup>Assistant Professor, <sup>2</sup>Senior Resident, <sup>3</sup>Civil Assistant Surgeon, Regional Eye Hospital/Kakatiya Medical College, Warangal, Telangana, India.

**Corresponding author:** Dr V. Sree Kumar MS, Assistant Professor, Regional Eye Hospital, Kakatiya Medical, College, Warangal, Telangana, India. 506007.

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Duration of diabetes	Number of cases examined	With out diabetic retinopathy	NPDR	PDR	Advanced DR	Percentage
< 10years	45	35	8	1	1	22.2%
11-15years	41	29	6	5	1	29.2%
16years and more	14	05	6	2	1	64.2%

**Table-2:** Severity of diabetic retinopathy

Fundus changes in dr	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Advanced DR
No. of cases	08	06	06	08	03

**Table-3:** Fundus changes

S. No.	Other risk Factors	Males	Females	Percentage
1.	Hypertension	29	08	37%
2.	Smoking	25	-	25%
3.	Alcohol	28	-	28%
4.	Obesity	22	06	28%
5.	High lipid profile	30	06	36%
6.	Nephropathy	03	-	03%
7.	Anemia	-	04	04%

**Table-4:** Diabetic retiopathy associated with other risk factors

family history of diabetes and 52% were with family history of diabetes. Diabetic retinopathy changes seen in duration of diabetes about less than 10 years were 22.2%. In diabetics of duration about 11-15 years of duration the retinopathy changes were seen in 29.2%. In duration more than 16years, 64.2% of cases the retinopathy changes were seen. 20 cases were of NPDR, 8 cases were of PDR and 3 cases were with advanced diabetic retinopathy (Table-2). 20% cases of NPDR were with CSME and 37% cases of PDR were with CSME. The most common cause of diminution of vision were cataract and macular edema. Table-3 shows fundus changes in patients. Of the total cased, 37% of cases had hypertension, 36% of cases had hyperlipidemia, 28% of cases were addicted to alcohol and obese, 25% of cases were smokers, 4% of cases had nephropathy and 3% cases had anaemia as risk factors. Among 100 cases, 77 cases were taking regular treatment (77%) and 23 cases were on irregular treatment (23%) (Table-4). The incidence of diabetic retinopathy was more in patients taking irregular treatment.

## DISCUSSION

This was a observational study conducted in 100 patients who attended the OPD of Regional Eye Hospital, from February 2014 to July 2015 and were diagnosed with diabetic mellitus. Among 100 Patients, 69 cases showed no evidence of diabetic retinopathy. 20% showed non proliferative diabetic retinopathy changes, 08% cases showed proliferative diabetic retinopathy changes and 03% cases showed advanced diabetic retinopathy changes. According to Mohan et al<sup>4</sup> patients suffering from NIDDM of 25years duration, DR was detected in 52% of patients. Non proliferative diabetic retinopathy was seen 41.7% and PDR in 10.3% of patients. In a clinic population of a cohort of 6792, the prevalence of DR was 34.1 % which included NPDR 30.5 % PDR 3.4% and DME 6.4% in type 2 diabetic patients attending a diabetes centre at Chennai in south India. In the present study 36% of cases had history of hyperlipidemia. According to study done by yanko et al.<sup>5</sup> it is found that the prevalence of retinopathy 11-13 years after the onset of type 2 diabetes was 23%; after 16years or more years, it was 60 %.

Klein et al<sup>6</sup> reported 67% of patients had retinopathy and 10% had PDR after 10years of diagnosis of type 2 diabetes.

Diabetic retinopathy (DR) is a Microvascular disease of Retina affecting 4 percent of the world's population, DR has been shown to be the cause of visual impairment in 86 percent of type 1 diabetic patients and in 33 per cent of type 2 diabetics In India. However this morbidity is largely preventable and treatable. If managed with timely intervention, the quality of life can be preserved. Almost half of whom have some degree of DR at any given time in 4 percent of the world's population. DR occurs in all type 1 and 75 per cent of type 2 diabetes after 15 year of duration.<sup>7,8</sup> However, due to the large number of diabetic type 2 subjects, DR is likely to have a public health problem in India. In India Occurrence of DM as Epidemic in type 2diabetes mellitus as reported by the World Health Organization (WHO)<sup>9</sup>, diabetic retinopathy is fast becoming an important cause of visual disability. DR is preventable and treatable if managed early and timely intervention is done.

A female to male ratio in this study was 1:1.6., i.e., among 100 patients 62 were males, 38 were females. Diabetic retinopathy was seen more in males because of more risk factors and precipitating factors like sedentary life style, obesity, alcohol, smoking and others etc. In a study by Mohan Rema et al<sup>10</sup>, the male to female ratio was 3: 2. A study conducted by Rema M and Pradeepa R, too showed a preponderance in men with a female to male ratio of 1:2. Study by khandekar et al<sup>11</sup> too showed that men are at higher risk of developing retinopathy. Majority of the cases i.e., 30 cases belong to 51-60 years of age group (30%), 26 cases belong to 41-50 years of age group (26%), 24 cases belong to 61-70 years of age group (24%), 12 cases belong to 35-40 years of age group (12%), 8 cases belong to 70 and above age group (8%). Majority of them fall in the middle age group (40-60years). Since these subjects are professionally and functionally more responsible, increased incidence in this age group is not good for society and country, as visual disability leads to economic loss and more burden upon the society. Therefore prevention of diabetes by changing life style, modifying the risk factors and early diagnosis and treatment of diabetic retinopathy is essential in order to preserve working resources of the society. In a study by R Khandekar et al<sup>11</sup> showed that the retinopathy rate was higher in age group 50-59 and 60-69 years.

Among 100 cases, 48 (48%) were without family history of diabetics, 52 (52%) were with family history. In this study it showed that the family history is not that significant. This might be due to the recent changes in the life style. The role of genetic factors in relation to retinopathy has been studied, as some patients develop DR irrespective of good glycaemic control.<sup>12,13</sup> In type 2 diabetes mellitus a study conducted in families of

322 patients, Rema et al<sup>12</sup> reported, a familial clustering of diabetic retinopathy among siblings of diabetic probands with and without DR was present. The odds ratio was 3.5 suggesting that siblings of the probands with DR had 3.5 times higher risk of developing retinopathy. It has also been demonstrated that in Mexican-American type 2 Diabetes.<sup>13</sup> In the present study, 37% of cases had history of hypertension, (29 male patients, 08 female patients). Increased blood pressure implicated to damage the retinal capillary endothelial cells in eyes with diabetes.<sup>14</sup> The possible mechanisms by which hypertension may affect DR are haemodynamic (impaired autoregulation and hyperperfusion) and through VEGF (vascular endothelial growth factor). One of the study by kornerup concluded that the raise of blood pressure was by no means an essential factor in the etiology of diabetic retinopathy. However, it is reported that retinopathy progresses more rapidly in patients with hypertension than those without it. According toraman et al in study of risk factors diabetic retinopathy in rural India showed that systolic hypertension is a risk for developing diabetic retinopathy. The UKPDS showed that the incidence of retinopathy was associated with systolic blood pressure.<sup>15</sup>

In the present study 36% of cases have history of hyperlipidemia (30 male patients 06 females). Individuals with increased total serum cholesterol, low-density lipoprotein (LDL) cholesterol or triglyceride levels are more likely to develop retinal hard exudates, with risk of vision loss, irrespective of the extent of macular edema.<sup>16</sup> Rema et al,<sup>17</sup> The ETDRS<sup>18</sup> and the WESDR<sup>19</sup> found in DR a significant association between elevated serum total cholesterol and LDL cholesterol and the severity of retinal hard exudation. A recent paper from the CURES<sup>20</sup> eye study showed an association of DR with total cholesterol and serum triglycerides

In the present study 28% male patients had the history of alcohol intake. Young et al.<sup>21</sup> reported heavy alcohol consumption to be a risk factor for development of DR in patients without retinopathy at baseline. The Casteldaccia Eye Study demonstrated that duration of alcohol intake was associated with DR.<sup>22</sup>

In the present study 22 male, 06 female patients were obese. The diabetes control and complications trial (DCCT) observed in Zhang et al<sup>23</sup> study, that BMI had a significant predictive value.

In the present study 04 females were anemic. In the ETDRS<sup>24</sup> for development of high risk PDR and visual impairment, low hematocrit was an independent risk factor.

The common causes of diminution of vision in diabetic retinopathy are cataract, moderate NPDR, PDR with CSME, macular edema, vitreous hemorrhage, retinal detachment. Most common causes of diminution of vision in this study were cataract and macular edema. The Palakkad Eye Disease Survey reported in diabetics, cataract (27.8%) was the leading cause for visual disability.

Among 100 cases, 77 cases were taking regular treatment (77%) and 23 cases were on irregular treatment (23%). Patients on irregular treatment were more prone to the diabetic retinopathy changes and severity of the retinopathy changes. According to study by United kingdom prospective diabetes study, intensive control of diabetes and blood pressure slowed the progression of diabetic retinopathy and reduced the risk of other microvascular complications of DR.

## CONCLUSION

The intensive control of hyperglycaemia and hypertension reduces the incidence and progression of diabetic retinopathy. Despite of knowing this many people are unable to maintain these things with in normal limits. Visual disability from DR is largely preventable if managed with prevention of unhealthy food preferences, good glycaemia control, regular screening of retinal examination for early detection of retinopathy changes and timely intervention by laser. DR has become another common cause of visual dysfunction among the middle age group (40-60years ) along with senile cataract and glaucoma. So early diagnosis and meticulous management is essential to prevent visual disability and diabetic retinopathy complications.

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# Cysticercal Encephalitis: an Unusual Differential in the List of Encephalitis

Singh Ajeet P<sup>1</sup>, Khurana Bhawna<sup>2</sup>, Kumari Anita<sup>3</sup>, Prasad PL<sup>3</sup>

## ABSTRACT

**Introduction:** Neurocysticercosis (NCC) is the most common infestation of Central Nervous System with majority of cases presenting with seizures.

**Case report:** Here we report a case of NCC in a young boy who presented as encephalitis which is a very rare initial presentation of the disease. MRI brain showed characteristic “starry sky pattern” with eccentric mural nodule specific for NCC. Cysticercal encephalitis is a very rare presentation of NCC which itself is an unusual cause of encephalitis.

**Conclusion:** It should be included in differential diagnosis of acute encephalitic cases apart from common causes especially in endemic countries like India. Early diagnosis and appropriate therapy can result in better outcome in this rare but commonly fatal neurological disorder.

**Keywords:** Neurocysticercosis, Cysticercal encephalitis

## INTRODUCTION

Neurocysticercosis (NCC) is the most prevalent parasitic infestation in India. Central nervous system (CNS) involvement is seen in 60–90% of all infested patients with wide variations in clinical manifestations.<sup>1</sup> 70 to 90% of cases present with seizures while other common manifestations are headache, neurological deficit, hydrocephalus and raised intracranial pressure.<sup>2,3</sup> Seizure can occur both with degenerating cysts or calcified lesions. Rare neurological manifestations are spinal cysticercosis, progressive cord compression, ophthalmic cysticercosis, migraine and altered mental state.<sup>3</sup> Cysticercal encephalitis, is a very unusual presentation of NCC which occurs when there is diffuse cerebral edema along with multiple parenchymal cyst.<sup>4</sup> These patients are at risk of severe neurological sequelae because of brisk inflammatory response secondary to massive infection. Both MRI and CT can show the presence of an eccentric mural nodule which is characteristic of NCC. Seizures, being the most common presentation are usually controlled with standard antiepileptic drugs. Cysticidal therapy usually hastens radiological resolution of cysts but sometime associated with an exacerbation of neurological symptoms and death in some patients who have multiple cysts. Cysticercal encephalitis as manifestation of disseminated neurocysticercosis is very rare and only 0.3% of all cases of NCC have been reported in one large series of Indian children.<sup>5</sup> We present a case of acute cysticercal encephalitis in a 12 year old boy with characteristic imaging findings.

## CASE REPORT

A 12 year old boy presented with complaints of progressive deterioration in consciousness since two days and single episode of seizure like activity one day back. There was history of on and off fever and headache for last 5 months with no history of head trauma, ear discharge, vomiting, jaundice or any history

of tuberculosis contact. On examination child was afebrile with Glasgow coma scale (GCS) of 4/15 while the vitals were pulse-110/min, RR-24/min, BP-130/70mmHg respectively. In CNS examination only positive finding was extensor plantar response and rest were unremarkable as GCS was very low. Chest examination revealed bilateral crepts while cardiovascular system and other systemic evaluation was within normal limit. In view of altered sensorium a differential diagnosis of encephalitis, encephalopathy or any space occupying lesions was made and investigated accordingly. Laboratory investigations showed Hb-10.9gm/dL, TLC-12x10<sup>9</sup> cells/L DLC-P90, L10, E10, platelet count- 650 ×10<sup>9</sup>/L, Blood sugar- 110mg/dL, Blood urea-15mg/dL, S.creatinine – 0.3mg/dL, S.sodium-137mmol/L and S.potassium-4.8mmol/L. Malaria serology and mantoux test were negative and chest X ray showed mild perihilar opacities. The protein, sugar and ADA levels in CSF were 90mg/dL, 50mg/dL, and 8U/L respectively while total cells were 50 (P 45, L 5). MRI brain was suggestive of disseminated cerebral cysticercosis in various stages of evolution in bilateral cerebral hemisphere giving it the characteristic “starry sky pattern” (figure-1). Enhancing scolex was also noted in many of the cystic lesion with flair images revealing diffuse cerebral edema (figure-2). Child was managed initially with anti-convulsant along with antibiotics for prevention of secondary lung infection. Dexamethasone was given interavenously for 5 days followed by oral prednisolone over next 4 weeks with tapering. Albendazole was not given initially as it is contraindicated in such cases but after one week of symptomatic improvement, it was given for 8 days in a dose of 15mg/kg. After seven days of admission, patient regained consciousness but remained highly irritable. He had variable paresis in all four limbs for which he was put on regular physiotherapy and later on discharged. On follow up after 6 weeks, child's behaviour improved remarkably but weakness and abnormal gait resolved only after 6 months. Repeat CT scan after 6 months showed only few ring enhancing lesions as compared to earlier scan (figure-3).

## DISCUSSION

Neurocysticercosis is the most common parasitic disease of the CNS caused by ingestion of foods contaminated with *Taenia solium*. The cysticercal larva after reaching the brain invokes only minimal inflammatory reaction and forms cyst which

<sup>1</sup>Senior Resident, <sup>2</sup>Junior Resident, <sup>3</sup>Professor, SRMS IMS, Bareilly, India

**Corresponding author:** Dr Ajeet P Singh, Senior Resident, Department of Pediatrics, SRMS IMS, Bareilly, India.

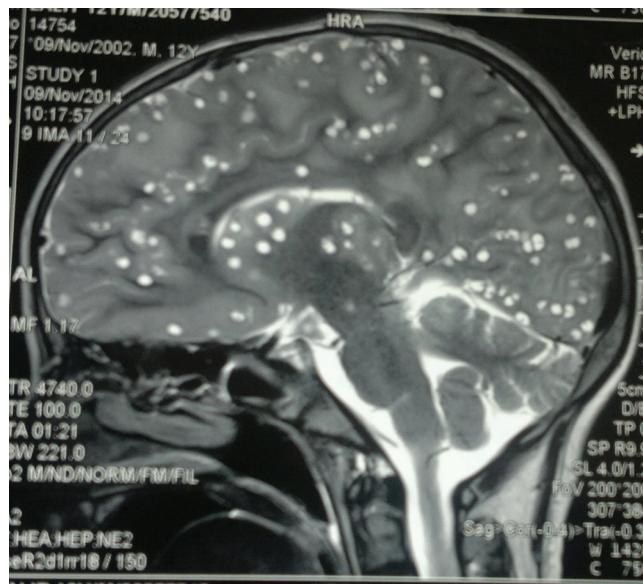
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later degenerates with thickening of wall and opacification which are easily picked up by neuroimaging as contrast enhancing ring like lesions. Cysticerci may be located in brain parenchyma, subarachnoid space, ventricular system or spinal cord causing pathological changes that are responsible for the pleomorphism of neurocysticercosis.<sup>6</sup> Though seizures are most common initial presentation of NCC but in the present case child presented in a state of altered sensorium for past two days with headache and insignificant history of single seizure like activity. Cysticercal encephalitis is a severe and rare form of neurocysticercosis. Besides that only few cases in children have been reported till yet.<sup>7</sup> It is characterized by altered sensorium, seizures, diminution of visual acuity, headache, vomiting, and papilledema as in the present case.<sup>4</sup> This occurs when there is massive cysticerci infection of the brain parenchyma and the host's immune system actively reacts against the parasites. Although enhancing lesions are typical of neurocysticercosis but they can be noted with tuberculomas, brain abscess and tumours. Accurate diagnosis of NCC is possible after interpretation of clinical data together with findings of neuroimaging studies and results of immunological tests. Despite the advances in neuroimaging and immune diagnostic tests, the diagnosis of neurocysticercosis is a challenge in many patients. Clinical manifestations are nonspecific, neuroimaging findings are often not pathognomonic, and serologic tests are faced with problems related to relatively poor specificity and sensitivity.<sup>8</sup> So a set of diagnostic criteria based on clinical, radiological, immunological and epidemiological data are used to diagnose patient with suspected NCC. This includes four categories of

Revised Diagnostic Criteria for Neuro-cysticercosis	
Absolute	
1.	Histological demonstration of the parasite from biopsy of brain or spinal cord lesion
2.	Cystic lesions with scolex on CT or MRI
3.	Direct visualization of subretinal parasite by fundoscopy
4.	Spontaneous resolution of small single enhancing lesions
Major	
1.	Lesions highly suggestive of NCC on neuroimaging
2.	Positive serum immuno blot for detection of anti-cysticercal antibodies
3.	Resolution of cysts after antiparasitic therapy
Minor	
1.	Lesions compatible with NCC on neuroimaging
2.	Clinical manifestations suggestive of NCC
3.	Positive CSF-ELISA for detection of anticysticercal antibodies or cysticercal antigens
4.	Cysticercosis outside the CNS
Epidemiologic	
1.	Individual coming from or living in an endemic area
2.	Evidence of household contact with <i>Taenia solium</i> infection.
3.	History of frequent travel to disease-endemic areas
Definitive	
1.	Presence of one absolute criterion or two major plus one minor and one epidemiologic criteria

**Table-1:** Criteria for NCC diagnosis

criteria- absolute, major, minor and epidemiological (Table-1).<sup>8</sup> Any suspected patient can be diagnosed as definitive case if there is presence of one absolute criteria and two major plus



**Figure-1:** MRI brain showing multiple solid and cystic lesion appearing hyperintense on T2 W image giving the characteristic "Starry sky appearance".



**Figure-2:** MRI brain showing multiple ring enhancing lesion with eccentric mural nodule in few of them



**Figure-3:** Repeat CT brain after treatment showing only few remnant calcified lesion.

one minor or one epidemiological criteria.<sup>8</sup> This case full fills criteria for definitive diagnosis. The current consensus is that patient with multiple parenchymal cysticerci should be treated with course of albendazole 15 mg/kg/day for 8 days along with simultaneous course of corticosteroids apart from anti-epileptics.<sup>9</sup> But in this case albendazole was given after one week, in view of their potential to exacerbate host inflammatory response. Patient with numerous cysticerci may require repeated courses of therapy and even surgery.<sup>10</sup>

## CONCLUSION

Accurate diagnosis and early appropriate therapy can result in better outcome in such rare but commonly fatal neurological disorder.

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# Clustering of Dental Caries and Risk of Obesity with Television Viewing among Bangalore North Adolescents

Jessy P<sup>1</sup>, Priya Nagar<sup>2</sup>, Pai Tanvi<sup>1</sup>, Mayuri Borse<sup>1</sup>

## ABSTRACT

**Introduction:** The time spent on television viewing has been implicated as a possible risk factor for developing dental caries, particularly to those related to sedentary life style. Study aimed to examine the potential association between excessive TV viewing and dental caries, and its risk of obesity among adolescents in Bangalore north.

**Material and methods:** A study sample of 250 students between 12-16 years of age were randomly chosen from a school situated in Bangalore north. A self-reported questionnaire was used to collect data on sociodemographic, and television viewing duration. Also a height and weight of the individual were measured along with the clinical dental examination and dental caries was diagnosed by WHO criteria. Comparative evaluation was done to examine the association between time spent viewing television and DMFT and untreated caries among 12-16 years-old adolescents.

**Results:** Higher caries prevalence was found among children who watched television excessively and asked for more food in-turn resulted in obesity.

**Conclusion:** Longer extent of television viewing was significantly and reliably associated with higher DMFT and higher risk of obesity among Bangalore north adolescents.

**Keywords:** Television viewing, Obesity, Dental caries, Adolescents

## INTRODUCTION

Dental caries affecting mankind still persisted as one of the most widespread, multifactorial diseases.<sup>1</sup> Its not only widespread among adults but also children, from 60% to 90% of them. In other words, six to nine children in every ten are affected by tooth decay.<sup>2</sup> Modern concept of dental caries includes social and behavioural factors regarding a particular individual.<sup>3</sup>

Childhood obesity has reached epidemic proportions.<sup>4</sup> Obesity is responsible for multiple complications and it is characterized by the energy and metabolism imbalance<sup>5,6</sup> In turn, obesity has been associated with diet, genetic, behavioural and psychological factors.<sup>4</sup> There is a strong dose-response relationship between the occurrence of overweight and hours of television viewed<sup>7</sup> In current trend, television has become a major part of children's lives and watching TV is the dominant recreational pastime at all ages, especially for children and adolescents. Presently most of the children have a regular access to TV along with portable handheld devices (computer, smartphone, laptop, tablet, i Pad) and they also routinely engage in two or more forms of screen viewing at the same time. As there is no studies done among Bangalore population. The aim of this present study was to examine the potential association between TV viewing and dental caries experience and also its risk of obesity, among adolescents from Bangalore north. This article throws a knowledge about the link between television viewing and dental caries and obesity.

## MATERIAL AND METHODS

Ethical committee clearance was taken from Institutional Ethics Committee, Krishnadevaraya college of dental science, Bangalore, Karnataka, India. Approval from the school authorities and informed consent from the parents were obtained. Children belonging to similar socioeconomic backgrounds and having television at home were included in the study. A cross sectional study was planned in which eight questionnaires were prepared and distributed among students of standard 7, 8, and 9 in their respective schools, followed by oral examinations. All examinations were carried out using mouth mirrors and standard explorers, by single examiner to avoid interexaminer variations. Dental caries of all the participating students were recorded using DMFT/dmft index. A total of 250 students aged 12-16 years in the schools of Bangalore north participated in the study. A questionnaire was administered to collect data on sociodemographic and television viewing duration. Also a height and weight of the individual were measured with digital scales (weight to the nearest 0.1 kg) and a portable stadiometer (height to the nearest 0.1 cm) while children were not wearing shoes. The body mass index (BMI) of each child was calculated along with the clinical dental examination and dental caries was diagnosed by WHO criteria.

## STATISTICAL ANALYSIS

Descriptive and analytical statistics were done. The *Chi-square test* was done to check differences in proportions between groups. SPSS (Statistical Package for Social Sciences) Version 20.1 (Chicago, USA Inc.) was used for analysis. DMFT scores were considered from the median values i.e 2 and 3. Interactions between dental caries, risk of obesity with television viewing were analysed.

## RESULTS

There were 250 adolescents aged 12-16 years out of which boys and girls ratio is 1:1.27.

Table-1A summarises the variables such as age, sex, BMI, ethnicity, area of residence, and source of entertainment where significant difference of dental caries experience was found between males and females at  $p < 0.05$  and also age and BMI

<sup>1</sup>PG Student, <sup>2</sup>Professor and Head, Department of Pedodontics and Preventive Dentistry, Krishnadevaraya College of Dental Sciences and Hospital, Hunasamaranahalli, Yelahanka, Bangalore- 562157, India

**Corresponding author:** Jessy P, KCDS Ladies Hostel, Krishnadevaraya College of Dental Sciences and Hospital, Hunasamaranahalli, Yelahanka, Bangalore- 562157, India

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shows statistical significant results at  $p < 0.01$ .

Table-1B exhibits duration of screen viewing and kind and duration of food consumption while viewing, significant results of increased DMFT were seen among those who watched TV for longer duration, at  $p < 0.05$ , and also increased DMFT were noted in students who preferred snacks while viewing TV (95.9%) at  $p < 0.01$ .

Table-2 shows the correlation between TV viewing, BMI and DMFT experience, where the statistical significant result was found as the increase in time spent on TV viewing leads

to increased BMI (overweight) and thereby increased caries experience.

Table-3 reveals odds ratios of high caries experience (DMFT  $\geq 3$ ) for 12-16 year olds and T.V. viewing, by age, sex, and BMI where females are commonly affected with the odds ratio of 1.911 significant at  $p < 0.05$

Figure-1 gives a perfect description of Caries experience (Low: DMFT  $\leq 2$ ; High: DMFT  $\geq 3$ ) and its relation with T.V. viewing and BMI for 12-16 year olds, in which the results shows that TV viewing of more than 2hrs/day causes increased caries

Variables		Total N (%)	DMFT $\leq 2$ N (%)	DMFT $\geq 3$ N (%)	P-Value
Sex	Males	110 (44.0)	28 (35.0)	82 (48.2)	0.033*
	Females	140 (56.0)	52 (65.0)	88 (51.8)	
Age	12-13 years	077 (30.8)	23 (28.7)	54 (31.8)	0.001†
	14 years	117 (46.8)	28 (35.0)	89 (52.4)	
	15-16 years	056 (22.4)	29 (36.2)	27 (15.9)	
BMI	Underweight	025 (10.0)	20 (25.0)	05 (02.9)	0.001†
	Normal Weight	065 (26.0)	16 (20.0)	49 (28.8)	
	Overweight	115 (46.0)	35 (43.8)	80 (47.1)	
	Obese	45 (18.0)	09 (11.2)	36 (21.2)	
Ethnicity	Originally from Bengaluru	238 (95.2)	73 (91.2)	165 (97.1)	0.133
	Native of Bengaluru	007 (2.8)	04 (5.0)	03 (01.8)	
	Migrated to Bengaluru	005 (2.0)	03 (3.8)	02 (01.2)	
Area of Residence	Urban	014 (5.6)	06 (7.5)	08 (04.7)	0.076
	Semi Urban	207 (82.8)	60 (75.0)	147 (86.5)	
	Rural	29 (11.6)	14 (17.5)	15 (08.8)	
Main Source of Entertainment	Television	134 (53.6)	44 (55.0)	90 (52.9)	0.114
	Computer	080 (32.0)	20 (25.0)	60 (35.3)	
	i-Pad	026 (10.4)	10 (12.5)	16 (09.4)	
	Any Other	010 (4.0)	06 (7.5)	04 (02.4)	

\* significant at  $p < 0.05$ ; † significant at  $p < 0.01$

**Table-1A:** Distribution of explanatory variables within groups by caries experience

Variables		Total N (%)	DMFT $\leq 2$ N (%)	DMFT $\geq 3$ N (%)	P-Value
Duration of watching T.V./ Computer/ i-Pad	< 30 Mins/day	054 (21.6)	23 (28.7)	31 (18.2)	0.046*
	30 Mins–1 hr/day	086 (34.4)	29 (36.2)	57 (33.5)	
	2 hr/day	071 (28.4)	23 (28.7)	48 (28.2)	
	2-3 hr/day	028 (11.2)	03 (03.8)	25 (14.7)	
	> 3 hr/day	011 (04.4)	02 (02.5)	09 (05.3)	
Preferred channels to watch	Sports	094 (37.6)	26 (32.5)	68 (40.0)	0.175
	News	006 (02.4)	04 (05.0)	02 (01.2)	
	Nat. Geographic / Discovery	012 (04.8)	06 (07.5)	06 (03.5)	
	Cartoon Channels	062 (24.8)	18 (22.5)	44 (25.9)	
	Movie / Songs	076 (30.4)	26 (32.5)	50 (29.4)	
Consume snacks while watching T.V./ Computer/ i-Pad	Yes	217 (87.5)	54 (69.2)	163 (95.9)	0.001†
	No	031 (12.5)	24 (30.8)	07 (04.1)	
Kind of snacks while watching T.V./ Computer/ i-Pad	Food	015 (6.8)	06 (10.7)	09 (05.4)	0.012†
	Snacks	148 (66.7)	28 (50.0)	120 (72.3)	
	Ice-cream	002 (0.9)	00 (00.0)	02 (01.2)	
	Drinks	57 (25.7)	22 (39.3)	35 (21.1)	
Duration of snacking while watching T.V./ Computer/ i-Pad	30 Mins–1 hr/day	142 (64.0)	36 (64.3)	106 (63.9)	0.080
	2 hr/day	056 (25.2)	18 (32.1)	38 (22.9)	
	2-3 hr/day	024 (10.8)	02 (3.6)	22 (13.3)	
Habit of eating snacks at night-time	Yes	112 (46.7)	13 (18.3)	99 (58.6)	0.001†
	No	128 (53.3)	58 (81.7)	70 (41.4)	

\* significant at  $p < 0.05$ ; † significant at  $p < 0.01$

**Table-1B:** Distribution of explanatory variables within groups by caries experience (cont.)

Hours of watching T.V.	BMI	Total N (%)	DMFT ≤2 N (%)	DMFT ≥3 N (%)	P-Value
< 30 Mins/day	Underweight	10 (18.5)	09 (39.1)	01 (3.2)	0.001 <sup>†</sup>
	Normal Weight	12 (8.7)	02 (32.3)	10 (22.2)	
	Overweight	21 (38.9)	11 (47.8)	10 (32.3)	
	Obese	11 (20.4)	01 (4.3)	10 (32.3)	
30 Mins–1 hr/day	Underweight	08 (9.3)	06 (20.7)	02 (3.5)	0.006 <sup>†</sup>
	Normal Weight	26 (30.2)	12 (41.4)	14 (24.6)	
	Overweight	39 (45.3)	07 (24.1)	32 (56.1)	
	Obese	13 (15.1)	04 (13.8)	09 (15.8)	
2 hr/day	Underweight	07 (9.9)	05 (21.7)	02 (4.2)	0.030*
	Normal Weight	17 (23.9)	02 (8.7)	15 (31.2)	
	Overweight	38 (53.5)	14 (60.9)	24 (50.0)	
	Obese	09 (12.7)	02 (8.7)	07 (14.6)	
2-3 hr/day	Normal Weight	06 (21.4)	00 (0.0)	06 (24.0)	0.186
	Overweight	14 (50.0)	03 (100.0)	11 (44.0)	
	Obese	08 (28.6)	00 (0.0)	08 (32.0)	
> 3 hr/day	Normal Weight	04 (36.4)	00 (0.0)	04 (44.4)	0.118
	Overweight	03 (27.3)	00 (0.0)	03 (33.3)	
	Obese	04 (36.4)	02 (100.0)	02 (22.2)	

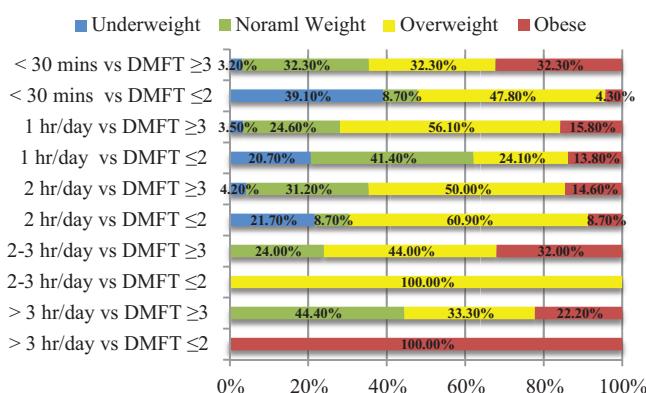
\*Significant at p < 0.05; † significant at p < 0.01

**Table-2:** Distribution of explanatory variables – hours of watching T.V. and BMI within groups by caries experience

Variables		Odds Ratio	95 % C.I.	P-value
Age (reference: 12-13 yrs)	14 years	3.71	1.58-8.67	0.002 <sup>†</sup>
	15-16 years	5.06	2.28-11.20	0.010 <sup>†</sup>
Sex (Male)	Female	1.911	1.00-3.62	0.047*
Watching T.V. (reference: < 30 mins)	30 Mins–1 hr/day	0.579	0.10-3.114	0.525
	2 hr/day	0.673	0.12-3.50	0.638
	2-3 hr/day	0.909	0.17-4.86	0.912
	> 3 hr/day	2.535	0.33-19.01	0.366
BMI (reference: Underweight)	Normal Weight	0.086	0.02-0.30	0.001 <sup>†</sup>
	Overweight	1.420	0.50-3.98	0.505
	Obese	0.620	0.25-1.51	0.294

\*Significant at p < 0.05; † significant at p < 0.01: model adjusted for age, sex, and BMI; log likelihood chi-square: 257.89, Prob > chi-square:<0.001, Pseudo R-square: 0.279

**Table-3:** Odds ratios of high caries experience (DMFT ≥3) for 12-16 year olds and T.V. viewing, by age, sex, and BMI



**Figure-1:** Caries experience (Low: DMFT ≤2; High: DMFT ≥3) and its relation with T.V. viewing and BMI for 12-16 year olds

experience with the higher risk of obesity.

## DISCUSSION

In India, Children between the ages of 6-17 viewing television more than 35 hours a week which could severely generate higher prevalence of dental caries and a greater risk of obesity amongst them. The following statistics are dreadful that so many children

today sit glued in front of the TV, being brainwashed by all sorts of demonic influences. According to the associated chamber of commerce and industry of India (ASSOCHAM), the average children watches more than 5 hours of TV each day (or 35 hours/week).<sup>8</sup>

The time spent on television viewing has been implicated as a possible risk factor for developing dental caries as they are more likely to consume more sweetened beverages and snacks while viewing TV.<sup>9-11</sup> Our findings are generally consistent with previous studies which have shown amplified viewing time to be linked with increased soft-drink consumption.<sup>3</sup> Thus in our findings higher caries prevalence was found among children who viewed television and asked additionally for more food and soft drinks. The other causative factor is type of channels viewed as it also has influence in dental caries and obesity.<sup>12</sup> About 50% of Cariogenic food advertisements were popular on children's favorite channels.<sup>13</sup> Fruit, vegetables, protein-rich foods products were rarely advertised, whereas foods frequently advertised are rich in fats and sweets, with candy being the most commonly advertised food.<sup>13,14</sup> The advertisement of high sugar products was 38.4% and low sugar products equated for only 17.0%. whereas the promotion of healthy living and oral hygiene

products accounted for only 1.8% and 0.3% respectively.<sup>15</sup> The current analysis also suggest the similar findings. Incidence of dental caries and obesity is directly proportional to viewing television<sup>6</sup> and we also found an inverse relationship between television viewing and rate of planned physical activity. Because those who watch television for extended periods are likely to be less active than those who watch less television.<sup>4</sup> In our findings Children viewing television more than 2hrs had low physical activity and are also linked to increased consumption of obesogenic foods which may be a indicator for risk of obesity. One of the study done by Ramesh K,2010 reveals that increase in weight was observed in 19.6% children signifying that the television viewing may prompt to childhood obesity. In 30.4% cases decrease in physical activity was found.<sup>16</sup> Thus there is a strong relationship between the hours of television viewed and prevalence of overweight, and decrease in viewing time could help prevent common chronic health condition.<sup>17</sup> Also another stronger marker of increased risk of being overweight is TV in the child's bedroom which is an added effect.<sup>18</sup>

## CONCLUSION

This study demonstrated that there is an strong link between Dental caries, obesity and TV viewing among adolescents in Bangalore north as there was a greater likelihood of having increased decayed teeth, risk of obesity with increasing time spent in viewing television.

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# Fungal Profiling in Patients with Chronic Suppurative Otitis Media: A Microbiological Study

Rajesh Kumar Yadav<sup>1</sup>, Kumar Gaurav<sup>2</sup>, Megha Bansal<sup>3</sup>, Abhishek Jaiswal<sup>4</sup>

## ABSTRACT

**Introduction:** One of the complications of acute otitis media is chronic suppurative otitis media although the risk factors responsible for this are unclear. Development of chronic suppurative otitis media may be related to the frequent infection of the upper respiratory tract and poor socioeconomic conditions. Long term antibiotic and steroidal therapy for its treatment are assumed to suppress the resident bacterial flora with a resultant increase in fungal growth. Hence; this study was undertaken to assess the fungal growth in patients with chronic suppurative otitis media.

**Material and Methods:** 214 clinically diagnosed patients of chronic suppurative otitis media who reported in the hospital from June 2012 to July 2014 were included in the present study. Patients presenting with tympanic perforation and ear discharge of more than 2 months were included in the study. Inoculation of the swabs of the patients was done on two sets of Sabouraud's dextrose agar slants with 0.05 mg/ml of chloramphenicol followed by incubation at 35°C and 28°C, respectively. Criteria of Lodder and Kreger-Van Rij and Rippon were used to identify the isolates based on colonial appearance, microscopic morphology in lactophenol cotton blue mount, slide culture preparation, and biochemical characters.

**Results:** Approximately 77% of the patient showed positive culture results for fungal growth. Remaining of the subjects showed absence of any fungal growth. Majority of the patients in which fungal growth was present belonged to age group of 21 to 30 years. More than 50 % of the patients received topical ear drops while remaining 48 % were on oral anti-microbial therapy. Out of all the patients receiving topical therapy, maximum of them were receiving ciprofloxacin followed by gentamicin. Candida albicans was the most frequently found fungal spp. followed by aspergillus spp.

**Conclusion:** Bacteria flora of the ear may get suppress by the prolonged use of antibiotics or steroidal drops which subsequently might lead to fungal growth.

**Keywords:** Fungal infection, Otitis media

## INTRODUCTION

Although the risk factors are unclear, chronic suppurative otitis media (CSOM) is assumed to be a complication of acute otitis media (AOM). Development of chronic suppurative otitis media may be related to the frequent infection of the upper respiratory tract and poor socioeconomic conditions (overcrowded housing and poor hygiene and nutrition).<sup>1-4</sup> However, a systematic review found no clear evidence that antibiotics are effective in preventing the progression of AOM to CSOM even among children who are at high risk for the disease.<sup>5</sup> An ear with perforated tympanic membrane and persistent drainage from the middle ear is the chronic discharging ear. Unlike otitis media with effusion which is common in the West,<sup>6-8</sup> chronic discharging ears are highly prevalent in the tropical regions including

South Asia. It may often be accompanied by complications<sup>9-12</sup> including septicaemia, meningitis, brain abscess, facial paralysis and mental retardation<sup>13</sup> and it is believed to be responsible for more than two-thirds of deafness in children. Unfortunately, the treatment protocol of the chronic discharging ear is still limited to the symptomatic treatment. i.e. regular clearing and dressing the ear until unless the lesion becomes completely dry<sup>14</sup> and in case complications occur, mastoidectomy is done.<sup>15,16</sup> Hence; this study was undertaken to assess the fungal growth in patients with chronic suppurative otitis media.

## MATERIAL AND METHODS

The present study included 214 clinically diagnosed CSOM patients who reported in the hospital from June 2012 to July 2014. From the institutional ethical committee, ethical clearance was taken. Patients presenting with tympanic perforation and ear discharge of more 2 months were included in the study. Subjects included were only those subjects who were on any antibiotics (oral, topical or systemic) and/or steroid ear drops for >14 days and still persisted with symptoms. Patients were not exposed to any kind of risk by following innocuous method of sample collection procedure. Exudates from the tympanic membrane were thoroughly soaked with sterile cotton swabs and were for further microbiological examination, were sent to the pathologic and microbiologic laboratory. Microscopic examination of the specimens was done in the laboratory in 10% KOH preparations and Giemsa stained smears and were evaluated to check the for the presence of pus cells, budding yeast cells, fungal hyphae (septate or aseptate) and spores, etc. Whenever and wherever required, use of special stains such as periodic acid-Schiff and Gomori's methanamine silver was done. Inoculation of the swabs was done on two sets of Sabouraud's dextrose agar slants with 0.05 mg/ml of chloramphenicol followed by incubation at 35°C and 28°C, respectively.

For checking the any king of mycotic growth in the cultural plates, thorough examination was done initially daily for seven days followed by examination after every three days for 4 weeks. The specimens were considered positive for fungus under following conditions:

<sup>1</sup>Associate Professor, <sup>4</sup>Tutor, Department of Microbiology, <sup>3</sup>Assistant Professor, Department of Pathology, TSMMC and H., Amausi,

<sup>2</sup>Assistant Professor Department of Ent, Amausi, Lucknow, Uttar Pradesh, India

**Corresponding author:** Rajesh Kumar Yadav, Associate Professor, Department of Microbiology, TSMMC and H., Amausi, Uttar Pradesh, India

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Number of isolates	Sex	Age group in years				
		Less than or equal to 10	11 to 20	21 to 30	31 to 40	More than 40
Culture positive for fungal growth	Male	16	22	34	18	8
	Female	10	18	30	8	2
Culture positive for fungal growth	Male	6	12	6	4	2
	Female	4	2	10	2	0

Table-1: Distribution of patients according to age and sex.

Treatment	Percentage of patients
Topical ointments	Ciprofloxacin
	Gentamicin
	Ofloxacin
	Steroidal formulation
	Unknown
Oral formulations	48

Table-2: Various treatments received by patients

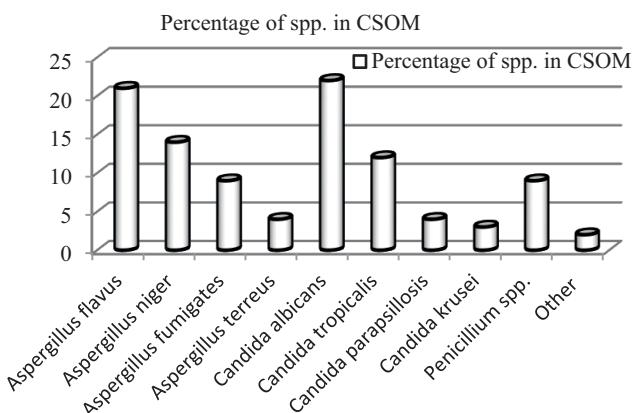


Figure-1: Distribution of various fungal isolates in the patients

- (i) When both the smear and the culture were positive,
  - (ii) When the smear was negative but culture was significant or repeatedly positive for same fungus, and
  - (iii) When smear was positive although culture were sterile.
- Criteria of Lodder and Kreger-Van Rij and Rippon were used to identify the isolates based on colonial appearance, microscopic morphology in lactophenol cotton blue mount, slide culture preparation, and biochemical characters.<sup>17,18</sup>

## STATISTICAL ANALYSIS

Microsoft office 2007 was used to make tables and graphs. Results of the study are based on descriptive statistics. Mean and percentages were calculated to infer data.

## RESULTS

Table-1 shows the demographic data of the study population. Approximately 77% of the patient showed positive culture results for fungal growth. Remaining of the subjects showed absence of any fungal growth. Majority of the patients in which fungal growth was present belonged to age group of 21 to 30 years. Table-2 shows various treatment modalities received by patients. More than 50 % of the patients received topical ear drops while remaining 48 % were on oral anti-microbial therapy. Out of all the patients receiving topical therapy, maximum of them were receiving ciprofloxacin followed by gentamicin. Figure-1 shows the distribution of various fungal isolates in the patients. *Candida albicans* was the most frequently found fungal

spp. followed by *aspergillus* spp.

## DISCUSSION

Chronic otitis media and CSOM are few of the common conditions encountered in a general otolaryngology clinic setting and its prevalence has been quoted to range from 9% to 27.2%<sup>20,21</sup> among patients who present with signs and symptoms of otitis externa and up to 30%<sup>22,23</sup> in patients with discharging ears. Chronic Otitis Media (COM) is the term used to describe a variety of signs, symptoms, and physical findings that result from the long-term damage to the middle ear by infection and inflammation. CSOM is the inflammation of the ear that causes recurrent ear discharge through a perforation of the ear drum.<sup>19</sup> It is worldwide in distribution with a higher prevalence in the hot, humid, and dusty areas of the tropics and subtropics.<sup>21-23</sup> Although rarely life threatening, the disease is a challenging and frustrating entity for both the patients and otolaryngologists as it frequently requires long-term treatment and follow up. Despite this, there could be recurrences.

In the present study the highest incidence of fungal CSOM was noted in second and third decades of life (more than 60%), and this observation was concurrent to the studies conducted by various other authors.<sup>24,25</sup> High exposure of the youngsters to the fungal spores might be responsible for high incidence of fugal infections in this specific age group.<sup>26</sup> Among the fungal etiology in CSOM, the most commonly isolated organisms are *Aspergillus* species and *Candida* species.<sup>27</sup> In the present study, *Aspergillus* species comprised of more than 45% of the total fungal isolates, whereas approximately 40% of the total microorganisms were species of *Candida*. *A. Flavus* and *A. Niger* were the most common *Aspergillus* species. Among the *Candida* species, the most common isolates were *C. albicans* and *C. tropicalis*. Earlier study from India,<sup>24</sup> reported higher isolation rate of *Aspergillus* species as compared to *Candida* species. A recent study by Aneja et al.<sup>28</sup> from India reported *Aspergillus* in more than 85% of patients with *A. niger* and *A. Flavus* as the most prevalent species. While some studies report *candida* to be the most common species.<sup>29</sup> Strauss and Fine reported two cases of *Aspergillus* otomastoiditis caused by *A. fumigatus*.<sup>30</sup> This mold has been considered more pathogenic than *A. niger* as *A. fumigatus* produces a hemolytic exotoxin which has the ability to alter skin resistance.<sup>31</sup> In artificial substrates, *Aspergillus* is one of the main organisms inhabiting the media.<sup>28</sup> Acidic pH of the ear canal is responsible for the growth of *Aspergillus* in these areas.<sup>32</sup> *Pseudallescheria boydii* is a saprophytic fungus capable of causing invasive fungal infections in humans. This fungus is morphologically similar to *Aspergillus* but is resistant to conventional systemic antifungal therapy with amphotericin B.<sup>33</sup> Because of appearance of lack of specific clinical characteristics of some of the fungal organisms like *aspergillus*, mycotic infections have become

more tedious to identify clinically and therefore, further these infections donot respond with traditional antimicrobial therapy and mycotic culture is used to identify such organisms in ear infections.<sup>34</sup> This substantiates the essentiality of fungal cultures for diagnosis. *Penicillium* species was isolated in eight cases. A study by Talwar et al.<sup>24</sup> found *Penicillium* in more than 10% of the cases whereas a study by Aneja et al<sup>28</sup> reported the same in less than 3% of cases. *Mucor* species was isolated in two cases, and both the patients were known diabetics. *Mucor* has a propensity to invade arterial walls in immunocompromised patients, especially in uncontrolled diabetes mellitus patients. Haruna et al.<sup>35</sup> reported a meningoencephalitis case caused by mycotic infection invading through temporal bone. They observed that fungal organisms with minimal of virulence like non-albicans *Candida* are also actively found in the ear infections. Fungal organisms apart from showing geographical distribution also show seasonal and time dependent variation in distribution. Prevalence of fungal infections of the ear during moist and humid conditions has been reported previously by several authors.<sup>36,37</sup> Dayasena et al studied the aetiological organisms for CSOM and also identified the effect of demographic factors on disease manifestation. They included a case series of 234 patients who had been admitted to National Hospital of Sri Lanka, with the complaint of ear discharge and from whom the specimens were sent for microscopy and culture at Department of Microbiology 1 January 2009 to 31 December 2009. From the results, they concluded that demographic does not seems to significantly alter the manifestation of the disease, though CSOM was more commonly seen among males and adults.<sup>38</sup>

## CONCLUSION

From the above results, it can be concluded that bacterial flora of the ear may get suppress by the prolonged use of topical antibiotics or antibiotics-steroids ear drops which subsequently might lead to fungal growth. Further studies are advocated to control the discomfort cause by this condition.

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# Dental Caries in Primary and Permanent Molars in 7-8-Year Old School Children Evaluated with Caries Assessment Spectrum and Treatment (CAST) Index from Bangalore North

Mayuri Borse<sup>1</sup>, Priya Nagar<sup>2</sup>, Jessy P<sup>1</sup>, Pai Tanvi<sup>1</sup>

## ABSTRACT

**Introduction:** Caries is a common biofilm-mediated chronic disease that affects all ages. So, the study was done to evaluate caries in primary and first permanent molars of 7-8-year-old children by the Caries Assessment Spectrum and Treatment (CAST) index and to find whether there was any correlation between the caries stages in such teeth.

**Materials and methods:** The study covered 100 7-8-year-old children from randomly selected schools in the North Bangalore. The prevalence of CAST categories was evaluated with regard to the first and second primary, and first permanent, molars. The Spearman's rank correlation coefficient was used to explore the correlation of the distribution of CAST codes among the evaluated teeth. This parameter is compared using Kruskal-Wallis non parametric test. The level of statistical significance was established at  $p < 0.1$ . The intra-examiner reliability was determined by the unweighted kappa coefficient.

**Results:** With regard to deciduous teeth, 70% subjects showed a dentin cavity (code 5) as the most serious caries stage. In 1<sup>st</sup> and 2<sup>nd</sup> primary molars, caries was most often recorded at the stage of cavitated dentin lesion. With regard to the permanent molars, enamel lesions were most prevalent (code 3) and most lesions were scored at the non-cavitation level. Teeth with pulpal involvement, sepsis and extracted due to caries were found to be more prevalent in first, and then in second primary molars. The strong correlation was found in teeth present in maxilla and mandible. The ' $r$ ' value was 0.217 and 0.109 in maxilla and mandible ( $p < 0.1$ ), respectively. For neighbouring primary and permanent molars ' $r$ ' values were lower than 0.1, which meant a weak correlation.

**Conclusion:** A strong correlation was found between the status of teeth from the maxilla and mandible. The study proved the usefulness of the CAST index in epidemiological surveys.

**Keywords:** Caries pattern, CAST index, Children

## INTRODUCTION

Untreated caries can lead to pain, loss of teeth and impaired quality-of-life. The development of a caries lesion is the result of a complicated interplay of many factors. In most cases, caries develops slowly and the process may arrest spontaneously. However, the disease is not usually self-limiting and without adequate treatment the process can continue until the tooth is destroyed. Therefore, there is increasing emphasis on the importance of effective early intervention and a prerequisite is reliable assessment of the presence and activity of a lesion at an early non-cavitated stage of the disease process.<sup>1,2</sup>

Dental caries remains a serious problem in many populations worldwide with a marked increase in prevalence over the last decade; hence a continued surveillance of the dental epidemiological status is of paramount importance. Dental

caries, if left untreated can lead to pain, loss of teeth, and impaired quality of life.

DMFT, the most commonly used tool, ignores the presence of precavitated lesions and is unable to categorize caries in different stages of its advancement. From the practical point of view, the most advantageous solution in epidemiological surveys is to use a single index describing the full continuum of a disease.

Hence, an innovative caries detection index namely Caries assessment spectrum and treatment (CAST) has been introduced, which has the integral capability to record the whole progressive spectrum of dental disease and also the inclusion of filled teeth in the category of sound teeth.<sup>3-5</sup>

Many initiatives were taken since late 19<sup>th</sup> century to develop an index that records the diverse spectrum of this pandemic disease.<sup>6</sup> One such remarkable step against the apparent need was taken almost a decade back, when a visual/tactile inspection based caries index was introduced as ICDAS (International Caries Detection and Assessment System). This index records both the restorative and the carious status from earliest visual change in enamel to the dentinal cavitation in a two digit coding system. However, ICDAS faced the reluctance for its application due to multiple reasons with its complicated recording criteria topping the list.<sup>7,8</sup>

Furthermore, the burden of dental caries in developing countries is fundamentally because of the untreated part of dental caries. Thus, as a perceptible need in 2010, PUFA/pufa (Pulpal involvement, Ulceration, Fistula, Abscess) was reported that pertinently record the later consequences of dental caries. However, PUFA was recommended to be used as an adjunct to standard caries indices.

Keeping in view the intricacy of ICDAS, restraint nature of PUFA and no potential ways to compare their outcomes with DMF, suggests the need for the introduction of a superior doorstep for the diagnosis of initial reversible stages of caries development. This goal was accomplished in 2011, when the potencies of ICDAS, PUFA and the DMF index were amalgamated by the faction of people from the Radboud University Nijmegen

<sup>1</sup>PG Student, <sup>2</sup>Professor and Head, Department of Pedodontics and Preventive Dentistry, Krishnadevaraya College of Dental Sciences, Bengaluru, India

**Corresponding author:** Mayuri Jaywant Borse, Room No 321, sir MVIT Ladies Hostel, Krishnadevaraya College of Dental Sciences, Hunsmaranhalli, New International Airport Road, via Yelahanka, Bengaluru 562157, India

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Medical Centre, The Netherlands (Jo E. Frencken, Rodrigo G. de Amorim) and from the University of Brasília, Brazil (Jorge Faber and Soraya C. Leal). This innovation has been given the title "Caries Assessment Spectrum and Treatment"

(CAST) as illustrated in table-1. This index is proposed to be used worldwide.<sup>7</sup>

CAST index reports the progressive nature of dental caries which will facilitate the health-care providers to present the real picture of preventable carious lesions, which up till now was just accounted as cavities in epidemiological studies.<sup>9</sup>

Hence the objective of the study was to evaluate caries in primary and permanent molars of 7-8 years old children from Bangalore North by the CAST index and to find whether there was any correlation between caries stages in such teeth.

## MATERIAL AND METHODS

The presented data is a part of a cross-sectional survey conducted in the North Bangalore. Parents or caregivers were asked to sign a written statement of consent for child's participation in the study. In total, 100 children aged between 7 and 8 years were examined during the study. Only those children who had all four permanent molars fully erupted were selected for a further analysis. We also excluded subjects with any of the premolars erupted because in those cases we were not able to determine whether a primary molar was exfoliated or extracted due to caries. The minimum size of the sample population was calculated with the help of sample size calculator software and size was determined to be 100 subjects.

### Dental examination

The dental examination was performed by one examiner. The teeth were evaluated according to the CAST recommendations mentioned in Table-1. The index has a hierarchical structure and covers the full spectrum of caries stages, from a sound surface, pit and fissure sealants, dental fillings, caries lesions in enamel and dentine, a pulpal and periapical inflammation, through to a tooth loss due to caries. The prevalence of particular conditions from tooth reversible premorbidity (Enamel lesions) through to tooth's mortality (Extraction) was calculated pursuant to the scheme suggested by Frencken et al.<sup>7</sup> Prior to the survey, a training session consisting of the theoretical and practical parts was conducted. The theoretical part included the study of the literature and materials provided by the authors of the CAST

index; then the extracted primary and permanent molars were evaluated with regard to the presence of CAST codes.<sup>10</sup>

During the survey, the children were examined in school rooms where an artificial light was used to illuminate the oral cavity. The status of each tooth surface was checked using a plane dental mirror and a periodontal probe ending with a 0.5 mm ball. The probe was also used for the removal of dental plaque or debris present despite prior tooth brushing. A dental examination was carried out for all teeth present in the child's mouth. The status of each tooth's surface was recorded separately on a form developed for this study (Table-2). If two conditions were present on the same surface, e.g. a filling in one pit and an enamel lesion in another, or an enamel lesion in one pit and a cavity in another, the higher score was recorded. If an abscess or a fistula was present, all surfaces with an open cavity were scored with code 7. The highest code for each tooth was selected for a further analysis. About 5% of the evaluated population was re-examined at the end of each day in order to determine the intra-examiner reliability.

## STATISTICAL ANALYSIS

The prevalence of each caries stage was evaluated with regard to all deciduous and permanent teeth, and separately to the first and second primary, and first permanent, molars. The Spearman's rank correlation coefficient was used to explore the correlation of the distribution of CAST codes between first and second primary molars, second primary and first permanent molars, the counterpart molar teeth from the right and left side of the dental arch and the molars located in the opposite jaws. The level of statistical significance was established at  $\alpha < 0.1$ . The intra-examiner reliability was determined by the unweighted kappa coefficient. The parameter is compared using Kruskal-Wallis non parametric test.

## RESULTS

With regard to deciduous teeth, 70% subjects showed a dentin cavity (code 5) as the most serious caries stage. In 1<sup>st</sup> and 2<sup>nd</sup> primary molars, caries was most often recorded at the stage of cavitated dentin lesion. Serious morbidity was found to be more prevalent in 1<sup>st</sup> and then in 2<sup>nd</sup> primary molar. Pulp involvement (Code 6) was more prevalent in 1<sup>st</sup> primary molar.

For permanent teeth, enamel lesions were most prevalent

Cast codes Characteristics	Code	Description	Concept of health
Sound	0	No visible evidence of a distinct carious lesion.	Healthy
Sealed	1	Pit and / or fissures are at least partially sealed with a sealant material	
Restored	2	A cavity is restored with a (in)direct restorative material	
Enamel	3	Distinct visual change in enamel only. A clear caries discolouration is visible with or without localised enamel breakdown	Reversible premorbidity
Dentin	4	Internal caries-related discolouration in dentin. The discoloured dentin is visible through enamel which may or may not exhibit a visible localised breakdown of enamel	Morbidity
	5	Distinct cavitation into dentin. The pulp chamber is intact.	
Pulp	6	Involvement of pulp chamber. Distinct cavitation reaching the pulp chamber or only root fragments are present.	Serious morbidity
Abscess/fistula	7	A pus containing swelling or a pus releasing sinus tract related to a tooth with pulpal involvement.	
Lost	8	The tooth has been removed because of dental caries.	Mortality
Other	9	Does not correspond to any of the other categories.	

Table-1: Caries assessment spectrum and treatment (cast) index

Group	N	Min	Max	Mean	Std. Deviation	U	Sig	p value
Upper Right	99	0.000	10.000	2.687	2.884	4423.500	NS	0.217
Upper left	99	0.000	12.000	3.343	3.114			
Lower Right	99	0.000	11.000	2.152	2.647			
Lower Left	99	0.000	12.000	1.727	2.910			

NS: Significant Note: This parameter is compared using Kruskal-wallis non parametric test

Table-2: Permanent molar with Primary molar

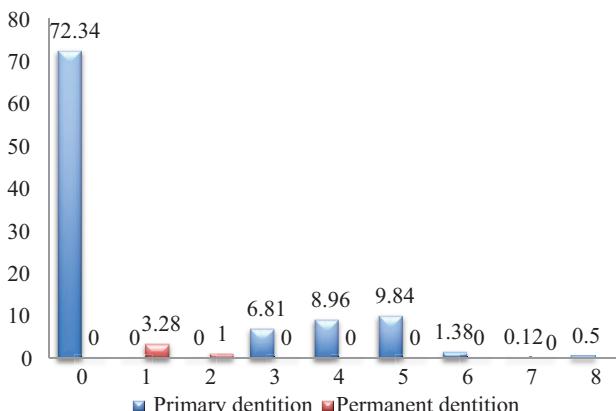


Figure-1: Enamel lesions

(code 3). No children could be put under categories 7 and 8 in permanent teeth (Figure-1). In permanent molars, most lesions were scored at the non cavitated level. The prevalence of sealants and restoration were very less. Results Strongly suggests lack of awareness for prevention of oral diseases is actually leading to the deteriorating oral health status. The strong correlation was found in teeth present in maxilla and mandible. The 'r' value was 0.217 and 0.109 in maxilla and mandible ( $p < 0.1$ ), respectively (Table-3). For neighbouring primary and permanent molars 'r' values were lower than 0.1, which meant a weak correlation.

## DISCUSSION

This study has been undertaken to evaluate the complete spectrum of dental caries experience using a new caries detecting tool CAST index. This index has the integral capacity to record the whole progressive spectrum of dental caries. Gives a modern approach to filled teeth due to their inclusion in the category of sound teeth. It is useful for prevention and risk assessment of caries. Promising index for epidemiological research studies.

This index was developed because of the need to find a reliable, pragmatic cohesive and easy to read reporting system which is based on the strengths of PUFA and ICDAS-II indices and provide a link to the widely used DMF index (M and F component). It covers the total dental caries spectrum – from no carious lesion, through caries protection (sealant) and caries cure (restoration) to carious lesions in enamel and dentine, and the advanced stages of caries lesion progression in pulpal and tooth surrounding tissue.<sup>6</sup> It does not record active and inactive carious lesions. The CAST index has not been validated, nor has its reliability been tested. It is also not suggested for use in clinical trials. Other limitation can be that it does not provide data on treatment or preventive measures required for each code. CAST index can be used to determine the level of dental caries, whether in enamel or in dentine. Enamel caries lesions in the CAST instrument are represented by one category only, in

ICDAS system, three different stages are represented as enamel lesions. Reporting of the caries status according to CAST allows for the presentation of a pre morbidity stage, which will be helpful in preventive care. CAST index is helpful in scoring Dentin lesions which can be treated at initial stages.<sup>11</sup>

We observed that the pulpal involvement, the category involving a cavity reaching the pulp or the presence of root fragments, was found to be the most serious stage in 10% (primary teeth) and 0.3% (permanent teeth) of the subjects.

The neglects in dental treatment with regard to the deciduous dentition have been observed worldwide. It was previously proven that the dmft level positively correlated with the number of teeth scored with the pufa (pulpal involvement-ulceration-fistula-abscess) index assessing the consequences of untreated dental caries.<sup>12,13</sup>

We decided to primarily concentrate on the correlations between the status of molars because of the considerable dynamics of front teeth exchange in children at the age of 7–8 years. we excluded incisors and canines from the analysis which helped us to keep the homogeneity of the study population. We observed that the percentage of teeth with enamel lesions was at a similar level for second primary and first permanent molars, but with regard to first primary molars the prevalence of code 3 was lower. The tendency that cavitated lesions were more prevalent in primary than in permanent molars was very clear. The presented results are in accordance with the study of Honcala et al.<sup>14</sup> On Estonian children aged 7 and 8 years who assessed molar teeth by the ICDAS criteria. The enamel lesions visible on wet teeth (ICDAS code 2), located on occlusal surfaces of first permanent molars (up to 17% of the teeth) were most prevalent in their study. The highest percentage of teeth with dentine lesions in Estonian children was observed for lower second primary molars. At the age of 7-8-years the factors causing dental caries act too short to induce the development of deep cavities in permanent teeth. Primary teeth are also more prone to a faster lesion progression from enamel to dentine and then to the development of pulpitis due to a lower thickness and a relatively larger pulp chamber in comparison to permanent teeth. In the present study, the percentage of molars with a serious morbidity (involvement of pulp and tooth surrounding tissues) was especially high for second primary molars, and these teeth also showed the highest tooth mortality (CAST code 5 and 6). This observation is in contrast to many previous studies where first primary molars were reported to be more affected than second ones. Occlusal surfaces of permanent molars and buccal pits of lower molars are most prone to the development of caries lesions. sealants are strongly recommended in the high risk populations.<sup>15</sup>

## CONCLUSION

CAST has introduced a new paradigm by reassessing the pathogenesis of dental caries. Paradigm has shift from curative

to preventive dentistry. On the basis of these results CAST index may be proposed to have the potential for scoring the whole spectrum of dental caries.

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# Impact of Obesity on Male Fertility in an Urban Nigerian Town

Obilahi Abhulimen TJ<sup>1</sup>, Ibrahim Isa A<sup>1</sup>, N. Ugwueke Thaddeus<sup>2</sup>

## ABSTRACT

**Introduction:** Obesity is gradually becoming an epidemic disease that is rapidly spreading in both developed and developing countries. Recently it has been linked with fertility problems in men. The aim of this study is to evaluate the effect of male obesity on semen quality.

**Material and Methods:** This was a prospective Cross-sectional multicenter study carried out over a period of six months (February to July 2011). Seminal fluid of 42 obese and 42 non obese male partners of infertile couples were analyzed.

**Results:** There was a statistically significant association between obesity, class of obesity with sperm count and motility ( $p = 0.0001, 0.0141, 0.0055, 0.0099$ ) (All  $p > 0.005$ ).

**Conclusion:** This study found obesity to be associated with poor semen quality. Hence tremendous efforts and health education is needed to curb the growing disease, obesity.

**Keywords:** Body mass index, male obesity, infertility, sperm quality.

## INTRODUCTION

Available evidence suggests that male infertility is an important but neglected reproductive health issue in Nigeria.<sup>1</sup> Published studies indicate that the male factor is present in between 20% and 70% of the causes of infertility in different parts of the country.<sup>2,3</sup>

Studies from several populations around the world indicate that smoking<sup>4</sup>, type of occupation<sup>5</sup>, alcohol and coffee intake<sup>5</sup> and nutritional factors<sup>6</sup> affect male fertility. Several sexually transmitted bacteria such as *Neisseria gonorrhoeae* and *Chlamydia trachomatis* have been linked with reduced fertility because of reduced sperm function.<sup>7</sup> Important local factors include infection such as tuberculosis<sup>8</sup> which can directly or indirectly damage the male reproductive system.

Abnormalities in semen production and quality have however been the main problem in majority of cases.<sup>9</sup> This emphasizes the importance of seminal fluid analysis as an indispensable laboratory diagnostic procedure.<sup>7,4</sup>

According to a commonly used definition, obesity is said to be present when more than 20% of the body weight is due to fat in men.<sup>9</sup> Normal value of fat is 12-18% for men.<sup>9</sup> Normal height and weight tables are also used extensively but an index that correlates better to body fat is the Quetelet index or body mass index {which is the body weight (in kilogram) divided by the square of the height (in metre)}<sup>9,10</sup>. The normal value for this index is 20-25kg/m<sup>2</sup>. Values greater than 30kg/m<sup>2</sup> denote obesity.<sup>9,10</sup> Obese class I is BMI of 30-34.9kg/m<sup>2</sup>, obese class II is BMI of 35-39.9kg/m<sup>2</sup> and obese class III is BMI of 40kg/m<sup>2</sup>.<sup>10</sup> In both sexes, obesity, particularly the abdominal obesity (truncal obesity) phenotype, may impair fertility.<sup>11</sup> This adverse effect appears to be mainly related to disorders of sex hormone secretion and/or metabolism, leading in turn to a condition of relative

hyperandrogenism in obese women and of hypotestosteronemia (and in some cases, a true hypogonadotropic hypogonadism) in obese men.<sup>11</sup> These hormonal alterations may also play an important role in the pathophysiology of different obesity phenotypes and associated metabolic and cardiovascular comorbidities.<sup>11</sup>

Obese men were found to exhibit reduced androgen and sex hormone binding globulin (SHBG) levels accompanied by elevated estrogen levels.<sup>12,13</sup> Reduced inhibin B levels correlate with the degree of obesity and are not accompanied by compensatory increase in FSH. The complexly altered reproductive hormone profile suggests that endocrine dysregulation in obese men may explain the increased risk of altered semen parameters and infertility. In other words, excess weight may be linked with altered testosterone, estradiol levels, poor semen quality and infertility.<sup>13</sup>

In view of the facts that the causes of male infertility are diverse, treatment of male infertility can be difficult and more importantly, the effect of obesity on semen quality has not been extensively studied in our sub-region before, it is imperative to undergo this study to generate local data, contribute to the global discourse on obesity and male infertility and invariably improve male reproductive health care in this centre and society, at large.

## MATERIAL AND METHOD

### Setting

The study was a multi-Centre study conducted at the University of Ilorin Teaching Hospital, Ilorin, Kwara State, Nigeria and Centre's that offer management for infertility in Ilorin which are Anchor Medical Centre, Royal Medical Centre, Surulere Medical Centre and Mid-land Fertility Centre.

### Study population

The study population were males with body mass index (BMI) greater or equal to 30kg/m<sup>2</sup> i.e obese male partners in infertile couples. The controls were non-obese male partners in infertile couples with BMI of 20-25kg/m<sup>2</sup>.

### Study design

The study was a prospective comparative analytical study. It involved recruitment of males attending these health Centre's

<sup>1</sup>Consultant, Department of Obstetrics and Gynaecology, Faculty of Clinical Sciences, Niger Delta University, Wilberforce Island, Bayelsa state,

<sup>2</sup>Consultant, Fertility Unit, lilly Hospital, Warri, Delta State Nigeria.

**Corresponding author:** Dr Ibrahim Isa. A, Consultant, Department of Obstetrics and Gynaecology, Faculty of Clinical Sciences, Niger Delta University, Wilberforce Island, Bayelsa state, Nigeria.

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for infertility who satisfied the inclusion criteria.

#### Inclusion criteria

The participants were healthy male partners of infertile couples with no known medical illness such as diabetes mellitus, epilepsy and hypertension.

#### Sample size determination

Sample size was determined by the Fisher's formula<sup>14</sup>

$$n = z^2 pq / d^2$$

Where n = sample size for the study

$z$  = standard normal deviation (a constant) which is 1.96 at 95% confidence interval

p = the prevalence of obesity amongst males in Nigeria which is 2%

$$q = 1-p$$

d = observed difference of 5% or more taken as being significant

$$n = 1.96^2 \times 0.02 \times 0.98$$

$$(0.05)^2$$

$$n = 30$$

Provision was made for attrition by adding 40% of sample size i.e 12. Thus, making a sample size of 42 for the study and control groups respectively.

#### Sampling technique

This was by multi-stage sampling technique. The first stage was proportional allocation to get the number of subjects from each of the five study centres. The second stage was systemic sampling technique to select subjects that were used from each of the study centres. Sampling interval was one in every two. Over the period of study (February to July 2011), with a systemic random sampling technique of one in every two, 26 obese male partners of infertile couples were recruited from UIITH, 13 from Mid-Land Fertility Centre and 1 from each of the other three centres.

#### Data collection

The selected patients were informed and counseled about the study. Only those who consented to participate in the fully explained study were included in the study.

Seven research assistants who were selected doctors, one from each of the three units in the department of Obstetrics and Gynaecology in UIITH as well as one for each of the other four centres, attending to the couples regularly in the Gynaecology Clinics, were trained and educated prior to administration of questionnaire with the study objectives and protocol in mind. Their duty was primarily to help recruit patients based on the study criteria for the researcher. These patients were later seen by the researcher who also carried out the clinical examination on these patients. Two laboratory scientists (research assistants) from the department of microbiology in UIITH, were involved in carrying out the analysis of the semen samples.

#### Collection and analysis of semen

The standard WHO guideline for semen analysis<sup>15</sup> was used. The participants abstained from sexual intercourse for three days before semen collection. The masturbation method was adopted for semen collection into the sterile wide mouthed container provided for the purpose. Semen sample was produced in a private room within the hospital and brought to the laboratory within thirty minutes of collection. The semen samples were examined within one hour of collection or as soon

as liquefaction occurred.

The information obtained was coded and transferred onto a proforma already designed for the study. Approval for this study was obtained from the ethical committee of the University of Ilorin Teaching Hospital.

Permission to use other study sites was also obtained from constituted authorities. Patients' data were treated confidentially. The study was explained to the subjects and their written informed consent was obtained before inclusion into the study.

#### STATISTICAL ANALYSIS

Data analysis was carried out using Epi-info version 6.0 software package. Descriptive analyses was used, mean±standard deviation (minimum-maximum) and percentage (number), whereas intergroup comparisons were done using chi-square test. The p<0.05 was considered to be significant

#### RESULTS

During the six months study period (1st of February to 31st of July 2011) 84 male partners in infertile couples were involved in the study; 42 of whom were obese (study group) while the remainder (control group) had normal BMI ( $20\text{--}25\text{kg/m}^2$ ).

Table-1 shows that the mean age of the obese males was  $38.7 \pm 6.3$  years. Age group 30-34 years accounted for 26.2% while age groups 35-39years and 40-44years accounted for 23.8% respectively. The age group of 35-39 years accounted for the highest proportion in the control group (28.6%). As shown, no statistical significant difference was observed in the age. All the subjects that participated in the study had at least primary education. Most of the subjects, however, had tertiary education (64.3% of the obese and 71.4% of the control). As shown, no statistical significant difference was observed in the educational status distribution of study and control groups. The average BMI of the study group was  $32.9 \pm 2.8\text{kg/m}^2$  while for the control while for the control was  $22.4 \pm 1.4\text{kg/m}^2$ . As shown,

Age group(y)	Obese (N=42)	Non-Obese (N=42)	p-value
25-29	2 (4.8)	3 (7.1)	*0.275
30-34	11 (26.2)	10 (23.8)	** 0.60
35-39	10 (23.8)	12 (28.6)	
40-44	10 (23.8)	10 (23.8)	
45-49	8 (19.0)	5 (11.9)	
50-54	1 (2.4)	2 (4.8)	
Mean	38.7±6.3	37.9±5.7	
Level of Education			
Primary	3 (7.1)	3 (7.1)	0.746
Secondary	12 (28.6)	9 (21.4)	** 0.59
Tertiary	27 (64.3)	30 (71.4)	
			** 21.01

Table-1: Distribution of Sample size according to Age and Educational level

Parameters	Obese	Non obese	P value
Sperm Count (M/ml)	$17.1 \pm 12.3$	$43.4 \pm 45.1$	0.000
Sperm Motility (%)	$37.4 \pm 21.8$	$48.6 \pm 20.8$	0.014

\*Values are reported as mean± SD

Table-2: Semen quality of study participants

Group	Frequency (%)	BMI (Kg/m <sup>2</sup> )	Sperm Count (M/ml)	Sperm Motility (%)
Non obese	42 (100)	22.4 ± 1.4	43.4 ± 45.1	48.6 ± 20.8
Class I Obese	33 (78.6)	31.7 ± 1.4	18.8 ± 11.7	38.8 ± 18.1
Class II Obese	7 (16.6)	36.5 ± 0.9	11.5 ± 14.2	33.3 ± 21.1
Class III Obese	2 (2.8)	41.6 ± 2.1	7.0 ± 9.9	10.0 ± 14.1
P value		0.000	0.006	0.009

\*Values are reported as mean ± SD; \*\*Obese class I= BMI 30-34.9kg/m<sup>2</sup>, obese class II = BMI 35-39.9kg/m<sup>2</sup> and obese class III BMI 40kg/m<sup>2</sup> or more.<sup>2</sup>

**Table-3:** Semen quality classified according to obesity class.

Semen parameter	Study Frequency (%) (n-42)	Control Frequency(%) (n-42)	Total Study Frequency(%) (n-84)
Semen Count (M/ml)			
0	3(7.1)	2 (4.8)	5 (6.0)
1-5	7 (16.7)	5 (11.9)	12 (14.3)
6-19	13 (31.0)	6 (14.3)	19(22.5)
≥20	19 (45.2)	29 (69.0)	48 (57.1)
Total	42(100.0)	42(100.0)	84(100.0)
Mean	17.1(±12.3)	43.4 (±45.1)	30.2(±35.4)
Semen Motility (% active)			
0-24	13(31.0)	5(11.9)	18 (21.4)
25-49	12(28.6)	10(23.8)	22(26.2)
≥50	17(40.4)	27(64.3)	44(52.4)
Total	42(100.0)	42(100.0)	84(100.0)
Mean	37.4(±21.8)	48.6(±20.8)	42.9(±21.9)

**Table-4:** Showing semen parameters in the study population

the difference is significant statistically.

Table-2 showed semen quality of study and control groups. The mean sperm count for the obese was 17.1 million spermatozoa per ml (oligozoospermia) as against 43.4 million spermatozoa per ml for the non obese and this was statistically significant. The mean sperm motility was 37.4% vs 48.6% for the obese against the non obese and was also statistically significant as 22.4 ± 1.4kg/m<sup>2</sup>. As shown, the difference is significant statistically. Table-3 showed a statistically significant association between the class of obesity and sperm count (p value-0.0055) as well as with sperm motility (p value-0.0099). The sperm motility and count decreased as obesity increased i.e inverse relationship between BMI and semen parameters (motility and count).

Table-4 shows that the mean sperm count for the obese subjects was 17.1 ± 12.3 million spermatozoa per ml and 43.4 ± 45.1 million spermatozoa per ml for the control. Azoospermia was commoner amongst the obese male partners in infertile couples (7.1% vs 4.8%). The same was noted for oligozoospermia (47.7% vs 26.2%). The mean sperm motility was 37.4 ± 21.8% for the obese; 31% of whom had asthenozoospermia. The control had sperm motility of 48.6 ± 20.8% with 11.9% of subjects with asthenozoospermia.

## DISCUSSION

This study was a multi-centered, prospective case-controlled study assessing the effect of male obesity on semen quality of male partners of infertile couples in Ilorin.

The interaction between obesity and fertility has received increased attention owing to the rapid increase in the prevalence of obesity in the developed world<sup>11</sup> and in near future, might become a public health issue in Nigeria and sub-Saharan Africa because of better economic opportunities in our own society.

In this study, obesity was associated with reduced sperm count ( $17.1 \pm 12.3$ M/ml vs  $43.4 \pm 45.1$ M/ml; p-0.0001) and reduced sperm motility (37.4 ± 21.8% vs 48.6 ± 20.8%; p-0.0141). A similar but less marked effect was noticed on sperm count but not on sperm motility, in a similar study<sup>16</sup> which revealed a reduction in sperm count of 23.9% (95% confidence interval 4.7 – 43.2%) as against a 60.6% reduction in sperm count noticed in this study. The marked reduction in sperm count in this study may not be unrelated to the small population size of this study and the ethnicity/race of the subjects studied. The findings of reduced sperm motility with obesity in this study was also similar to that of some studies<sup>16-18</sup> which showed a negative association between BMI and sperm motility. Other studies however, noted no significant correlation between BMI and sperm count<sup>17,19,20</sup> as well as sperm motility.<sup>19,20</sup> These varying results may be attributed to the population sizes of these studies. Amongst the obese group, majority (78.6%) had class I in obesity. There was an inverse relationship between increasing obesity class and semen parameters {sperm count p-0.0055 and sperm motility p-0.0099}. This was similar to the findings in a study<sup>16</sup> which noted a p-0.0055 for the association between increasing BMI and percentage of motile sperm. Also, participants with class III obesity had reduced average sperm motility of 10%. This emphasizes the role of life style modification i.e, dietary control and weight reduction, as important management protocol in male infertileThe prevalence of oligozoospermia in the obese men compared with normal BMI men was also high{47.7% vs 26.2%}. This was similar but more than that reported in a similar study<sup>16</sup> which found a prevalence of 24.4% vs 21.7% for oligozoospermia in over-weight and obese men compared with normal-weight men. The reason for the increase in this study may also be related to the small population size of this study. The prevalence of 7.1% reported for azoospermia amongst the obese male partners of infertile couples in this study was however, less than 23.4% reported in a similar study carried out in this environment<sup>19</sup> about ten years ago. The marked decrease in the prevalence of azoospermia could be attributed to better health seeking behaviour of these men in addition to the increased number of accessible health facilities in Ilorin.

Overall, this result is an important addition to the emerging evidence of the relationship between obesity and male infertility.

## CONCLUSION

This study has demonstrated an inverse but significant relationship between male obesity and semen parameters (sperm count and motility) amongst male partners of infertile couples in Ilorin. This suggests that male obesity has an adverse effect on the quality of semen amongst male partners of infertile couples.

Concerted effort should be made to prevent excessive weight gain as well as reduce weight amongst the obese as this is a recognized management option for altered semen parameters seen in the obese.

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# Retrospective Study of Clinico- Immunological Progress of Human Immunodeficiencyvirus/Acquired Immune Deficiency Syndrome Patients on Antiretroviral Therapy at Central India

Ayush Dubey<sup>1</sup>, Jeetandra Sharma<sup>2</sup>, Lokendra Dave<sup>3</sup>, Hemant Verma<sup>4</sup>, Bhavishya Rathore<sup>5</sup>

## ABSTRACT

**Introduction:** Human immunodeficiency virus infection (HIV) remains a worldwide health crisis. Nearly 40 million people infected, 95% of them lives in developing countries like India, Africa etc. Aim of study is to assess immunological and clinical progress of human immunodeficiency virus/acquired immune deficiency syndrome (HIV/ AIDS) patients on antiretroviral therapy (ART).

**Material and Methods:** This was the retrospective study which was carried out in ART plus center at Gandhi medical college and Hamidia hospital Bhopal from March 2008 to March 2016. This enabled patient's follow-up for WHO clinical stage, weight and functional status of all these patients for minimum of one year.

**Results:** Total of 5295 HIV/AIDS patients were registered while 1903 patients were shown to take ART and were regularly follow up visit to the ART Center. Follow up status after 1 year on ART revealed that, 89.65% patients were still active and 71.4% had "good" adherence level. Median weight of the patients increased to 58 kg (improved by 12%). Change in CD4+ cell count was 104.5 (45.24%) and 199.75 cells/mm<sup>3</sup> (86.47%) after 6 and 12 months on ART respectively. Functional status as working improved by 20.71%.

**Conclusion** Immunological and clinical improvements as reported by increase in weight, CD4+ cell count and functional status of patients after initiation of ART.

**Keywords:** human immunodeficiency virus, acquired immune deficiency syndrome, antiretroviral therapy, highly active antiretroviral therapy.

Combination ART has reduced morbidity and mortality, and its access has increased in recent years, achieving a goal to have 15 million people on treatment by 2015.<sup>6</sup> Globally, only 40% of people with HIV are receiving treatment, out of which 41% are adults and 32% are children.<sup>6</sup> Approximately 76% of all people in sub-Saharan Africa receiving ART therapy shows very suppressed viral replication and so less chance of transmitting the infection.<sup>6</sup> The percentage of pregnant women receiving ART for the prevention of mother-to-child transmission of HIV increased to 73% in 2014, up from 36% in 2009. Highly active antiretroviral therapy (HAART) is currently the most effective way to treat acquired immune deficiency syndrome (AIDS). HAART can dramatically suppress the replication of human immunodeficiency virus (HIV), rebuild the immune function of infected patients, and reduce the incidence of opportunistic infections.<sup>7,8</sup> HAART has significant effect on HIV and reduces the incidence of AIDS and death.<sup>9</sup> Currently 15.8 million people are receiving antiretroviral therapy (June 2015) The treatment efficacy of HAART is mainly evaluated by the decrease in viral load and improvement in the immune system.<sup>10</sup> HAART is now widely available in most developed countries; As treatment with HAART, once started, is likely to be life long, it is important that models for prognosis are updated as longer follow-up time becomes available. In this paper we evaluated the effect of ART that estimate immunological and clinical progression up to minimum of 1 years after starting HAART, first according to CD4 counts measured at baseline and then on, second incorporating the successive clinical response to treatment.

This study was done with the objective to evaluate the improvement in immunological and clinical scenario of Human immunodeficiency virus/acquired immune deficiency syndrome (HIV/ AIDS) patients on antiretroviral therapy (ART) at ART plus center in Gandhi Medical College and Hamidia Hospital Bhopal.

<sup>1</sup>Department of Neurology, Sri Aurobindo Institute of Medical Sciences, Indore, <sup>2</sup>Postgraduate, Department of Medicine, <sup>3</sup>Professor and Head, Department of TB and Chest, <sup>4</sup>Senior Medical Officer, ART Plus Center, <sup>5</sup>Postgraduate, Department of Community Medicine, Gandhi Medical College Bhopal (MP) India

**Corresponding author:** DR. Jeetandra Sharma, Postgraduate, 3<sup>rd</sup> year student, Department of Medicine, Gandhi Medical College Bhopal (MP), India

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## MATERIAL AND METHODS

After taking permission from institutional ethical board a retrospective medical records review design was conducted to determine the immunological and clinical progress of HIV/AIDS patients on ART. The study population included all patients who came to the Hamidia hospital Bhopal from March 2008 to March 2016. Data was collected from the medical records of HIV/AIDS patients who were registered in ART plus center in Gandhi Medical College Bhopal, Madhya Pradesh, India. This enabled retrospective follow-up of records of all these patients for minimum of one year. Records of patients on their WHO clinical stage, weight and functional status were reviewed by the investigators at 12 month and CD4 Count at 6 month and 12 month successively. In addition, data was collected regarding the age and sex.

Total 5295 were registered during this period out of which 3314 were eligible for ART treatment (CD4 count <350 cell/mm<sup>3</sup>). Out of 3314 patients 1903 patients have attend regular follow up visit to examine their clinical and immunological status while remaining patients had opted out, transfer out, died, lost of follow up and 160 patient were registered in 2016 march so their follow up remains to begin . The medical records of HIV/AIDS patients who were under follow-up in the institution for their progress after ART initiation served as sources of data The exclusion criteria for study were being on ART for less than one year, incomplete medical records of patients, who initiated ART in another institution and transferred in and those who started in the institution and were transferred out to another institution since complete records were not available and died within one year of registration. Data collected was kept confidential and used strictly to purpose the study.

S. no.	Clinical outcome	Before art n=1903(%)	After 1 year of art n=1903(%)
A.	Weight (In kg)		
1.	<40	182(9.2%)	109(5.72%)
2.	40-49	664(34.85%)	485(25.48%)
3.	50-59	780(41.0%)	929(48.83%)
4.	60+	277(14.55%)	380(19.97%)
B.	Functional status		
1.	Working	634(33.31%)	1028(54.02%)
2.	Abulatory	901(47.35%)	678(35.63%)
3.	Bedridden	368(19.33%)	197(10.35%)
C.	WHO Clinical stage of AIDS		
1.	Stage I	161(8.46%)	142(7.45%)
2.	Stage II	435(22.86%)	725(38.11%)
3.	Stage III	940(49.4%)	756(39.73%)
4.	Stage IV	367(19.28%)	280(14.71%)

**Table-1:** Clinical progress (weight, who clinical staging, functional status) at 12 months of art

## STATISTICAL ANALYSIS

Data was entered in MS excel and analyzed by Epi-info software version 7. Descriptive statistics like mean and percentages were used to interpret results.

## RESULT

### Patients' condition at initiation of ART

A total of 5295 medical records of HIV/AIDS patients who registered ART plus center from the start of the program in March 2008 till the end of March 2016 were used in study. The mean age was 33.40 years and standard deviation $\pm$  11.84 years, it ranged from 0.5 to 82 years, most of the patients belong to the age group between 30-39 year (36.31%) followed by 20-29 years (25.58%)and the number of males were 3441 (64.98%), females formed 1829 (34.54%), while transgender were 25 (0.47%). Out of 5295 patients 3314 patients had started ART in which 1903 patients on ART are those who continue to be present at their follow up visit for regular clinical and pathological check up (for weight, WHO clinical staging, functional status and CD4 count). At the start of ART the weight of most of the patients (75.89%) was between 40 - 49 kg. Of these, 41.00% were between 40 and 49 kg, whereas 34.89% being between 50 and 60 kg. The overall median weight of the patients was 50 kg (Table-1). Regarding functional status most of the patients, 47.35% were ambulatory and 33.31% were working, the remaining being bed ridden at the start of ART (Table-1). At the initiation of ART, around 49.4% were in WHO Clinical Stage III followed by Stage II (22.86%) and Stage IV (19.28%), stage I(8.46%) respectively (Table-1). The mean CD4+ cell counts of the patients at the time of initiation of ART were 231 cells/mm<sup>3</sup> (Table-2). Distribution of patients by regimen shows that maximum patients (more than 90%) were on TLE (tenofovir/ lamivudine/ efavirenze) and ZLN(zudovudine / lamivudine/ nevirapine) regimen at the initiation of ART.

### Patients' conditions after 6 and 12 months of ART initiation

The follow up status after 1 year on ART indicated that 89.65% of the patients were still active and 71.4% were recorded to have had "Good" adherence level and 25.4% had "Fair"adherence level out of those who remained active on treatment. The overall median weight of the patients increased to 58 kg (improved by 12%) after 1 year on ART (Table-1). The change in functional status after 1 year on ART showed that 54.02% (improved by 20.71%) were on working status. The percentage of working patients has changed from 33.31% to 54.02% and 11.72% patients were improved from ambulatory to working status. which shows a clear improvement in the quality of life of the patients respectively. In case of bedridden patients 8.98% had improved to working or ambulatory status after the 1 year of antiretroviral therapy (Table-1). At the initiation of ART, the clinical stage of the patients shows, that around 72.26% of patients were in WHO Clinical Stage III and II which became

S No.	CD4 Count	At initial stage (Cells/mm <sup>3</sup> )	1 <sup>ST</sup> Follow up at 6 Month (Cells/mm <sup>3</sup> )	2 <sup>ND</sup> follow up at 12 months (Cells/mm <sup>3</sup> )
1.	MEAN*	231	335.5	430.75
2.	Improvement in CD4	-	104.5 (45.24%)	199.75 (86.47%)

\*Mean CD4 count from 2008 to 2015

**Table-2:** Immunological progress (mean cd4 count) at 6 months and 12 months of art

77.84% after one year of ART means improved in the number of patients by 5.58%. While 4.57% Stage IV patients were shifted to Stage III/II (Table-1). After 6 months of ART, the mean CD4+ cell count increased to 335.5 cells/mm<sup>3</sup> and after 1 year of therapy, this count increased to 430.75 cells/mm<sup>3</sup>. The overall change in the CD4+ cell count was 104.5 and 199.75 cells/mm<sup>3</sup> after 6 and 12 months on ART respectively (Table-2).

## DISCUSSION

Gandhi medical college and Hamidia hospital Bhopal ART plus center is active in central India hence it reflects the HIV/AIDS patients in central India.

In this study, 1903 HIV/AIDS patients who were on ART in the health center were involved. 80.67% patients were active at the time of initiation of ART and 89.65% patients were still active after one year of ART follow up, improved by 8.98%. This number was greater as compared to a study occurred in west Kenya which involved 2059 HIV positive on pregnant, where after 10 months of follow upon HAART 70% of the patients remained active on treatment.<sup>11</sup> this may be attributed to the improvements in weight, functional status and CD4+ cell count after initiation of ART which helped in improving the overall health conditions of patients thereby decreasing the chance of occurrence of death. The median weight increased by 8 kg for patients who were on ART after 12 months which is higher than the study done in USA, which showed increase in about 0.8 kg after a follow up duration of 5 months.<sup>12</sup> This shows good response of ART concerning weight. The median CD4+ cell count among the patients increased by 104.5 cells/mm<sup>3</sup> in the first 6 months on ART. This was lower compared to a prospective study done in South India where the CD4+ cell change after 6 months of HAART was increased by mean of 140 cells/mm<sup>3</sup>.<sup>13</sup> The CD4+ cell count changed during the first 6 months of HAART was also lower than that of the change described in a retrospective study done in Yirgalem Hospital southern Ethiopia where the CD4+ cell count change after 6 months of ART was about 175 cells/mm<sup>3</sup>.<sup>14</sup> After 1 year of ART the functional status of the patients improves significantly which shows that improvement in the quality of life of the patients.

## Limitations

In this study, information regarding opportunistic infections and medications adverse reactions was not available in a complete manner among the medical records of the patients, which hindered the analysis of ART outcomes in relation to these conditions.

## CONCLUSION

This study showed that more than three fourth of the patients who started the therapy were active after 1 year of ART. There were improvements both immunologically and clinical condition of patients as increase in the weight, CD4+ cell count and the improvement in the functional status of the patients after 1 year of ART initiation. Based on the objective of evaluating the immunological and clinical progress of HIV/AIDS patients, this study concluded that the patients involved in ART were shown to experience improved health status in general.

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# Evaluation of the Antibacterial and Antifungal Activity of Three Retrograde Filling Materials: An In Vitro Study

Meghna S. Chopra<sup>1</sup>, Meenal N. Gulve<sup>2</sup>

## ABSTRACT

**Introduction:** Retrograde filling materials are used with the purpose of obtaining root end sealing in the endodontic surgeries. In addition to improving the sealing of the existing root canal filling, these materials should possess antimicrobial properties to prevent the movement of bacteria and their products from the root canal system to the periapical tissues for the success of the endodontic surgeries. Study aimed to evaluate the antibacterial and antifungal properties of mineral trioxide aggregate (MTA) compared to bioceramic and resin modified glass ionomer cement (RMGIC).

**Material and methods:** Pellets of MTA, Bioceramic and RMGIC were prepared to test the influence of these cements on the growth of strains of *Enterococcus faecalis*, *Staphylococcus aureus* and *Candida albicans* using the agar diffusion method. Wells were formed by removing agar and the test materials were manipulated and placed in the wells. The growth inhibition diameter around each material against the tested organism was measured after 24 hour incubation at 37°C. The data was analysed statistically using analysis of variance (ANOVA) and unpaired t-test to compare the differences among the three cements.

**Results:** Inhibition zones for Bioceramic against *E. faecalis* and *C. albicans* significantly larger ( $P<0.01$ ) when compared to MTA and RMGIC. However RMGIC showed significantly larger ( $P<0.01$ ) zone of inhibition against *S. aureus* but no zone of inhibition against *C. albicans*.

**Conclusion:** All materials showed antimicrobial activity against the tested strains except RMGIC against *C. albicans*. Bioceramic had a greater antimicrobial activity compared to MTA and RMGIC.

**Keywords:** Antibacterial activity, Bioceramic, Inhibition zone, Mineral Trioxide Aggregate.

## INTRODUCTION

Microorganisms are considered to be the primary etiological agents in the development and progression of pulpal and periapical diseases as well as in endodontic treatment failure.<sup>1</sup> When the healing is not achieved after non-surgical endodontic therapy, and when the retreatment is not possible or failed, surgical approach is required to conserve the tooth. This procedure involves exposure of the involved apex, root resection, preparation of a class I cavity at the resected root end and insertion of a root end filling material in the prepared cavity. The root end filling material should provide an apical seal at the end of the resected root, preventing the movement of the bacteria and the bacterial products from the root canal system to the periapical tissues.<sup>2</sup>

An ideal root end filling material should produce a complete apical seal, be non toxic, biocompatible, non-resorbable, dimensionally stable, easy to manipulate, radio-opaque and well tolerated by the periapical tissues. In addition to these, the

root end filling materials should have some antibacterial and antifungal activity to prevent the bacterial and fungal growth.<sup>3</sup> Glass ionomer cement(GIC) is one of the well known root end filling material which has unique properties such as adhesion to moist tooth structure, low shrinkage and biological acceptance but low antimicrobial activity.<sup>4</sup> In order to overcome the problems of conventional GIC's such as moisture sensitivity, low initial mechanical properties and inferior translucency, a hybrid material combining the technologies of glass ionomer cement and resin composites, Resin modified glass ionomer cement(RMGIC) was developed. RMGIC overcomes the disadvantages of GIC and at the same time maintain their clinical advantages of fluoride release and adhesiveness.<sup>5</sup> Mineral trioxide aggregate (Angelus,Londrina,PR,Brazil) is marketed as gray and white preparations both of which are composed of 75% Portland cement clinker, 20% Bismuth oxide and 5% gypsum by weight. MTA consists of fine hydrophilic particles that, in the presence of water or moisture forms colloidal gel that solidifies to form hard cement within approximately 4 hours. The white colour preparation lacks tetra calcium aluminoferrite as a result of which, it is more aesthetic.<sup>6</sup> Bioceramic (Septodont) is a calcium based cement recently introduced new endodontic material. The powder mainly consists of tricalcium and dicalcium silicate as well as calcium carbonate. The liquid consists of calcium chloride in aqueous solution with a mixture of polycarboxylate which sets in 12 minutes.<sup>7</sup> Many root end filling materials like amalgam, resin reinforced zinc oxide eugenol cement (Super EBA), Intermediate restorative material (IRM) have been used in the past but due to low sealing ability and antimicrobial activity, there arose a need for the development of these newer retrograde filling materials.

The purpose of this study was to investigate and compare the antibacterial and antifungal effects of MTA, Bioceramic and RMGIC on *Enterococcus faecalis*, *Staphylococcus aureus* and *Candida albicans* microorganisms.

## MATERIAL AND METHODS

The study was performed in the Department of Microbiology at the Karmaveer Bhaurao Patil (KBP) College, Vashi, Navi Mumbai, India. The test materials- MTA (Angelus,

<sup>1</sup>PG Student, <sup>2</sup>Professor and Head, Department of Conservative Dentistry and Endodontics, MGV's KBH Dental College and Hospital, Nashik, Maharashtra, India

**Corresponding author:** Dr. Meghna S. Chopra, 705, Natasha Towers, 7 Bungalows, Andheri(west), Mumbai-400061, India.

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Londrina, PR Brazil), Biodentine (Septodont) and RMGIC (Vitremer, 3M ESPE, St.Paul, MN, USA) were manipulated strictly in accordance to the manufacturer's instructions. The antimicrobial activity of the endodontic cements was evaluated by the agar diffusion method against three strains: Enterococcus faecalis (ATCC 29212), Staphylococcus aureus (ATCC 25923) and Candida albicans (ATCC 10231). Bacteria were diluted to obtain a suspension of approximately  $5 \times 10^6$  colony forming units/ml in sterile Trypticase Soy Broth (TSB) obtained by spectrophotometer. 10 ml of Mueller Hinton agar was poured in Petri plates to form a base layer. When it solidified, a second layer or seed layer containing 10 ml of Mueller Hinton agar and 200  $\mu$ l of the microbial standardized suspensions was poured over it. After solidification of the second layer, three wells of 7 mm of diameter (one for each material) were obtained by removing a standardized portion of the agar in equidistant points with the aid of sterilized cork-borer and immediately filled with freshly manipulated test materials. After prediffusion of the test materials for 2 hours at room temperature, all the plates were incubated at 37°C and evaluated at 24 hours.

## STATISTICAL ANALYSIS

Microbial inhibition zones were measured with a 0.5mm precision ruler and results were expressed as mean and standard deviation. The data was analysed statistically by one way analysis of variance (ANOVA) at 95% confidence interval and 2 degrees of freedom and Unpaired t-test using Statistical Package for Social Sciences (SPSS) software version 21 (SPSS Inc, Chicago, IL, USA).

## RESULTS

The antimicrobial activities of MTA, Biodentine and RMGIC and the mean and the standard deviation values are shown are listed in Table-1. The inhibition zones shown by MTA, Biodentine and RMGIC are shown in figure-1, figure-2 and figure-3 respectively. Biodentine showed significantly (greater activity against all the three microorganisms when compared to MTA ( $P<0.01$ ). The difference was significant ( $P<0.01$ ) when compared to RMGIC against E.faecalis and C.albicans. RMGIC significantly ( $P<0.01$ ) inhibited S.aureus when compared to MTA and Biodentine, however it was incapable of inhibiting C.albicans.

## DISCUSSION

The strains evaluated in this study were E.faecalis, S.aureus and C.albicans, which are frequently isolated during routine endodontic treatment of an infected root or from teeth with periapical pathology. They have been found with higher frequency in cases in which treatment had been protracted, in flare-ups and in failing cases. These micro-organisms can enter the root canal system before or after treatment and may then cause secondary infections. E.faecalis was chosen as the test organism because it is associated with persistent apical

inflammation in clinical situations. It has been used extensively in endodontic research because it has been found in infected canal and has been associated with failed root canal treatment.<sup>8</sup> S.aureus is predominantly found in persistent or refractory periapical lesions in teeth subjected to periapical surgery.<sup>9</sup> Fungi such as C.albicans may gain access to the root canal from the oral cavity as a result of poor asepsis during endodontic procedures, or because of coronal leakage. C. albicans has the ability to form biofilms on different surfaces and may be involved in cases of persistent and secondary infection.<sup>10</sup> The agar diffusion method has been widely used method for evaluation of antimicrobial activity in vitro and reflects intrinsic antibacterial activity and diffusivity of the materials examined.

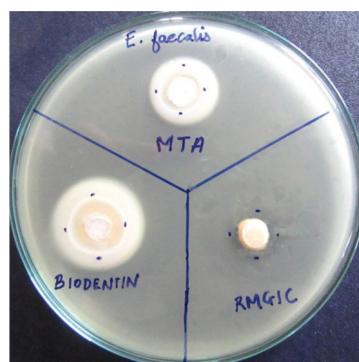


Figure-1: Inhibition zones against E.faecalis by the three test materials

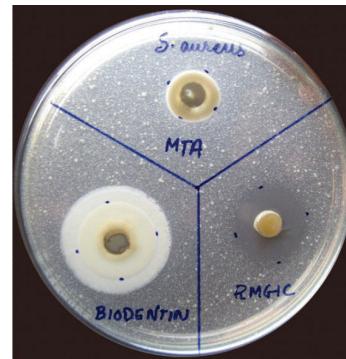


Figure-2: Inhibition zones against S.aureus by the three test materials



Figure-3: Inhibition zones against C.albicans by the three test materials

Test material	E.faecalis		S.aureus		C.albicans	
	Mean	S.D	Mean	S.D	Mean	SD
MTA	13.16	0.28	14.5	0.5	18.16	0.28
Biodentine	14.66	0.57	21.16	0.28	24.33	0.57
RMGIC	12.33	0.28	22.5	0.5	0	0

Table-1: Mean and standard deviation (S.D) of inhibition zones in Millimeters

It allows direct comparison of medicaments against the test microorganisms, indicating which medication has the potential to eliminate bacteria from the root canal system.<sup>11</sup>

In the present study, Biodentine showed higher inhibition halos against *E.faecalis* and *C.albicans* as compared to MTA and RMGIC. Biodentine is available in the form of powder and liquid which can be mixed in an amalgamator. The main component of powder is a tricalcium silicate, with the addition to the powder of Calcium carbonate ( $\text{CaCO}_3$ ) and Zirconium oxide ( $\text{ZrO}_2$ ). The liquid is a solution of Calcium chloride ( $\text{CaCl}_2$ ) with a water reducing agent. On setting it forms a gel structure which results in the ionic exchange. Compared to other calcium based cements, it presents a faster setting time of about 12 minutes and higher mechanical properties as the compressive strength is 241 MPa and flexural strength is calculated to 34 MPa. Thus it is mechanically stronger, less soluble, gives a tighter seal preventing microleakages. Antimicrobial efficacy of Biodentine can be assumed to be the result of hydration of tricalcium silicate resulting in formation of colloidal gel and release of calcium hydroxide, which provides the ability to inhibit micro-organisms.<sup>12</sup> Hence in this study Biodentine had a significantly higher antimicrobial activity as compared to MTA.

MTA contains calcium oxide, which when mixed with water, forms calcium hydroxide, inducing an increase of pH by dissociation of calcium and hydroxide ions. Antimicrobial action of MTA is attributed to its high initial pH of 10.2 which rises to 12.5 in 3 hours.<sup>13</sup> MTA showed antifungal activity against *C.albicans* which was in agreement to the study by Al-Nazhan and Al-Judai.<sup>14</sup>

RMGIC has formed the highest inhibition zone against *S.aureus* as compared to MTA and Biodentine whereas no inhibition zone was formed against *C.albicans*. The inclusion of Fluorite and/or cryolite as fluxes for firing purposes in the RMGIC may enhance the release of fluoride ions into the matrix during the setting reaction in the initial 24 hour period. Furthermore, the liquid component of RMGIC conventionally contains hydroxyethyl methacrylate, which in part may aid the antibacterial effect by providing a low initial pH. The initial mix of the cement is also of low pH (2.2-3.6) and rises to neutrality during the progress of the setting reaction. This early acidity may play a major role in its antibacterial effect.<sup>15,16</sup> No previous studies have evaluated the antifungal activity of RMGIC. Anna Carolina et al., demonstrated no activity of GIC against *C.albicans* which could be due to the fluoride concentration released by the material.<sup>17</sup> The results of this study suggest that *Candida* is resistant to RMGIC as there is no significant zone of inhibition formed around it.

## CONCLUSION

All the materials showed antimicrobial activity against the tested strains except RMGIC on *Candida albicans*. Biodentine created larger inhibition zones against *E.faecalis* and *C.albicans* compared to MTA and RMGIC. Biodentine significantly inhibited all the microorganisms. Thus we conclude that Biodentine has a greater antimicrobial activity as compared to MTA and RMGIC. However variations in agar medium, bacterial strains, diffusion capacity of inhibitory agents and cellular density may interfere with the formation of inhibition

zones around materials used in antimicrobial testing.

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# Organophosphate Induced Delayed Neuropathy: A Case Report

Praneet Ansal Mundu<sup>1</sup>, Manish Kumar<sup>2</sup>, Rajendra Prasad Satapathy<sup>1</sup>, J. K. Mitra<sup>3</sup>

## ABSTRACT

**Introduction:** Acute organophosphorous poisoning is one of the most common poisonings that we come across in emergency medicine producing significant mortality and morbidity. The sinister spectrum of organophosphorous poisoning is not only related to an initial life threatening acute cholinergic crisis but also to the delayed neurological symptoms which can be potentially debilitating. Accidental or suicidal exposure with these anticholinesterase compounds results in three well defined syndromes i.e. initial acute cholinergic crisis, intermediate syndrome (12-96 hours after exposure) and a organophosphorous induced delayed neuropathy (3-4 weeks after initial exposure).

**Case report:** Herein we describe a 22 year old male patient who after ingestion of large amount of (250 ml) Chlorpyriphos based insecticide had an acute cholinergic crisis and intermediate syndrome followed by development of paraesthesia and lower limb weakness 3 weeks after initial exposure to organophosphorous. Pyramidal tract involvement was also observed as the patient developed spastic paraparesis in lower limbs. Electrophysiological study was characterized by motor axonal polyneuropathy.

**Conclusion:** This was a case of organophosphate induced delayed polyneuropathy with Corticospinal tract involvement leading to spastic paraparesis. Hence all patients with organophosphorous poisoning should be under regular follow up and examined for neurological involvement.

**Keywords:** Organophosphorous, Intermediate syndrome, organophosphorous induced delayed neuropathy, Spastic paraparesis, motor axonal polyneuropathy.

## INTRODUCTION

Organophosphorous poisoning is the most common poisoning in an agriculture based country like India, where the easy availability of several organophosphorous based insecticides account for its rampant misuse. In India organophosphorous (OP) compounds are among the most commonly used agents for suicidal poisoning accounting for half of hospital admissions due to poisoning.<sup>1</sup> The pathophysiological basis of for the clinical manifestation of OP poisoning is inactivation of the enzyme, acetylcholinesterase at the peripheral muscarinic and nicotinic nerve terminals and junctions. Additionally these agents also inhibit the enzyme neuropathy target esterase (NTE) which is responsible for the delayed polyneuropathy in some of the patients.

## CASE REPORT

A 22 year old previously healthy male student consumed a large amount of organophosphorous insecticide (Chlorpyriphos 200 ml) with a suicidal intent around three weeks before being admitted to this hospital. At the time of that admission he was having frothing, nausea, vomiting, and respiratory distress. He was having miosis, bronchorrhoea, bradycardia and was in altered sensorium. He was having signs of cholinergic crisis and was managed vigorously by gastric lavage, inj Atropine, and

pralidoxime yet the symptoms persisted for the whole day. In the next two days the patient improved and the dose of atropine was gradually tapered when he started showing signs of atropinization.

On the third day of his hospital stay the patient suddenly complained of weakness of neck flexors and he also had bilateral ptosis. Fasciculations were observed in the thigh and calf muscles. Injection Atropine was being continued at 1 ml/ hour at this time. The next day the patient complained of breathing difficulty and was shifted to Medical ICU. The patient had developed flaccid paralysis and respiratory muscle weakness (Intermediate syndrome).

He was given proper oxygenation and his airway was secured. Injection Atropine and other symptomatic treatment were continued with close monitoring of his oxygen saturation and pulse rate. He symptomatically improved in a period of 8-10 days. Power in the lower limb gradually improved and he started walking. The patient was discharged with proper medical advice.

After remaining asymptomatic for three weeks he started having tingling sensation in his right foot specifically on the lateral border of right foot and little toe. Two days after this the patient complained of weakness in right lower limb and he started having difficulty in walking. Gradually he also developed weakness of left lower limb in subsequent two to three days. He then started walking with support. Tingling and numbness which was his initial complaint resolved during this period but weakness in both lower limbs persisted.

There was no history of fever, back ache, joint pain, and swelling of joints prior to this event. There was no history of root pain, girdle like sensation or bowel and bladder involvement. On neurological examination the patient had normal higher mental function and cranial nerves functions were intact. Motor system examination revealed weakness of both lower limbs however the power in upper limb was normal. Tone of the lower limb muscles was increased. There was clasp knife spasticity. Ankle jerk and knee jerk were exaggerated but biceps, triceps and supinator jerks were normal. Babinski sign was present, abdominal, cremasteric and anal reflexes were present. Ankle and patellar clonus was present. Touch, temperature, pain and proprioception was preserved there was no sensory impairment. Investigations of this patient revealed normal blood investigations (table-1). CSF analysis was normal(table-1). MRI spine was

<sup>1</sup>Junior Resident, <sup>2</sup>Senior Resident, <sup>3</sup>Associate Professor, Department of General Medicine, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India

**Corresponding author:** Dr. Praneet Ansal Mundu, 89, Anandpur, P.O.- Doranda, Ranchi-834002, Jharkhand, India

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normal however nerve conduction velocity studies showed features suggestive of Motor Axonal Polyneuropathy (table-2). Sensory Nerve studies were within normal range. Both peroneal and tibial CMAP'S show delayed latency. CMAPs were smaller in both peroneal and left tibial nerves. Other parameters were within normal limits. Sensory nerve action potentials were within normal limits. 'F' wave study showed delayed response in tested nerves.

**Impression:** Suggests Motor Axonal Polyneuropathy.

**MRI of whole spine:** Loss of lumbar lordosis.

## DISCUSSION

Organophosphates are a large group of compounds which exerts its toxicity due to inhibition of the enzymes cholinesterase, acetylcholinesterase and neuropathy target esterase. The organophosphorous compounds are rampantly used as insecticides, pesticides, industrial plasticizers and petroleum additives. Poisoning with organophosphorous compounds is serious problem worldwide. According to WHO one million serious unintentional poisonings occur every year and an additional two million people are hospitalized for suicidal attempts with pesticides.<sup>2</sup> Other common modes of OP poisoning include ingestion of contaminated fruits and vegetables, exposure to skin as well as inhalational routes. Organophosphorous associated with neuropathy are Tri-o-cresyl phosphate (TOCP), chlorpyriphos, trichlorphos, malathion, parathion, metriphonate and metamidophos. The most dangerous OP ester is TOCP.<sup>3</sup>

The clinical syndromes following an acute organophosphorous poisoning is divided into three types:

First is the acute cholinergic crisis which occurs due to excessive stimulation of muscarinic receptors by Acetylcholine due to blockade of acetylcholinesterase by an organophosphorous. The symptoms usually manifest within hours heralded by the onset of nausea, vomiting, fasciculations, increased sweating, lacrimation and salivation. Clinical examination reveals bradycardia, miosis and bronchorrhea proportionate to the amount of poison ingested. Excessive exposure may sometimes causes irritability, altered sensorium, convulsions and coma.

Second is the Intermediate syndrome which usually appears after 24-96 hours after poisoning on the recovery of cholinergic crisis. This is caused by the dysfunction of the neuromuscular junction caused by the down regulation of presynaptic and postsynaptic nicotinic receptors due to the release of excessive Acetylcholine and Calcium.<sup>4</sup> The main features comprise of muscle weakness affecting the proximal muscles and neck flexors. Cranial nerve involvement is common during this phase. Intermediate syndrome may also involve the respiratory muscles and patients may require ventilatory assistance. The clinical course usually lasts from about 5 to 18 days. Recovery from intermediate syndrome is usually complete though intermediate syndrome does carry death risk due to Type 2 respiratory failure.<sup>5</sup>

Third is the Organophosphorous induced delayed neuropathy (OPIDN) which usually develops two to three weeks after the initial symptoms. It is characterized by a distal motor axonal neuropathy with minimal or no sensory loss. The earliest symptoms to be seen are paraesthesia and calf pain. Weakness initially develops in the distal leg muscles causing foot drop, later it may extend proximally. Cranial nerve and autonomic involvement are absent. OPIDN is pathophysiological related

Parameters	Normal level	Value
Total leucocyte count	4000–11000/ cumm	4240 Cells/ cumm
Neutrophils	40–70%	46.5%
Lymphocytes	20–40%	39.4%
Monocytes	1–8%	8.7%
Eosinophils	1–4%	5.2%
Basophils	0–1%	0.2%
Haemoglobin	13–18g/dl	10.8 g/dl
MCV	77–95 fL	63.5 fL
Blood urea	7–20 mg/dl	16 mg/dl
Serum creatinine	0.6–1.2 mg/dl	0.7 mg/dl
Serum bilirubin total	0.3–1.9 mg/dl	1.52 mg/dl
SGPT	7–56 IU/L	92 IU/L
SGOT	5–40 IU/L	59 IU/L
Serum cholinesterase level	5320–12920 U/L	
On second day of poisoning		140.7 U/L
After 3 weeks of poisoning		4670.2 U/L
HIV		Non-Reactive
HbSAg		Non-Reactive
Serum sodium	135–145 mmol/l	143 mmol/l
Serum potassium	3.5–5 mmol/l	4.2 mmol/l
Serum calcium	2.2–2.7 mmol/l	1.21 mmol/l
Vit. B12 Level		>2000 pg/ml
Blood glucose (Fasting)	>125mg/dl	80 mg/dl
CSF Glucose	45–80 mg/dl	37 mg/dl
CSF Protein	40–80 mg/dl	70 mg/dl
Cells	0–5	03/cumm

Table-1: Investigation reports

Nerve	Normal NCV value (m/s)	Result
Right median	>52	54.59
Left median	>52	70.62
Right ulnar	>57	53.74
Left ulnar	>57	52.62
Right peroneal	>44	43.64
Left peroneal	>44	46.7
Right tibial	>48	47.39
Left tibial	>48	45.14
Ulnar cmap	>4	61
Median cmap	>4	37.4
Peroneal cmap	>2	2.4
Tibial cmap	>2	4.6

Table-2: Nerve conduction velocity study.

to inhibition of a carboxyesterase called neuropathy target esterase. OP compounds that do not inhibit this enzyme do not induce OPIDN. NTE is present in brain, spinal cord and peripheral nerves as well as some non neural cells. The natural history of this neuropathy has revealed that it is subacute in onset with slow progression. Clinical involvement of the corticospinal tract and the dorsal column becomes apparent when the peripheral neuropathy improves.<sup>6</sup> The prognosis of the patients with mild neuropathy is generally good but majority of patients with severe neuropathy and pyramidal tract involvement are left with residual disabilities like spasticity and ataxia.

After ingesting chlorpyriphos our patient presents with all these three syndromes i.e., an initial cholinergic crisis, intermediate syndrome and finally after a symptom free interval of three weeks he developed organophosphorous induced delayed

neuropathy.

Luiz Felipe R Vasconcellos et al in their case report described a 39 year old female with Dichlorvos based insecticide poisoning who later on developed organophosphorous induced delayed neuropathy.<sup>7</sup> However she developed flaccid paralysis of both upper and lower limbs. The striking dissimilarity in our case was the development of spastic paralysis with increased tone, exaggerated deep tendon reflexes and well sustained ankle clonus.

Nand et al in their case report described a 19 year old man who developed OPIDN following Dichlorvos ingestion. He later on developed spastic weakness of lower limbs.<sup>8</sup>

Pyramidal tract involvement in OPIDN is quite rare in itself and very few cases have been reported in India. Thiamine and methylprednisolone have been used in these cases but with variable success.

## CONCLUSION

Neurological manifestations in organophosphorous poisoning is an uncommon finding. Our patient presented with all three syndromes of acute organophosphate poisoning. In addition to the classical symptoms and sign our patient also demonstrated pyramidal tract involvement which is quite rare. Hence regular follow up of patients of organophosphorous poisoning is important for detection of organophosphate induced delayed polyneuropathy. This particular patient was managed symptomatically as there is no definite treatment for this condition.

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# Antibacterial Efficacy of Collagen and Foetal Barrier Membranes

Prutha Vaidya<sup>1</sup>, Swapna Mahale<sup>2</sup>, Pallavi Badade<sup>1</sup>, Alisha Panjwani<sup>1</sup>, Agraja Patil<sup>1</sup>, Ayushya Warang<sup>1</sup>

## ABSTRACT

**Introduction:** A wide range of barrier membranes are used in guided tissue and bone regeneration for reconstructing lost periodontium. One of the main reasons for unsuccessful regenerative procedures is the colonization and penetration of bacteria through barrier membrane into the treated site. Certain bacteria have high adherence to GTR membranes with periodontal pathogens showing greater affinity. Antibacterial properties of amniotic fluid are well documented and demonstrated. No such factors have yet been found in amniotic membranes. The antibacterial activity if present in GTR membranes can control inflammatory lesion and collagenolytic activity of bacteria increasing the life of the membrane and treatment outcome. Study aimed to investigate the antibacterial properties of collagen and foetal barrier membranes.

**Material and methods:** Three membranes (Collagen, Chorion, Amnion) were tested against three bacterial strains (*S. aureus*, *A. actinomycetemcomitans*, *P. gingivalis*) using direct contact test. The optical densities of bacterial growth were evaluated using Spectrophotometry.

**Results:** There was no statistical significant difference in the growth of bacteria for Amnion and Collagen membrane. However there is a statistically significant increased growth of *P. gingivalis* and *A. actinomycetemcomitans* on Chorion membrane.

**Conclusions:** Thus chorion membrane enhances the growth of periopathogens in vitro and maybe a potential risk to regeneration.

**Keywords:** periodontitis, antibacterial, barrier, membranes, regeneration, resorbable

associated with GTR, with prevalence between 50% and 100%.<sup>1</sup> Once membrane exposure is clinically detected, efforts should be directed to prevent or treat local infection as many studies have shown that exposed membranes are contaminated by bacteria.<sup>2,3</sup> Contaminated membranes are associated with reduced clinical outcomes.

Thus post exposure the nature of the surface of the BM and the adsorption of organic materials from saliva or serum, could provide a potential interface for cell colonisation.<sup>4</sup> After placement, bacteria from the oral cavity may colonize the coronal part of the membrane. Frequently, this results in recession of the gingival tissues, which allows colonization of the membrane material further apically. In addition, "pocket" formation may occur on the outer surface of the membrane due to apical migration of the epithelium on the inner surface of the covering gingival tissue. This may allow bacteria from the oral cavity to colonize the subgingival area.

Certain bacteria have high adherence to collagen membranes with periodontal pathogens showing greater affinity.<sup>5</sup> Certain bacteria have high adherence to collagen membranes with periodontal pathogens showing greater affinity. The proteolytic activity of the bacteria may result in rapid degradation of the membranes and thus impair the regenerative potential.<sup>6</sup>

Antibacterial properties of amniotic fluid are well documented and the presence of many potentially antibacterial factors has been demonstrated.<sup>7</sup> No such factors have yet been found in amniotic membranes.

Talmi et al. (1991) have demonstrated an inhibitory effect of amniotic membranes on agar plates.<sup>8</sup> Kjaergaard et al. (2001) tested the antibacterial properties of amnion and chorion against diverse panel of bacteria. He concluded that amnion had marked inhibitory properties against most of the bacteria however on the other hand chorion showed a marginal inhibitory effect.<sup>9</sup> M. Parthasarathy (2014) confirmed the antimicrobial effect of both amniotic and chorionic membranes against several bacterial and fungal pathogens and found that among the two membranes, the maximum activity was recorded by amniotic membrane.<sup>10</sup> Slutzkey et al (2015) found that collagen barrier membranes possess no antibacterial properties and tested 3 different collagen BMs BioGuide (non cross-linked), OsseoGuard (cross-linked) and CopiOs (non cross-linked) and concluded that OsseoGuard (cross-linked) showed bacterial enhancing effect.<sup>11</sup>

The antibacterial activity if present can control inflammatory lesion and thus increase the life of the membrane and treatment

<sup>1</sup>PG Student, <sup>2</sup>HOD, Department of Periodontology, MGVs KBH Dental College, Nashik, Maharashtra, India

**Corresponding author:** Dr. Prutha Vaidya, P 1- 7 Krishna Kamal, Sus Road, Pashan, Pune-411021, India

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outcome.

The aim of this study is to investigate the antibacterial properties of collagen and foetal barrier membranes i.e amnion and chorion.

## MATERIAL AND METHODS

The study was conducted in Maratha Mandal's NGH institute of dental sciences and research centre, Belgaum.

### Membranes tested

- Collagen membrane (Healiguide)
- Chorion membrane (Tata memorial tissue bank)
- Amnion membrane (Tata memorial tissue bank)

### Bacteria tested

- *Staphylococcus aureus*
- *Aggregatibacter actinomycetemcomitans*
- *Porphyromonas gingivalis*

### Method of bacterial growth evaluation

#### Direct Contact Test (DCT)

The DCT is measured by determining growth on a 96 well microtiter plate. The outgrowth kinetics in each well was recorded continuously by measuring optical densities at 650 nm at specific time intervals i.e 30 min, 60 min, 90 min, 120 min, 150 min, 180 min and finally at 24 hrs.

Two samples of each membrane were taken for each of the three organisms. This was designated as group A. They were attached to the walls of the wells. Bacterial suspension was placed on each piece of membrane. It was then incubated for 1 hour at 37 degree C for bacterial fluid suspension to evaporate and to ensure close and direct contact between membrane and the bacteria. After 1 hour the respective culture media for each strain was added to each of group A well and gently mixed. Then some amount of suspension was transferred from group A wells respectively to adjacent set of wells and these wells were designated as group B. The transfer was such that equal volume of liquid media was maintained in both experimental groups A and B so that the bacterial outgrowth could be monitored and compared, both in the presence and the absence of test membrane.

One set of three wells served as positive controls i.e they had similar bacterial inoculum of the three strains as in the duplicates of group A but without the membrane in the wells. It was processed similar to the experimental group.

One set of three wells formed the negative control and contained the test membranes as in experimental group A and an equal volume of uninoculated fresh media. This negative control was treated as baseline. Then the outgrowths were monitored at 650 nm at 30, 60, 90, 120, 150, 180 minutes and at 24 hrs. Data was recorded in optical densities.

### Data processing

The OD values from the negative control well were considered baseline and were subtracted from the respective experimental data which were then plotted as growth curves. The curves for each well were analyzed, and a regression line was calculated on the ascending linear portion of the curve, expressed by the simple function  $y = ax + b$ . The formula of the linear portion provided two parameters: the slope, indicating growth rate; and the constant, correlating with the number of bacteria at time zero.

## STATISTICAL ANALYSIS

SPSS version 21 was used for statistical analysis. Analysis of variance (ANOVA) was applied to compare the growth rate.

## RESULTS

### Bacterial growth in presence of membranes

Table-1 indicates the growth rates derived from slopes of the linear regression. The growth of each bacteria on each membrane was compared to its respective positive control.

*S aureus* - The membrane samples of collagen, amnion and chorion in the suspension did not disrupt the growth of *S aureus* as compared to control.

*P gingivalis* - All three membranes did not disrupt the growth of *P gingivalis* as compared to control. However chorion membrane accelerated the growth of *P gingivalis* as compared to control group ( $P < 0.05$ ).

*A actinomycetemcomitans* - All three membranes did not disrupt the growth of *A actinomycetemcomitans* as compared to control. However chorion membrane accelerated the growth of *A actinomycetemcomitans* as compared to control group ( $P < 0.05$ ).

## DISCUSSION

The results showed that the membranes did not disrupt the growth of tested bacteria as compared to control groups. Thus they had no antibacterial properties. However chorion membrane accelerated bacterial growth. The DCT, which was used in this study, is an accepted method for testing antibacterial activities of dental materials. Most studies that tested the antibacterial properties of dental materials used the Agar Diffusion Test. An antibacterial activity measured by this kind of technique is not necessarily positive because insoluble components will show negative results.

Collagen is an important constituent of all the 3 membranes. Some of the bacteria that colonize the membranes were found to have the ability to rapidly degrade collagen by proteolytic activity.<sup>6</sup> In addition, the colonizing bacteria can pass through membranes accompanied by fibroblasts and giant cells or

	Positive Control	Collagen		P value	Chorion		P value	Amnion		P value
		Sample 1	Sample 2		Sample 1	Sample 2		Sample 1	Sample 2	
S. aureus	0.035	0.032	0.037	0.865	0.017	0.012	0.123	0.031	0.029	0.227
P. gingivalis	0.063	0.058	0.066	0.908	0.026	0.025	0.017 *	0.054	0.045	0.315
A. a	0.026	0.032	0.035	0.181	0.004	0.002	0.026*	0.029	0.035	0.457

\* statistically significant (P value < 0.05)

Table-1: Growth of bacteria

invade the membrane and colonize its internal surface.<sup>12</sup> Higher affinity of bacteria to certain materials is due to their increased hydrophilicity. It can be speculated that the collagen membrane used in this study was more hydrophilic due to its crosslinked structure.<sup>11</sup> Thus there was an enhanced growth of *S. aureus*, *P.gingivalis* and *A. actinomycetemcomitans* as compared to control, however it was not statistically significant.

Amniotic membranes have the ability to produce  $\beta$ -defensins, elafin and secretory leukocyte protease inhibitor. It also exhibits cystatin E, the analogue of cysteine proteinase inhibitor.<sup>9</sup> Thus in the present study amnion membrane reduced the growth of *P.gingivalis* whose one of the virulence factors is Gingipains which is a cysteine protease. However the dehydration process for clinical use decreases the concentration of antimicrobial factors and hence the reduction was not statistically significant. There is a lack of literature regarding the exact antimicrobial properties of chorion membrane. However a major constituent of chorion membrane is Laminin-5 which is a component of Extra Cellular Matrix with a high affinity for cellular adhesion. It has been hypothesized that there is an increased interaction between periopathogens and these ECM proteins leading to their increased growth. These interactions fail in presence of blood however during membrane exposure the risk increases. Thus in this study there was an increased growth of all 3 microorganisms, however there was a statistically significant increased growth of *A.a* and *P. gingivalis*.

## CONCLUSION

In clinical situations where definitive closure of gingival flaps is not predicted or hard to achieve for example socket preservation procedures chorion membrane should be avoided. The collagen membrane tested had no antibacterial properties. Nonetheless, the crosslinked collagen membranes should be used with caution. Amnion membrane is a suitable membrane as it caused least bacterial growth and had some inhibitory effect on *P. gingivalis*. However, studies have showed that maintenance of good oral hygiene and minimal gingival inflammation demonstrated consistently better regenerative response. Hence the key to any successful regeneration is to provide an environment non conducive for the growth of harmful bacteria, and since their elimination is an impossible concept we can atleast reduce their load and attempt to prevent their excessive growth.

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# Prevalence of Anaemia in Female Students of Pharmacy College and its Association with Various Socio-Demographic Variables: A Study Conducted in Rural Teaching Institute, Kasegaon

Ghorpade V V<sup>1</sup>, Shinde P P<sup>1</sup>, Madhekar N S<sup>2</sup>, Pol V S<sup>3</sup>

## ABSTRACT

**Abstract:** Nutritional anaemia though global in occurrence is more of concern in the developing countries because of the high prevalence in these regions. In India, this silent emergency is rampant among women belonging to reproductive age group (15-49 yrs). Objectives: 1. To estimate the prevalence of anaemia among girl students of rural Pharmacy College. 2. To find out any association between socio-demographic variables, dietary habits and menstrual history

**Material and methods:** A cross sectional institution based study was conducted in Rajarambapu Patil College of Pharmacy, Kasegaon from 15 Jan 2016 to 30 Jan 2016. In total 168 respondents participated. A pre designed and pretested self administered questionnaire interview method was used. Information on socio demographic factors, dietary habits and menstrual history was obtained. Data collected was analysed and interpreted with the help of percentage and chi square test.

**Results:** In present study only one fourth i.e.44 (26.19%) of study subjects had normal haemoglobin, while three fourth i.e. 124(73.81%) had one or other grade of anaemia. Among anaemics majority i.e. 70.23% contributed between mild to moderate category. Consumption of GLV & fruits, menorrhagia & passing clots during menses were significantly associated with anaemia prevalence.

**Conclusion:** Present study revealed high prevalence of anaemia in college going girls.

**Keywords:** Prevalence, Anaemia, Young female students.

## INTRODUCTION

Nutritional anaemia is a worldwide problem with the highest prevalence in developing countries. It is found among women of child-bearing age, young children, during pregnancy and lactation.

Nutritional anaemia though global in occurrence is more of concern in the developing countries because of the high prevalence in these regions.<sup>1</sup> Anaemia is attributed to dietary inadequacy due to poor purchasing power, illiteracy, ignorance regarding nutritional value of available cheap food, cultural taboos, superstition, large families etc.

In India, this silent emergency is rampant among women belonging to reproductive age group (15-49 yrs). As per District Level Health Survey (DLHS 2002-2004) prevalence of anaemia in adolescent girls is very high (72.6%).<sup>2</sup> In adolescent girls, educational or economic status does not seem to make much of a difference in terms of prevalence of anaemia. Prevention, detection or management of anaemia in adolescent girls has till now not received much attention.

Iron deficiency can arise either due to inadequate intake or poor bioavailability of dietary iron or due to excessive losses of iron from the body e.g. in women loss of considerable amount of

iron during menstruation.

Iron deficiency anaemia in adolescent girls is significant risk factor for maternal mortality, high incidence of low birth weight babies, high perinatal mortality and fetal wastage, which ultimately results in higher fertility.<sup>3</sup> It can even cause lack of concentration, irritability and impair academic performance of students.

Adolescence, a period of transition between childhood and adulthood, occupies crucial position in the life of human being.<sup>4</sup> It is considered as most appropriate time to intervene. Behaviour change messages embarrassed by this group can contribute to sustained health impact.

So the present study was planned to ascertain the prevalence of anaemia and its association with various factors among young female students of Pharmacy College and to suggest intervention strategies.

## Aims and objectives

To estimate the prevalence of anaemia among female students of rural Pharmacy College.

To find out any association between socio-demographic variables, dietary habits and menstrual patterns with prevalence of anaemia among female students of rural Pharmacy College.

## MATERIAL AND METHOD

The present cross sectional institution based study was carried out in Kasegaon Education Society's "Rajarambapu Patil Pharmacy College, Kasegaon" Tal- Walwa, Dist- Sangli.(M.S.). Total strength of Boys and Girls students was 352, out of which 194 were girls forming universal sample. Out of 194 girl students 168 participated in present study. Inclusion criterion – those who were present and willing to participate in study, informing about 1cc blood collection by prick. Exclusion criterion: those who were not willing to participate in study. The study period was from 15 January 2016 to 30 January 2016. Written consent was obtained from The Head of Institution and purpose of study was explained to him. Ethical clearance was taken from Institutional Ethical Committee, IMSR Mayani. A pre designed and pretested self administered questionnaire interview method was used after obtaining informed consent of students. Information on

<sup>1</sup>Associate Professor, <sup>2</sup>Professor and HOD, <sup>3</sup>Statistician, Department of Com. Medicine, IMSR Mayani, India

**Corresponding author:** 1Associate Professor, Department of Com. Medicine, IMSR Mayani, India

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socio demographic factors, dietary habits and menstrual history was obtained. Haemoglobin was measured by experienced laboratory technician using Sahli's method. Privacy of data was strictly maintained to protect physical, mental and social integrity of participants. The standards set by the WHO used to detect anaemia were used.

## STATISTICAL ANALYSIS

Collected data was analysed and interpreted using Chi-square test with the help of SPSS version 21. p value of < 0.05 was considered to indicate statistical significance.

In present study, majority i.e. (70.60%) belonged to age group between 20 years to 22 years. About half participants in this study (59.53%) belonged to middle socio-economic group. Percentage of participants staying at home was slightly more (by 13.09%) than percentage of participants staying at hostel (table-1).

In present study only one fourth 44 (26.19%) of study subjects had normal haemoglobin level, while three fourth 124(73.81%) had one or other kind of anaemia. Out of anaemics, 118 (95.16%) contributed for mild & moderate anaemia together (table-2).

Prevalence of anaemia among vegetarian & consuming mixed type of diet were 75.68% & 72.34% respectively. 93 (90.29%) and 108(84.38%) girls were anaemic who do not consume green leafy vegetables and fruits regularly respectively. Most significant associations in present study was found between anaemia and not regular consumption of fruits and green leafy vegetables daily ( $p<0.001$ ). No significant association was found between anaemia and habits of regular breakfast, doing fast & type of diet (table-3).

Study subjects in present study showed significant association ( $p<0.001$ ) between anaemia with duration of menstrual flow >5 days & passing clots in menstrual flow, while age at menarche & irregularity of menstrual cycle showed no association. 85(91.4%) & 78(85.71%) study subjects were having menstrual flow for more than 5 days & h/o passing clots during menstruation respectively (table-4).

## DISCUSSION

According to WHO, if the prevalence of anaemia is more than 40% it is considered as problem of high magnitude.<sup>5</sup> Present study highlights the fact that the problem of anaemia is far wider than expected among females especially from rural settings and needs immediate attention.

In present study Table-2 shows that only 44 (26.19%) participants were with normal haemoglobin level that is >12 gm/dl. While 124(73.81%) participants had one or other form of anaemia. The findings are comparable with 62.63%, 76% and 75% girls with one or other form of anaemia in studies done by Arun V Panant et al<sup>6</sup>, Satha A et al<sup>7</sup> and Sharda Sindhu et al<sup>8</sup> respectively. In present study mild, moderate and severe anaemia were found in 57(33.93%), 61 (36.31%) and 6 (3.37%) respondents respectively. Findings slightly differ from results mentioned by Kamal Mehta<sup>9</sup>, who found prevalence of mild, moderate and severe anaemia in 46.67%, 19.16% and 0.83% respectively and Sartha A et al<sup>7</sup> who found mild, moderate and severe anaemia in 56.67%, 19.33% and 0% respectively.

Table-3 shows that, as far as diet concerned, in present study no statistical significance was associated between dietary

pattern (veg. or mixed) and practice of fast with prevalence of anaemia. However significant statistical association ( $p<0.0001$ ) was found between non consumption of GLV and fruits with prevalence of anaemia. Similar findings were mentioned by Sartha A et al<sup>7</sup> and Kaur M et al.<sup>10</sup>

Regarding menstrual history, in present study, Table-4 shows that duration of menstrual flow > 5 days and history of passing clots during menstruation had significant association with prevalence of anaemia ( $p< 0.001$ ), while no significant association was found between age of menarche and regularity of menses with prevalence of anaemia. Manjula VD et al<sup>11</sup> also mentioned significant association between menstrual flow more than 5 days and passing of clots during menstruation and anaemia while Sartha A et al<sup>7</sup> found no association between above variables.

## CONCLUSION

Prevalence of anaemia and its severity is influenced by several independent but overlapping factors. Lack of proper diet and excessive blood loss during menstruation are major contributory factors for anaemia in females. In present study only 26.19% participants had normal haemoglobin levels on the contrary 73.81% had anaemia. Majority of anaemics, i.e. 90.29% &

Variable	Frequency	Percentage
Age group (in years) n= 168		
19	33	19.64
20	42	20.00
21	48	28.57
22	37	22.03
23	8	04.76
Socio-economic status* n= 168		
Upper(I)	48	28.57
Upper middle (II)	72	42.86
Lower middle (III)	28	16.67
Upper lower (VI)	12	07.14
Lower lower (V)	8	04.76
Residential status		
Hostel	73	43.45
Home	95	56.54
Type of family		
Joint	93	55.36
Nuclear	75	44.64
*Socio-economic classification as suggested by B G Prasad and modified; as per The All India Consumer price index (AICPL) of May 2014.		
<b>Table-1:</b> Distribution of study subjects according to Socio-demographic variables		

Grade of Anaemia	No of girls (%)
Non-anaemic (Hb >12gm/dl)	44 (26.19)
Grade I – Mild Anaemia (Hb 10.0 to 11.9 gm/dl)	57 (33.93)
Grade II- Moderate Anaemia (Hb 7.0 to 9.9 gm/dl)	61 (36.31)
Grade III – Severe Anaemia (Hb <7 gm/dl)	6 (3.57)

**Table-2 – Prevalence of anaemia as per grades in study subjects (n=168)**

Indicators	Anaemic n = 124	Non-anaemic n = 44	Total N= 168	p value
Diet type				
Vegetarian	56 (75.68%)	18 (24.32%)	74	
Mixed	68 (72.34%)	26 (27.66%)	94	p> 0.05
Regular Breakfast				
Yes	41 (66.12%)	21 (33.87%)	62	
No	83 (78.30%)	23 (21.70%)	106	p> 0.05
Consuming GLV regularly				
Yes	31 (77.69%)	34 (52.31%)	65	
No	93 (90.29%)	10 (09.71%)	103	p<0.001
Consuming Fruits daily				
Yes	16 (40%)	24 (60%)	40	
No	108(84.38%)	20 (15.62%)	128	p<0.001
Practising fast				
Yes	51 (70.84%)	21 (29.16%)	72	
No	73 (76.05%)	23 (23.95%)	96	p>0.05

**Table-3:** Association between Anaemia and Certain Diet habits in study subjects

Indicators	Anaemic n = 124	Non anaemic n = 44	Total n= 168	p value
Regular menses				
Yes	82 (76.64%)	25 (23.36%)	107	
No	42 (68.855)	19 931.15%	61	p>0.05
Duration of menstrual flow				
≤ 5 days	39 (52.00%)	36 (48.00%)	75	
> 5 days	85 (91.40%)	08 (08.605)	93	p<0.001
H/o passing clots				
Yes	78 (85.71%)	13 (14.29%)	91	
No	46 (59.74%)	31 (40.26%)	77	p<0.001
Age of menarche				
<14 years	32 (80.00%)	08 (20.00%)	40	
14-16 years	88 (72.73%)	33 (27.27%)	121	
>16 years	04 (57.14%)	03 (42.86%)	07	

**Table-4:** Association between anaemia and menstrual patterns in study subjects

83.10% had unhealthy diet preferences like non consumption of GLV & fruits respectively even though belonged to rural settings where these are freshly available.

## RECOMANDATIONS

Need to include iron rich food in diet of girls.

Efficient utilization of government programmes like ICDS, Nutrition programme for underweight adolescent girls, Kishori shakti yojana, Weekly iron folic acid supplementation for adolescent girls.

Health education, seminars on menstrual hygiene should be conducted at regular intervals.

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# Comparative Evaluation of Femoral Nerve Block and Intravenous Fentanyl for Positioning During Spinal Anaesthesia in Surgeries of Femur Fracture

Amisha Vats<sup>1</sup>, Monika Gandhi<sup>2</sup>, Parul Jain<sup>3</sup>, K.K. Arora<sup>4</sup>

## ABSTRACT

**Introduction:** Spinal anaesthesia is preferred to fix femur fracture. Extreme pain does not allow ideal positioning for this procedure. We conducted this study to compare analgesic effect provided by femoral nerve block and intravenous fentanyl prior to positioning for spinal anaesthesia in patients undergoing surgeries of femur fracture.

**Material and Methods:** In this observational study 100 patients scheduled for fracture femur surgery under subarachnoid block at M.Y Hospital, Indore for 1 year were included. Patient consent and ethics committee permission obtained. Patients observed as 2 groups-FNB and FENT. 5 min prior to positioning, FNB group patients received Femoral nerve block 20 ml lignocaine+adr (1.5%) via nerve stimulator and FENT group received fentanyl 1 µg/kg IV. If either group reported pain scores ≥4 during positioning, IV fentanyl 0.5 µg/kg was given every 5 min until the pain score decreased to <4 (maximum dose 3 µg/kg). Spinal block was performed, visual analog scores before and during positioning were observed. Statistical analysis done with SPSS 20 computer software. Z-test applied to compare the means and P < 0.05 taken as significant.

**Results:** VAS during positioning: FNB: 1.72 ± 0.783 versus FENT 2.14 ± 0.92 (P = 0.000). Time to perform spinal: FNB: 2.30 ± 0.61 min versus FENT 3.29 ± 0.95 min (P = 0.000). Quality of patient positioning was better in FNB group. Patient satisfaction same in both group. No major side-effect.

**Conclusion:** Femoral nerve block provides better analgesia, satisfactory positioning during spinal anaesthesia in patients of fracture femur

**Keywords:** Anaesthesia, femoral nerve block, femur fracture, fentanyl, spinal block, positioning during spinal block

been used for allaying the pain preoperatively and thereby improving the position of these patients.<sup>3,4</sup> Although the present studies fail to demonstrate superiority of femoral nerve block over intravenous fentanyl, previous studies have shown the superiority of the femoral nerve block over intravenous fentanyl.<sup>5,6</sup> Thus, we conducted the following study to compare the analgesic efficacy of Femoral Nerve Block and Intravenous Fentanyl just before positioning for central neuraxial block in patients undergoing femur fracture surgeries.

## MATERIAL AND METHODS

Institutional approval and written informed consent was taken from the patients before the study. Patients of both sexes within 18–70 years age group having weight more than 45 kgs and American Society of Anesthesiologist's physical status I to II, scheduled for fracture femur operation under central neuraxial (spinal) block, but unable to sit due to pain were included in the study. Patients with ASA III and IV, those who could sit comfortably, refused for participation in the study or having any contraindication to spinal anaesthesia, FNB or use of local anaesthetic, history of cardiac or respiratory compromise were excluded. Patients were observed as two groups; FNB and IV FENT. We calculated our sample size based on earlier studies.<sup>7</sup> Their pilot study showed that FNB group was more effective in reducing pain, and the mean score was 2 in FNB group. Based on  $\alpha = 0.05$ ,  $\beta = 0.20$  and considering a significant difference at mean difference of 2.2 in pain score, with standard deviation (SD) of 3.0, a sample size of 30 per group was required for one-tailed testing. We took 50 per group as sample size for our observational study. IV line was secured and fluid started, monitors attached and baseline parameters were recorded. FNB group patients received FNB guided by a peripheral nerve stimulator, 5 min prior to positioning. Point of needle entry was infiltrated with 1 ml 1% lignocaine first and then an insulated 50 mm 22 gauge needle was introduced identifying following landmark lying 1 cm lateral to femoral artery and 1.5 cm below inguinal ligament. 20 mL drug in a concentration of 1.5% lignocaine with adrenaline (1:200,000) aspirated and carefully injected (15 mL 2% lignocaine diluted with 5 ml distilled

<sup>1</sup>P.G Resident, <sup>2</sup>Associate Professor, <sup>3</sup>Assistant Professor, <sup>4</sup>Professor and Head of the Department, Department of Anaesthesia, M.G.M Medical College, Indore, India

**Corresponding author:** Dr. Amisha Vats, C/O Mr. Bagdi, 190, Jaora compound, Indore, India

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water) at the site after eliciting a quadriceps contraction at the stimulating current intensity of 0.3–0.5 mA. Whereas, patients of the FENT group were given injection fentanyl 1 µg/kg IV 5 min before positioning. After 5 min, if it was found that any patient in either of the groups had pain scores ≥4 during positioning, IV fentanyl 0.5 µg/kg was given further every 5 min till the pain scores reduced to <4 or maximum dose of 3 µg/kg was achieved (whichever first); still if pain score ≤ 4 remained, patients were excluded. Thereafter, subarachnoid block was given via midline/paramedian approach at the L2/L3/L4 level, according to the anaesthesiologist's preference. Pain scores before and during positioning using visual analog scale were noted (where 0 = no pain, 10 = maximal pain). Other parameters were additional fentanyl required during positioning, time taken to achieve position to perform block, satisfaction of the anaesthesiologist with respect to position maintained for performing spinal block (0 = not satisfactory, 1 = satisfactory, 2 = good, 3 = optimal) and whether the patient was satisfied or not with pain relief. Basic hemodynamic parameters of the patients such as heart rate (HR), mean arterial pressure (MAP) (non-invasive) and oxygen saturation ( $\text{SpO}_2$ ) was monitored strictly at specified time intervals.

### STATISTICAL ANALYSIS

Statistical analysis was performed with SPSS version-20 computer software. Parametric variables were described as mean ± SD; qualitative variables were described as number (percentage) and as median and range. Paired t-test, Unpaired

t-test or Mann Whitney test were used as appropriate to compare the two groups. P < 0.05 was considered as statistically significant.

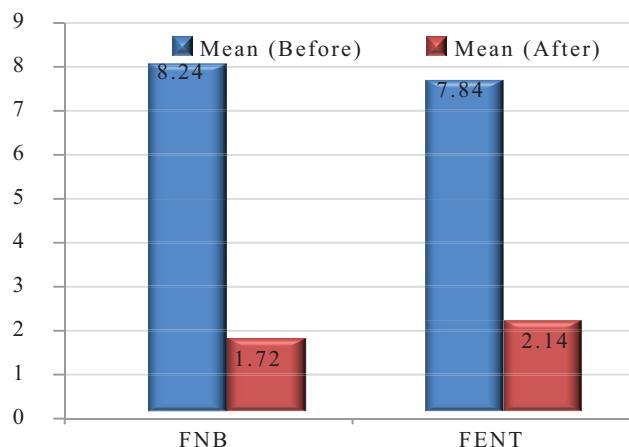
### RESULT

50 patients were observed in each group for various parameters. Demographic data and base line values for HR, MAP,  $\text{SpO}_2$  and type of surgery were comparable in both the groups (Tables-1 and 2). There was no significant change noticed in HR between two groups (P = 0.622); however, MAP was significantly lower in FENT group 5 min after the intervention (P = 0.0081). Visual analog scale during positioning (median ± SD) was lesser in group FNB: 1.72±0.783 versus FENT 2.14± 0.92 (P = 0.022) (Figure-1). Time required to perform spinal (mean ± SD) was shorter in group FNB: 2.30 ± 0.61 min versus 3.29 ± 0.95 min (P = 0.000). Quality of patient positioning for spinal anaesthesia as per anaesthesiologist (mean rank) was higher in group FNB 59.62 versus FENT 41.38 (P = 0.000). Patient satisfaction was same in both groups. No patient required additional dose of fentanyl. Excessive sedation was seen in 2 patients in FENT group. Although no patient in both the groups had  $\text{SpO}_2$  < 95 % during the procedure (Tables-2 and 3).

### DISCUSSION

Spinal anaesthesia is universally accepted and preferred technique of anaesthesia for surgeries of fracture femur.<sup>8</sup> It has gained popularity over general anaesthesia in femur surgeries because of early ambulation with spinal anaesthesia, reducing

	FNB Group (N=50)	FENT Group (N = 50)
AGE (years)		
18-30 years	9	12
31-50 years	15	15
51-70 years	26	23
SEX (male/ female)	37/13	36/14
Fracture site		
Neck of Femur	14	11
Intertrochanteric	21	24
Subtrochanteric	2	1
Shaft (Upper Third)	5	5
Shaft (Middle Third)	5	3
Shaft (Lower Third)	2	5
Suprachondylar	1	1
FNB – Femoral nerve block; FENT – Fentanyl		
<b>Table-1:</b> Demographic Data		



**Figure-1:** Mean of Visual Analogue Score before and after Intervention in Both Groups

	FNB (N=50)	FENT (N=50)	P Value
MAP at T0	96.68 ± 7.28	96.62 ± 10.92	0.974
MAP during positioning	97.64 ± 6.80	97.38 ± 8.16	0.863
MAP 5 min after intervention	89.4 ± 7.42	85.82 ± 7.60	0.041
HR at T0	86.56 ± 12.85	87.74 ± 11.87	0.544
HR during positioning	89.29 ± 11.63	88.14 ± 10.40	0.622
HR 5 min after intervention	88.66 ± 10.51	81.30 ± 10.14	0.659
$\text{SpO}_2$ at T0	98.925 ± 0.764	98.750 ± 0.63	0.267
$\text{SpO}_2$ during positioning	98.625 ± 0.774	98.725 ± 0.679	0.541
$\text{SpO}_2$ 5 min after intervention	99.050 ± 0.677	98.975 ± 0.862	0.666
T0 – Baseline value; MAP – Mean arterial pressure; HR – Heart rate; FNB – Femoral nerve block; $\text{SpO}_2$ – Oxygen saturation; FENT – Fentanyl			
<b>Table-2:</b> Vital clinical parameter before analgesia and during positioning			

	FNB (N = 50)	FENT (N = 50)	P- Value
VAS score at T0	8.24 ± 1.299	7.84 ± 1.23	0.111
VAS score during positioning	1.72 ± 0.751	2.14 ± 0.92	0.022
Time taken to achieve position (min)	2.31 ± 0.61	3.29 ± 0.95	0.00
Anaesthesiologist's satisfaction (0-3) Mean rank	59.62	41.38	0.00
Patient satisfaction (%)	100	100	-
Additional fentanyl required during positioning (mcg)	0	0	-
Complication: Excessive Sedation	0	2	-

T0 – Baseline value; FNB – Femoral nerve block; FENT – Fentanyl; VAS – Visual analog scale

**Table-3:** VAS scores, Time for spinal, Quality of position as per anaesthesiologist and Patient

chances of deep vein thrombosis, thereby reduction in morbidity and mortality.<sup>9,10</sup>

Sandby-Thomas et al. found that the most frequent agents used were midazolam, ketamine, and propofol which aided in positioning patients for the subarachnoid block. Other less preferred agents were fentanyl, remifentanil, morphine, nitrous oxide, and sevoflurane, whereas nerve block techniques were seldomly used worldwide.<sup>11</sup> Use of Femoral nerve block to relieve pain from a fracture of the femur at various other situations<sup>12,13</sup> is well known and now, is being used for positioning during spinal anaesthesia.<sup>14-17</sup>

In our study, the patients were comparable in relation to the age and sex distribution and types of femur fractures had similar representation in both groups i.e both the groups had majority patients of femur fracture of proximal site (fracture neck of femur, intertrochanteric fracture and shaft (upper third) rather than distal site femur fractures) as is evident from Table-1. The visual analogue scale values in FNB were significantly lower than fentanyl (Table-3). Many other studies also reported significantly low pain scores with FNB compared to IV fentanyl. A study by Iamaroon et al. did not find any significant difference between FNB and fentanyl. Possibly because they used 0.3% bupivacaine for FNB and positioned the patients 15 min after block instead of lidocaine whose effect comes in 5 min however; onset of analgesic effect of bupivacaine is variable and may take 25–30 min for full effect.

One of the important finding in our study was the superiority of femoral nerve blockade in terms of analgesia as compared to IV fentanyl in fracture femur along with greater anaesthesiologist satisfaction for positioning during spinal anaesthesia. Iamaroon et al. used 0.5 µg/kg fentanyl as the initial dose and average additional dose of fentanyl in FENT group was 17.1 ± 18.4. The total additional doses required by IV fentanyl group in our study is found to be zero. In our study, doses of FENT 1.0 µg/kg was given incrementally in 5 min interval because titrated doses of fentanyl reduce any serious side-effects, such as hypoventilation or apnea especially in older age group without affecting the analgesic effect<sup>18</sup> however, interval more than five minutes could have prolonged the anaesthetic procedure. We had used lidocaine for femoral nerve block because of its shorter time onset over long-acting local anaesthetic. Long-acting local agents have advantage of more effective and longer postoperative pain relief.

Pulse variation was statistically insignificant in both groups. Although bradycardia is known with fentanyl but because of premedication with anticholinergic (glycopyrrolate) causing opposing vagal mediated bradycardia, no significant change was observed. Mean arterial pressure was reduced significantly

in both groups after 5 minutes of intervention ( $P = 0.081$ ) MAP fell more in FENT group. This effect was seen because of pain relief to both groups (reduced sympathetic stimulation) as well as fall in arterial pressures due to added factors associated with fentanyl like myocardial depression, venodilation, bradycardia. Only two patients in FENT group had drowsiness as side-effect due to excessive sedation which required more persons for holding the patient during positioning. Excessive drowsiness was seen in elderly age group patients only. Our findings correlated with the study of Jadon et al<sup>19</sup> with respect to visual analogue score, additional fentanyl required, time taken to achieve position, quality of positioning and patient satisfaction.

## CONCLUSION

Both femoral nerve block and intravenous fentanyl are effective in relieving pain during patient positioning for spinal anaesthesia in surgeries of femur fracture but femoral nerve block provides better analgesia, more optimal positioning for central neuraxial blockade in less time and with no major hemodynamic instabilities and complications

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# Comparative Evaluation of performance of Mannheim Peritonitis Index (MPI) and Multiple Organ Failure Score in Patients with Peritonitis

Salamat Khan<sup>1</sup>, V P Singh<sup>1</sup>

## ABSTRACT

**Introduction:** Secondary bacterial peritonitis is a life threatening condition if not well managed. It is associated with high morbidity and mortality. Early stratification by scoring system will allow in predicting the possible outcome and providing more critical care services to the serious patients. Aim: This study was done to evaluate the performance of Mannheim Peritonitis Index (MPI) score and MOF score in patients with secondary peritonitis.

**Material and Methods:** This is a prospective, observational evaluation of MPI and MOF score which was conducted on 105 consecutive patients of peritonitis who were admitted in our institution and underwent appropriate surgical treatment. Patient's characteristics, clinical, laboratory findings, operative findings and postoperative outcome were noted.

**Results:** Overall, mortality was 11.4%. The highest prediction of mortality rate of 85.7% was at MPI score of >27. The prediction of mortality of MOF score was 80% (12/15). Non-survivors had mean score of MPI and MOF was  $28.50 \pm 3.6$  and  $3.46 \pm 2.19$  respectively whereas survivors had mean MPI and MOF of  $17.48 \pm 5.8$  and  $0.82 \pm 0.115$  respectively. The Score sensitivity of mortality were 100% and 83.33% for MPI score >20 and MOF score respectively. The lower sensitivity of MOF score was due to death of some cases above 50 years of age without organ failure. These deaths were due to sudden cardio-respiratory arrest.

**Conclusion:** Increasing MPI and MOF score were associated with poor outcome. Both MPI and MOF were good predictors of mortality in cases of peritonitis. However, MPI scoring system is better (sensitivity 100% Vs. 83.3%) predictor of mortality than MOF score.

**Keywords:** MPI score, MOF, Peritonitis, Mortality, Stratification, Morbidity

to be more practical and simple than other scoring systems like APACHE-II, which is time-consuming and not possible to apply in the setting of secondary bacterial peritonitis.<sup>7</sup> A multicenter trial including 2003 patients has also confirmed that MPI has good sensitivity and specificity.<sup>8</sup>

Organ dysfunction and failure develops with secondary bacterial peritonitis.<sup>9</sup> So it is routinely monitored in Intensive Care Unit (ICU). Multiple organ grading score system which was developed in 1985 grades the MOF patients into 3 point scale (Table-2).<sup>10</sup> The MOF scoring system includes 8 systems. These are cardiac, pulmonary, hepatic, renal, central nervous system, gastrointestinal system and haematological. The aim of the present study was to compare the performance of MPI and MOF prognostic scoring system in secondary peritonitis.

## MATERIAL AND METHODS

This was prospective observational study conducted at universal college of medical sciences and Career institute of medical science and hospital at Lucknow, a tertiary academic center with well-equipped ICU, during a period of 2 years (November 2013- October 2015). Ethical clearance was taken from college ethical committee and informed consent was obtained from each patient. *Exclusion criteria* were patients with tuberculous peritonitis, due to chemical peritonitis due to post-operative bile leak and cases with primary peritonitis (renal or hepatic failure), laparotomy done elsewhere for peritonitis or transferred out to continue treatment elsewhere. Informed consents were obtained. Clinically suspected cases of peritonitis were admitted and diagnosis was confirmed by laboratory and radiological investigations. The 110 confirmed cases were subjected to appropriate treatment and per-operative findings were noted. Operated cases were shifted to postoperative ward or ICU where monitoring is done. Data was collected on pre-structured format. Out of 110 cases, 5 cases were excluded and finally 105 cases were selected for study.

The sample size was calculated using 16% incidence from previous study using formula  $n = z^2 p q/d^2$  where  $n$  = required sample size,  $z = 1.96$  at 93% confidence interval,  $p$  = estimated incidence from previous study,  $q = 100-p$ ,  $d$  = maximum tolerable error 7%.<sup>1</sup> The sample size obtained was 105. Data were collected on a prepared format of all patients registered.

<sup>1</sup>Assistant Professor, Career Institute of Medical Sciences and Hospital Lucknow, India

**Corresponding author:** Dr. Salamat Khan, 21/204 Malhar Type Sahara States, Jankipuram, Lucknow, India

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Risk factor	Weightage (if any)
Age >50years	5
Female gender	5
Organ failure*	7
Malignancy	4
Preoperative duration of peritonitis>24 hours	4
Origin of sepsis non colonic	6
Diffuse generalized peritonitis	6
Exudates	
Clear	0
Cloudy/purulent	6
Fecal	12

\*Definition of organ failure, Kidney: Creatinine>117 µmol/L, Urea:>167 µmol/L, Oliguria:<20 mL/h, Lung: pO2<50 mmHg, pCO2>50 mmHg, Shock: hypodynamic or hyper dynamic Intestinal obstruction (only if profound), paralytic ileus >24 or complete mechanical ileus

**Table-1:** Mannheim Peritonitis Index<sup>4</sup>

Socio-demographic, clinical, laboratory results (haematological, biochemical) and surgical findings and outcome were noted. MPI score and Organ failure score were recorded on admission, after surgery, and during postoperative management. Patients were followed up until death or 30 days after discharge.

## STATISTICAL ANALYSIS

Compiled data was analyzed using SPSS version 21 and result considered significant if P was equal or less than <0.05. Chi square test and relative risk were used to check for the difference.

## RESULT

The mean preoperative duration of symptoms was 3.71 days and ranged from 12 hours-15 days with median of 3 days. The vast majority of patients (73.30%) presented during the first week after the onset of the symptoms (Table-3).

Acute appendicitis was the commonest cause of peritonitis, 56 (55.31%), followed by appendicular perforation 16 (15.23%), small bowel perforation 15 (14.28%), and peptic ulcer perforation 14 (13.32%). Other uncommon causes include uterine perforation, caecal gangrene and perforation (figure-1).

The mean preoperative duration of symptoms was 3.71 days and ranged from 12 hours-15 days with median of 3 days. Majority of patients (73.30%) presented during the first week after the onset of the symptoms (Table-3). With regards to the extent of peritonitis, 45 (42.85%) cases had generalized peritonitis and 60 (57.14%) had 1/4th peritonitis. Out of the 12 mortality,

10(83.33%) had generalized peritonitis and 2 (16.66%) had localized peritonitis (Table-4). Death of 2 cases of localized peritonitis occurred due to development of septicemia and multiple organ failure. Organ dysfunction and failure was observed in 15 (14.28%) patients. Out of 12 deaths 10 were associated with organ failure and rest 2 cases died due to sudden cardio-respiratory arrest. Death occurred due to multiple organ failure. The decreasing order of organ dysfunction/failure were, renal (15), cardiac (13), respiratory (12), liver dysfunction (9), and haematological (7) cases.

Local complication was observed in 22 cases. The overall morbidity rate was of 20.95%. Of 22 cases, 14 cases had superficial surgical site infections (SSSIs), 8 cases had septic shock, 4 cases had chest infection, one case had wound dehiscence, five had prolonged paralytic ileus. None of the case had intra-abdominal abscess, re-perforation, anastomotic leak and DVT. The commonest complication was surgical site infection (SSSI) (15.3%), followed by septic shock (8.60%), prolonged postoperative ileus up to 3-4 days (5.37%), chest infection (4.3%) and wound dehiscence (1.075%).

Relative Risk (RR) of the mortality recorded was higher inpatients aged >50 years (risk ratio 4 (CI 0.1075-0.755), Small bowel perforation 1.8 (CI 0.436-6.597) and PPU 1.5 (CI 0.58-7.59), >24 hour of pre-operation duration of symptoms 1.3 (CI 0.375-0.76.) Patient with >29 MPI score had high risk of mortality 59 (0.116-2.22).

Non survivors had higher

Organ	Normal function	Organ dysfunction	Organ failure
Lung	0 point No mechanical ventilation	1 point Mechanical ventilation with PEP<10 with FiO2<0.4	2 point Mechanical ventilation with PEP>10 with FiO2>0.4
Heart	Normal blood pressure (systolic)	BP systolic >100 mmHg with low dose of vasoactive drugs <sup>a</sup>	Periods of BP systolic <100 mmHg with high dose of vasoactive drugs <sup>b</sup>
Kidney	Serum creatinine<2 mg /dL (<150 µmmol/L)	Serum creatinine>2 mg /dL (>150 µmmol/L)	Hemodialysis and peritoneal dialysis
Liver	Normal AST and bilirubin	AST >25 unit/L Bilirubin >2mg/dL (>30 µmol/L)	AST >50 unit/L Bilirubin >6 mg /dL (>100 µmol/L)
Blood	Normal count	Leukocytes >30,000/µL Platelet count<50000/µL	Leukocytes >60,000 or <2500/µL
GIT	Normal	Stress ulcer Acalculous cholecystitis	Bleeding ulcer/necrotizing enterocolitis and or pancreatitis
CNS	Normal	Diminished responsiveness	Severely disturbed responsiveness/ Diffuse neuropathy

<sup>a</sup>=Dopamine hydrochloride <10 µg/kg/min or nitroglycerine >20 µg/kg/min and/or nitroglycerine >20 µg/kg/min volume loading; <sup>b</sup>=Dopamine hydrochloride >20 µg/kg/min volume loading; GIT=gastrointestinal tract.

**Table-2:** The Multiple Organ Failure (MOF) score<sup>10</sup>

Character	Frequency (n,%)	Mean (SD)	Median	Minimum duration	Maximum duration
Age group (years)					
<9	03(2.85)	27.28±13.4	20	66	7
10-19	33(31.42)				
20-29	17(16.19)				
30-39	17(16.19)				
40-49	13(12.38)				
>50	22(20.95)				
Sex					
Male	64(60.95)				
Female	41(39.04)				
Duration of symptoms					
≤24 hour	18(17.13)				
2-7 days	77(73.30)				
8-15 days	08(07.61)	3.7±3.26	3	12 hours	15
>15 days	02(03.80)				
Duration of hospital stay (days)					
1-7	65(61.88)				
8-14	35(33.32)	7.85±1.59	8	3	40
15-21	02(1.90)				
≥22	03(2.80)				

**Table-3:** Characteristics of the subjects (N=105)

MPI score	Generalized peritonitis		Localized peritonitis		Total
	Survivors	Death	Survivors	Death	
≤20	22	00	57	00	79
21-29	12	06	01	02	21
>29	01	04	00	00	05
Total	35	10	58	02	105

**Table-4:** Distribution of peritonitis in 3MPI groups

Parameter	Mortality rate	Risk ratio (95%CI)
Age (years)		
<50	8.64%(7/81)	Base line
>50	41.61(5/12)	4.8(0.1075-0.755)
Cause of peritonitis		
AA and AP	1.4(1/71)	Base line
SBP	2.6(4/15)	1.8(0.436-6.597)
PPU	2.1(3/14)	1.5(0.58-7.59)
Interval till surgery		
<24 hour	10(2/20)	Base line
>24 hour	13.6(10/73)	1.36(0.375-0.76)
MPI score		
<21	1.38(1/74)	Base line
21-29	28.8(7/18)	20.7(0.35-6.61)
>29	86.0(4/1)	59.59(0.116-2.22)

a=AA, acute appendicitis, AP, appendicular perforation. b=SBF, small bowel perforation. c=PPU, peptic ulcer perforation

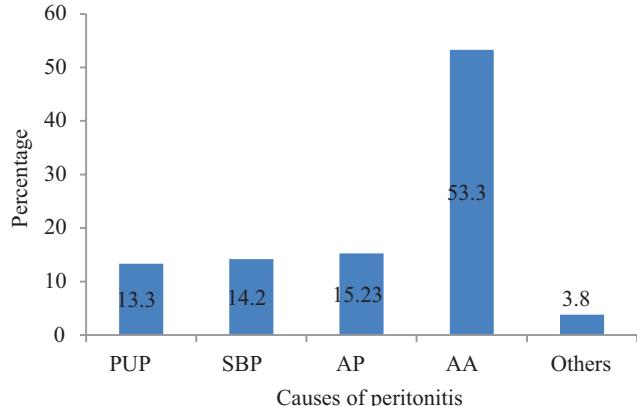
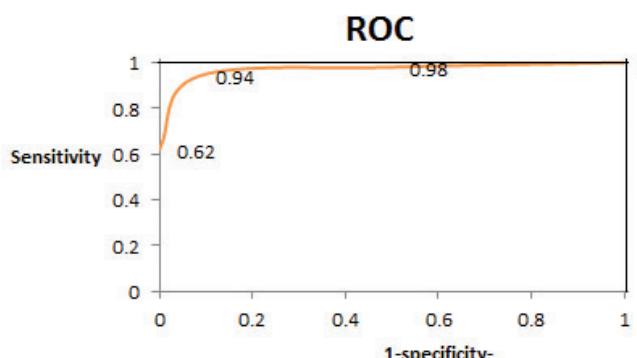
**Table-5:** Relation of patient's parameters to death

Parameter	Survivors (n =93)	Non survivors (n=12)	P-value
MOF score	0.82±0.115	3.80 ±1.74	<0.001
MPI score	17.48±5.8	28.50±3.6	<0.001

**Table-6:** Distribution of MOF score and MPI score among survivors and non survivors

Score	Sensitivity
MPI score at 20	100%
MOF score	83.3%

**Table-7:** Sensitivity of score for mortality

**Figure-1:** Distribution of cases in different etiologies**Figure-2:** Mortality ROC curve for sensitivity and specificity. Area under the curve is 0.922 with a sensitivity of 50.0% and specificity of 98.5% at an MPI of 27 points.

mean( $5.9 \pm 0.831$ ) compared to survivors ( $3.25 \pm 0.95$ ). This difference is statistically significant ( $P < 0.001$ ). Similarly, non-survivors had higher MPI mean( $28.50 \pm 3.6$ ) compared to survivor ( $17.48 \pm 5.8$ ). This difference is statistically significant ( $P < 0.001$ ) (Table-6).

The area under the curve (AUC) of the receiver operating characteristic(ROC) curve analysis for predictive power of MPI was 0.922 with sensitivity of 50% and specificity of 98.5% at an MPI of 27 points in hospital mortality (figure-2)

## DISCUSSION

Previous reports of studies conducted at multiple centers have confirmed mortality rates in peritonitis continues to be high ranging from 19.5% to 60% despite advances in antimicrobials, critical care management and aggressive surgical techniques.<sup>1-4</sup> In the present study, mortality rate was 11.4%. This lower rate of mortality was because of sample demographics as it constituted localized and generalized peritonitis.

Present study showed increasing mortality rates with increasing MPI score. Mortality rate of 0%, 61.5% and 80% was observed at MPI score of  $\leq 20$ , 21-29 and  $> 29$ . On stratifying patients in 2 MPI score of  $\leq 27$  and  $> 27$ , mortality rates were 6.1% and 85.7% respectively. The lowest (0%) mortality was at  $\leq 20$  and highest (85.7%) at  $> 27$  MPI score. This shows that there was strong association between increasing mortality with increasing MPI score. Sensitivity and specificity of MPI score at  $> 27$  and  $> 29$  were 50%, 33% and 98%, 9% in both scores respectively.

The cutoff point of zero mortality and highest mortality and sensitivity and specificity of MPI score for predicting mortality varies in different studies.<sup>11-13</sup> This difference could be because of demographics of sample.

Organ dysfunction and failure was observed in 15 (14.28%) patients. Out of 12 mortality recorded, 8 had multiple organ failure. The difference in the mortality between presence and absence of organ failure was statistically significant ( $P < 0.001$ ). The decreasing order of organ dysfunction/failure were, renal (15), cardiac (13), respiratory (12), liver dysfunction (9), and haematological (7) cases. There were 2 cases of CNS dysfunction in non-survivors and none in survivors. There was no a single case of GI failure as defined in MOF score. There was very low incidence of CNS and GI failure and rarely associated with poor outcome. This finding is consistent with reports of previous workers.<sup>1</sup> Due to lack of clear definition and poor incidence original MOF was revised in 2002 that does not include GI and CNS system.<sup>15</sup> Non- survivors had mean MOF score  $5.90 \pm 0.831$  and survivor had a mean of  $3.25 \pm 0.95$ . This difference is statistically significant ( $P < 0.001$ ).

Age as risk factor was associated with outcome. Patients  $< 50$  years of age with three or four organ failure and patients  $> 50$  years of age with 1 or 2 organ failure carry poor prognosis. None of the patient  $< 50$  years of age died without organ failure whereas 2 of the patient  $> 50$  years of age died suddenly due to cardio-respiratory failure. These finding suggests that age plays an important role in mortality. The mortality rate of 50% and 6.4% was associated with  $> 50$  and  $< 50$  years of respectively. Patients with MPI  $> 29$  score with one failing organ and or age  $> 60$  years had poor outcome. There is strong association in mortality with increase in MPI and MOF score.<sup>1,11-13</sup>

Previous studies have confirmed that mortality prediction of

MPI scoring system is comparable to the other scoring system like APACHE II.<sup>12,14</sup> In the present study, both MPI and MOF scoring system have shown increasing mortality with increasing MPI and MOF score. The Score sensitivity of mortality were 100% and 83.33% for MPI score 20(cutoff point) and MOF score respectively (Table-7). The lower sensitivity of MOF score was due to death of some cases above 50 years of age without organ failure. The present study shows that MPI had higher sensitivity in prediction of mortality than MOF. To the best of my knowledge this finding was not reported by previous workers.

## CONCLUSION

Increasing MPI and MOF score were associated with poor outcome. Both MPI and MOF scores were good predictors of mortality in cases of peritonitis. However; MPI scoring system is more sensitive than MOF score.

## Recommendation

MPI score is easy, more sensitive, can be used in stratification of cases of peritonitis for choosing appropriate treatment and prognosticating outcome.

## Limitation

The study included both localized and generalized peritonitis. The cases of generalized peritonitis are less in number. Further studies are required to validate the finding of the present study

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# Comparison of Morphometric Parameters in Suprabasal Cells in Epithelial Hyperplasia, Leukoplakia and Squamous Cell Carcinoma: an Image Analysis

Shilpi<sup>1</sup>, Shaleen Chandra<sup>2</sup>, Fahad M Samadi<sup>3</sup>, Gadiputi Sreedhar<sup>4</sup>, Jiji George<sup>5</sup>, SH Thippeswamy<sup>6</sup>

## ABSTRACT

**Introduction:** Computerized image analysis (CIA) based assessment of routine H and E staining pattern enables objective interpretation and quantification for differential diagnosis of the state of pathology elucidated by the tissue being investigated. Aim and objectives: The aim of this study was to establish the morphometric parameters of normal oral epithelial cells in the supra-basal cell layers.

**Material and methods:** This was a comparative study conducted on H and E stained tissue sections from epithelial hyperplasia, dysplasia, squamous cell carcinoma and normal oral mucosa. The Morphometric analysis of Images captured using digital camera under 10x magnifications was done using image analyzer software, IMAGE PROPLUS 4.1. The software automatically calculated cell and nuclear area with manually traced cells. The N/C ratio was calculated manually.

**Results:** Quantification of suprabasal cells gave accreditation for identification of cell layers. Morphometric parameters showed significant variations to differentiate grades of dysplasia and sites of oral epithelium.

**Conclusion:** The simple, inexpensive and easy morphometric analysis method can make the histomorphological study of tissues with premalignant lesions a more objective and practically applicable one for the early detection of cancer. Thus, morphometric analysis could serve as a discriminatory model and help in more accurate assessment of lesions which are highly proliferating and dysplastic and their malignant potential.

**Keywords:** Morphometry, OSCC, suprabasal cells

## INTRODUCTION

Oral cancer is the sixth most common cancer worldwide and has been marked by high morbidity and poor survival rates that have changed little over the past few decades. Beyond prevention, early detection is the most crucial determinant for successful treatment, better prognosis, and survival of cancer. Yet current methodologies for cancer diagnosis based upon pathological examination alone are insufficient for detecting early tumor progression and molecular transformation.<sup>1</sup> In India, approximately 94% of oral malignancies are those of oral squamous cell carcinomas (OSCC) whose etiology is multifactorial with various intrinsic and extrinsic factors.<sup>2</sup>

Computerized image analysis (CIA) based assessment of immunostaining pattern enables objective interpretation and quantification for differential diagnosis of the state of pathology elucidated by the tissue being investigated. Yaziji and Barry<sup>3</sup> in their investigations on Diagnostic Immunohistochemistry reported the main biases in conventional methods of semi-quantitative diagnostic reporting viz. reaction bias (in specimen fixation, tissue processing, antigen retrieval and detection system) and interpretation bias (in the selection of antibody panels,

sensitivity of the chosen panel, choice of antibody types and clones, results and literature interpretation).

The quantitative and qualitative analysis of several parameters such as nuclear cytoplasmic ratio and cellular/nuclear area, may reveal incipient cellular changes and thus offer high reliability over routine histopathological examination, in impending and frank malignancies of the oral cavity, in terms of early diagnosis and better treatment.

The aim of this study was to establish the morphometric parameters of normal oral epithelial cells in the supra-basal cell layers.

## MATERIAL AND METHODS

This was a comparative study conducted in the Department of Oral Pathology and Microbiology, Babu Banarsi Das College of Dental Sciences, Lucknow. The study was approved by the Ethical Committee of the Institute and consent from each individual was taken before enrolling in the study. The study was conducted on tissue specimens retrieved from the archives and from freshly biopsied formalin fixed tissues. The control group (n=20) comprised normal tissue from healthy adult individuals irrespective of age with no habits. The tissue was retrieved from adjacent to surgical area during routine surgical procedure. The study group consisted of 60 paraffin blocks with tissues obtained during biopsy which were confirmed histopathologically for Epithelial hyperplasia, Dysplasia and Squamous Cell Carcinoma, 20 each.

### Inclusion and exclusion criteria

Healthy individuals without any systemic and mental ailments and without any habit, irrespective of age and gender were included in the study. Clinically diagnosed white lesions with histological evidence of epithelial hyperplasia and without histological evidence of epithelial dysplasia were included in the study. Clinically diagnosed cases of leukoplakia, with histological evidence of epithelial dysplasia and histopathologically

<sup>1</sup>Senior Resident, <sup>2</sup>Professor and Head, <sup>3</sup>Assistant Professor, Department of Oral Pathology and Microbiology, King George Medical University, <sup>4</sup>Professor and Head, <sup>5</sup>Professor, <sup>6</sup>Ex Reader, Department of Oral Pathology and Microbiology, Babu Banarsi Das College Of Dental sciences, India

**Corresponding author:** Dr. Shilpi, B.D.S, M.D.S., Senior Resident, Department Of Oral Pathology and Microbiology, King George Medical University, Lucknow – 226003, India

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confirmed cases of oral squamous cell carcinoma, irrespective of its aetiology were included in the study. For every case, the most representative areas were selected from sections which could be subjected to morphometric analysis. Those patients with hyperkeratinized tissue were excluded. Improperly fixed tissues were excluded.

All biopsy specimens were fixed in 10% formalin for 24 hours, dehydrated in increasing concentrations of ethanol, cleared in Xylene, impregnated in paraffin wax and embedded in paraffin wax and tissue block were prepared. Tissue sections of 5  $\mu\text{m}$  thickness were cut using a soft tissue microtome. The sections obtained were stained with Harris Hematoxylin and Eosin. The stained sections were observed under microscope using WHO 2005 criteria to establish the grade of Epithelial Dysplasia.

#### Morphometric technique

##### Morphometric analysis of tissue sections

For morphometric analysis, images were captured using digital camera attached to a Binocular research microscope with a 4x objective. The actual measurements were done using the Image Proplus 4.1 after accurate calibration. Images were captured, stored and arranged according to the study groups.

Microscopic fields were selected randomly, commencing with first representative field on the left hand side of the section, then moving the stage to the next field and then continuing the selection to include a minimum of 7 fields from each section. For each section, the selected field included representative largest cells where distinct cellular and nuclear outlines were seen avoiding areas of overlapping cells. Histologically identifiable non-keratinocytes were not measured. The images were classified, transferred and stored in the computer. The measurements were done using Image Proplus 4.1 on the same fields (figure-1).

##### Measurements of morphometric parameters

**Cell area (CA):** It was measured in microns Square. For measurement, the cell perimeter was traced and software automatically calculated the cell area. For each field 5 largest cells with clear outlines were selected.

**Nuclear Area (NA):** Similar to cell area, nuclear outlines of the same cells which were used for cell area were traced.

The 5 largest cells and nuclei in each compartment were selected on the assumption that the plane of section would have passed through the centre of the cell or nuclei being measured and would more closely represent the actual size. This method also assumed that the cells in one compartment were more or

less of similar size.

##### Nuclear-Cytoplasmic ratio (N/C):

The Nuclear cytoplasmic ratio was calculated as below:

N/C = Nuclear area/ Cell area- Nuclear area

The outline of cells and nuclei where a complete outline could be clearly seen was traced on the screen. The cellular and nuclear measurements were carried out using measurement toolbars of the software.

#### STATISTICAL ANALYSIS

The results are presented as mean area and the data collected in this study were analyzed statistically by computing descriptive statistics, viz., mean and standard deviation. The differences in the control group and study groups for various diagnostic variables were compared by means of analysis of variance (ANOVA) followed by Turkey's test for pairwise comparisons. The comparison of morphometric parameters between buccal and gingival mucosa were compared by using Unpaired t-test. The results were considered statistically significant whenever  $p<0.05$ . All the analysis was carried out by using SPSS 16.0 version (Chicago, Inc., USA).

#### RESULTS

The analysis of variance showed that there was significant ( $p=0.0001$ ) difference in the cell area in suprabasal cells among the groups. The post-hoc intergroup comparison test revealed that there was significant ( $p=0.0001$ ) difference in cell area between pair of groups. The cell area was found to be lower in SCC ( $144.71\pm1.17$ ) than dysplasia ( $155.27\pm1.37$ ), hyperplasia ( $159.72\pm2.03$ ) and controls ( $149.50\pm1.37$ ). However, the nuclear area was observed to be lower in controls than controls ( $50.68\pm1.06$ ) than hyperplasia ( $51.91\pm1.64$ ), dysplasia ( $61.36\pm1.21$ ) and OSCC ( $68.74\pm1.01$ ) which statistical significant ( $p=0.0001$ ). Similar observation was found in the ratio of nuclear/cytoplasmic area in suprabasal cells among the groups (Table-1).

There was significant ( $p<0.01$ ) difference in the cell and nuclear area among different grades of dysplasia in suprabasal cells. The cell area was significantly ( $p=0.001$ ) lower in normal ( $149.50\pm1.37$ ) than mild dysplasia ( $155.98\pm1.88$ ), moderate dysplasia ( $156.17\pm1.95$ ) and severe dysplasia ( $157.19\pm1.26$ ). The similar pattern was observed for nuclear area and Nuclear - Cytoplasmic ratio (Table-2).

The cell and nuclear area were significantly lower ( $p=0.0001$ ) in buccal mucosa than gingival mucosa in suprabasal cells. However, reverse relationship was found for Nuclear - Cytoplasmic ratio (Table-3).

#### DISCUSSION

In this study, the suprabasal cell area in well differentiated OSCC ( $144.71\pm1.17 \mu\text{m}^2$ ) was reduced in comparison to normal mucosa and dysplasia ( $149.50\pm1.37 \mu\text{m}^2$ ,  $155.27\pm1.37 \mu\text{m}^2$ ). The findings of our study are in accordance with Ramesh et al<sup>14</sup> who has observed the decreased cell area from normal >dysplastic > SCC. The reason for the same was explained by Gao et al<sup>15</sup> that as the carcinogenesis progresses shrinkage of cell junctions lead to increase in intercellular spaces and ultimately there is decrease in cell area.

Suneet et al<sup>6</sup> found increased NA in smears from keratinocytes

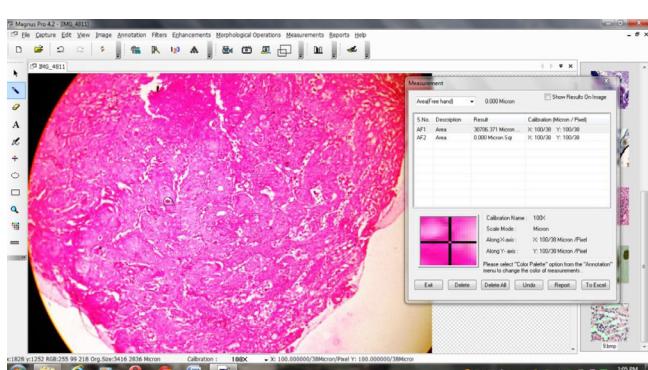


Figure-1: Shows software for image analysis and measurements

Groups	Cell area (in micron square)	Nuclear area (in micron square)	Nuclear-Cytoplasmic area ratio
Control	149.50±1.37 <sup>a</sup>	50.68±1.06 <sup>a</sup>	0.51±0.01 <sup>a</sup>
Epithelial Hyperplasia	159.72±2.03 <sup>a</sup>	51.91±1.64 <sup>a</sup>	0.48±0.04 <sup>a</sup>
Dysplasia	155.27±1.37 <sup>a</sup>	61.36±1.21 <sup>a</sup>	0.65±0.01 <sup>a</sup>
OSCC	144.71±1.17 <sup>a</sup>	68.74±1.01	0.90±0.02
ANOVA p-value	0.0001*	0.0001*	0.0001*

\*Significant, <sup>a</sup>p=0.0001

**Table-1:** Comparison of morphometric parameters in suprabasal cells

	Cell area	Nuclear area	Nuclear - Cytoplasmic ratio
Normal ( control )	149.50±1.37 <sup>a</sup>	50.68±1.06 <sup>a</sup>	0.51±0.03 <sup>a</sup>
Mild dysplasia	155.98±1.88 <sup>a</sup>	60.98±2.01 <sup>a</sup>	0.64±0.01 <sup>a</sup>
Moderate dysplasia	156.17±1.95 <sup>a</sup>	61.76±1.27 <sup>a</sup>	0.65±0.02 <sup>a</sup>
Severe dysplasia	157.19±1.26 <sup>a</sup>	61.98±0.57 <sup>a</sup>	0.65±0.03 <sup>a</sup>
ANOVA p-value	0.0001*	0.001*	0.001*

\*Significant, <sup>a</sup>p=0.001

**Table-2:** Comparison of cell, nuclear area and nuclear - cytoplasmic ratio in suprabasal cells of different grades of dysplasia

	Cell area	Nuclear area	Nuclear - Cyto-plasmic ratio
Buccal	149.50±1.37	50.68±1.06	0.51±0.02
Gingival	187.27±1.56	58.02±0.99	0.44±0.01
p-value <sup>1</sup>	0.0001*	0.0001*	0.0001*
<sup>1</sup> Unpaired t-test			

**Table-3:** Comparison of Cell and Nuclear area between Buccal and Gingival mucosa in suprabasal cells

of OSCC and concluded that increased NA is due to increased DNA synthesis. Callimeri and Smith<sup>7</sup> found that an increased nuclear to cytoplasmic ratio was one of the consistent findings during progression from benign to a state of malignancy.

In a morphometric study on gastric precancerous lesions, morphometry was effective in distinguishing mild, moderate, severe epithelial dysplasia and carcinoma. The carcinogen induced cellular changes in epithelia. There was progressive increase in size and number of progenitor cells with slight increase in the more matured cells.<sup>8</sup>

Abdel – Salam et al<sup>9</sup> conducted an image cytometry study in oral hyperplasia and dysplasia. They found that nuclear area is a useful parameter for discriminating among the various groups. Overlap between the moderate and severe dysplasia group were seen. There was increase in cell area, nuclear area and N/C ratio in suprabasal cell layers of dysplastic epithelium as compared to normal. Morphometric parameters showed intergrade difference to differentiate among grades of dysplasia with significantly highest nuclear area in severe dysplasia and lowest cumulative values in mild dysplasia. The findings of the present study is similar to the above mentioned study.

The site wise variation in the N: C ratio was explained by Jin. et al<sup>10</sup> that the mean N: C ratio in palatal mucosa was 0.618±0.98. It was observed that N:C ratio in palatal mucosa are higher compared to the values of normal buccal mucosa in our study. There are many qualitative studies on the cellular morphology of normal and abnormal epithelia, but few have recorded actual size or area of individual cell types, with very few studies involving oral epithelium. Hence, no comparisons could be made with their data.

## CONCLUSION

The simple, inexpensive and easy morphometric analysis

method can make the histomorphological study of tissues with premalignant lesions a more objective and practically applicable one for the early detection of cancer. Thus, morphometric analysis could serve as a discriminatory model and help in more accurate assessment of lesions which are highly proliferating and dysplastic and their malignant potential.

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# Diagnostic Utility of Bone Marrow Aspiration and Biopsy in Paediatric Age Group

Lalita Y. Patil<sup>1</sup>, Yoganand V. Patil<sup>2</sup>, Grace D'Costa<sup>3</sup>, Arvind Valand<sup>4</sup>

## ABSTRACT

**Introduction:** Bone marrow examination required for differential diagnosis of various myelo and lymphoproliferative disorders; their prognostic classification and assessment of status during and after therapy, staging of lymphoma and marrow infiltration. Study aimed to evaluate the contribution of bone marrow aspiration and trephine biopsy to the final diagnosis.

**Material and methods:** Two and half year study of BM trephine biopsy lesions in pediatric population (0 to 18 yrs). BM biopsy processed with H and E stain and special stains.

**Results:** maximum cases were male s and from age group of 12-18 yrs, fever is the most common symptom and pallor is most common sign encountered, majority cases were anemias followed by infectious disease, Leukemias and ITP. BM aspiration and BM Biopsy are complimentary to each other in 72.5% cases.

**Conclusion:** Bone marrow Aspiration and BM Biopsy are confirmative for tissue diagnosis and plays important role in clinical diagnosis, prognosis and also to decide line of management.

**Keywords:** Pediatric Bone Marrow Aspiration, Bone marrow Biopsy

## INTRODUCTION

During the past decades there have been major advances in the understanding of disorders of the blood accompanied by increasing recognition of the complex structural and hormonal interrelations between the cellular and tissue elements of the marrow. Improvements in biopsy technique as well as technical progress in their preparation have provided additional impetus to the study of the bone marrow as an organ with architecture and components intact in their natural spatial context.<sup>1</sup> The indications stem from many fields including hematology, immunology, oncology and rheumatology. Improved needles permit the simultaneous performance of aspiration and biopsy. The former is particularly useful for cytological details, cyto-chemical stains and immunological markers while the latter permits a complete assessment of marrow architecture. In hematology, bone marrow examination is needed for the differential diagnosis of various myelo- and lymphoproliferative disorders; their prognostic classification and assessment of status during and after therapy, staging of lymphomas and marrow infiltration by foreign cells.<sup>1-3</sup> In this study we aim to demonstrate the utility of the bone marrow trephine biopsy, assess its contribution to the final diagnosis in the pediatric population and demonstrate the spectrum of lesions encountered in the pediatric age group in a large general tertiary care teaching hospital.

## MATERIAL AND METHODS

This study comprises a two and a half year study of bone marrow trephine biopsy lesions in the pediatric population

(age group 0 to 18 years) in Grant Medical College and Sir J.J. Hospital Mumbai. Total 120 cases were included in the study based on the inclusion and exclusion criteria. Institutional ethical committee has approved the study. A detailed clinical history, general and systemic examination were noted and this information was recorded in the Performa. Every case is investigated with peripheral blood smear, complete blood count along with haematological parameters like bleeding time (BT), clotting time (CT), aspiration and bone marrow biopsy. A written informed consent was taken in all cases. A bone marrow aspiration and biopsy from the posterior superior iliac supine were done using the aspiration needle and Jamshidi needle respectively. The bone marrow aspiration needle no 18 was introduced and when the marrow cavity was entered, a 20 cc plastic syringe was attached to the needle after withdrawing the stiletto and suction was applied to obtain the bone marrow aspirate. Smears were made of the aspirate immediately and stained with Leishman's stain. A small nick was made with the scalpel blade and the Jamshidi needle (No.11) with the stilette locked in place was advanced through the lesion pointing in the direction of anterior superior iliac supine into the bony cortex into clockwise and anticlock wise motion was made to obtain the bone marrow core. the needle was rotated completely several times along its long axis and removed with alternating rotary motions. Gauze was held at the biopsy site giving pressure for a few minutes. The biopsy specimen was expelled through the proximal end. It was put in buffered formalin fixative and taken for routine processing. In all cases routine H and E stain was done. Special stains, like Reticulin stain, Masson Trichrome and Prussian Blue were done wherever necessary.

## STATISTICAL ANALYSIS

Descriptive statistics like mean and percentages were used to interpret results.

## RESULTS

This was two and half years prospective study of bone marrow trepene biopsy lesions encountered in the pediatric population.

<sup>1</sup>Associate Professor, Department of Pathology, T.N. Medical College and B.Y. Nair Hospital, <sup>2</sup>Sr. Pathologist, Jagjivan Ram Hospital (W. Rly) Mumbai Central, <sup>4</sup>Professor and Head, Department of Pathology, Grant Medical College and Sir J. J. Hospital, Mumbai, <sup>3</sup>Professor and Head, Department of Pathology, SRTG Government Medicine College, Ambejogai, Maharashtra, India

**Corresponding author:** Dr. Lalita Yoganand Patil, Department of Pathology, T.N. Medical College and B.Y. Nair Hospital, Mumbai Central, Mumbai 400008, India

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An analysis of the age distribution pattern indicates that the maximum number of cases was in older age groups, the maximum being 57/120 cases (47.5%), in oldest age range of 12-18 years. This was followed by the age range 5-12 years i.e. 31/120 cases (25.83%) and 1-5 years 28/120 cases (23.33%). The minimum number of cases 4/120 (3.3%) were in the age group of less than 1 year. No neonates were encountered in the study. The sex distribution pattern indicates a higher percentage of males 75/120 cases (62.50%) compared to females 45/120 cases (37.5%). Male to female ratio being 1.66. An analysis of clinical symptomatology indicates that the fever was the commonest symptom encountered, seen in 68/120 cases (56.6%) followed by general debility – 46/120 cases (38.3%). GI disturbances like anorexia, nausea, abdominal distension, and bleeding tendencies were the next most commonly seen symptoms 29/120 cases (24.2%) and 22/120 cases (18.3%) respectively. The various types of bleeding tendencies encountered were epistaxis, bleeding gums, malena, hematemesis, hemoptysis, menorrhagia, ecchymotic patches and the commonest was epistaxis. The least frequently encountered symptoms were pica and amenorrhea cases 1/120 (0.8%). An analysis of the signs elicited recorded that pallor was the commonest clinical sign encountered – 112/120 cases (93.3%) cases. The sites of pallor being conjunctiva, tongue, palm etc. this was followed by hepatosplenomegaly seen in 34/120 cases (28.3%) cases. The next commonest sign encountered was isolated splenomegaly 18/120 cases (15%). This was followed by icterus 13/120 cases (10.8%) and edema 12/120 cases (10%). The commonest site of edema was feet. The least frequent elicited sign was sternal tenderness 4/120 cases (3.33%). A broad analysis of the combined findings of the peripheral smear, bone marrow aspirates and trephine biopsy showed that the majority of cases were of anemias 74/120 cases (61.66%). This was followed by infectious diseases 14/120 cases (11.66%). We encountered only 10 cases of leukemias and ITP each (8.33%). Of the 10 cases of leukemia, 8 were ALL, 3 being L1 and 1 L2 and 2 were AML- one being M4 and other M6. Split up of ITP was – 8 cases of acute ITP and 2 of Chronic ITP. We encountered 4/120 cases (3.33%) of marrow eosinophilia which were clinically diagnosed as hypereosinophilic syndrome. The least frequently encountered lesions were metastasis, storage disorders, myelofibrosis and hypersplenism 2/120 cases each (1.66%). The metastasis seen were both from malignant small round cell tumor i.e. neuroblastoma and PNET. The storage disease split up was – one case of Gaucher's and one case of Niemann Pick disease each the 2 cases of myelofibrosis included 1 primary and the other secondary to Hodgkin's disease. Both the cases of hypersplenism were secondary to pancytopenia. Of the 74 cases of anemias the majority i.e. 45/74 cases (60.81%) were dimorphic anemias followed by iron deficiency anemias 10/74 cases (13.51%), This was followed by haemolytic anemias 9/74 cases (12.16%), the subgroups being thalassemia 4/9 cases (44.44%), sickle cell disease 2/9 cases (22.22%) and elliptocytosis 1/9 cases (11.11%); the cause of the other two was unknown. Hypoplastic/aplastic anemias constituted 7/74 cases (9.45%). Pure megaloblastic anemia was infrequently encountered 3/73 cases (4.05%). An analysis of the spectrum of infections encountered reveals that in the majority of cases the cause was non specific with marrow showing evidence of

myeloid hyperplasia 6/14 cases (42.9%). Specific infections like malaria and kala-azar were seen in 4/14 cases (28.6%) and 3/14 cases (21.4%) respectively. We had a single rare case of haemophagocytic syndrome (7.1%). Correlation of the clinical diagnosis and bone marrow diagnosis showed that in the majority of cases 57/120 cases (47.5%) the aspirate and biopsy both confirmed the clinical diagnosis. The biopsy and/or aspirate alone gave the diagnosis in a significant 51/120 cases (42.5%) while it was non contributory in a smaller number of cases i.e. 12/120 cases (10%) where the biopsy was inadequate. A comparative evaluation of bone marrow aspiration and biopsy showed that both the procedures were complementary to each other in majority of the cases – 87/120 (72.5%) the bone marrow trephine alone gave diagnosis in 17/120 cases (14.16%) the majority of which yielded a dry tap on aspiration either due to hypocellular marrow the cause being hypoplastic anemia, myelofibrosis; or hypercellular marrow as in the cases of leukemia and metastasis. The aspirate was dilute in a few cases and thus inconclusive for opinion. Bone marrow aspirate alone gave the diagnosis in 16/120 cases (13.33%). Out of these 16 cases, in 12 cases biopsy was inadequate; two cases were of kala-azar and two of malaria where the LD bodies and schizonts could not be detected on the trephine biopsy.

## DISCUSSION

In recent years, the indications for bone-marrow biopsy have broadened so that they have now been employed in the investigation of many disorders in hematology, internal medicine, oncology and osteology. The upsurge of interest was spurred by improvement in instrumentation for taking the bone marrow biopsy as well as in processing techniques. The most frequent indication for bone marrow examination was unexplained anemias – 42/120 cases (35%) with or without organomegaly mainly hepatosplenomegaly – 18/120 cases (15%) and PUO – 6/120 cases (5%). This contrasts with the study of Githang et al<sup>3</sup> who got the maximum number of requisitions for bone marrow examination for hematological and non-hematological malignancies – 46%. We encountered only 10 cases of leukemias, 8.33% out of which 8 were ALL constitutes 85% of childhood hematological malignancies and AML – 15%, Miller et al<sup>2</sup> However the study of Hasenbegvoic et al found<sup>4</sup> an equal frequency of ALL and AML and a lower percentage of leukemias – 2.66% compared to our figure of 8.33%. One of the patients presented with pancytopenia (subleukemic leukemia) and bone marrow aspirate and biopsy confirmed the diagnosis. Out of 8 cases of ALL, 3 were L1 (27.5%) and 5 were L2 type (72.5%); here the proportion is in reverse compared to literature which states that the percentage of L1 is higher, but this variation can be because more of our patients were in older age group as this fact is well documented by the study of Vienna MB<sup>5</sup> and Lilleyman JS<sup>6</sup> who found that an age more than 10 years was associated with L2 and a poorer prognosis. 2 of our patients were diagnosed as AML the subtype being – M4 and M6 – one case each. Neither of these cases were clinically suspected as AML; the clinical suspicion being CML in one case and ITP/ aplastic anemia in other because of confusing clinical features and ultimately the bone marrow examination gave the diagnosis. According to Caplin C et al,<sup>7</sup> the risk of missing leukemias in patients having typical features

of ITP is less than 1% and they did not find even a single such case in a study of 332 cases who presented with ITP like features. But we found one such case. Batra et al<sup>8</sup> have also described bleeding manifestations and thrombocytopenia of short duration in ¼ (25%) of in the pediatric age group constituting only 2-7% of AML cases, the clinical presentation being similar to adult patients. We did not encounter a single case of described in the literature- Hann et al.<sup>9</sup> We encountered 10 cases – 8.33% of ITP and subcategorized these into acute – 8 cases and chronic – 2 cases. All the patients were under 15 year of age. This is in correlation with the literature 2 which describes acute ITP in children more frequently compared to adults and chronic ITP more frequently in adults. There were 4 cases showing eosinophilia in the peripheral blood and clinically suspected to be having hypereosinophilic syndrome; all the 4 demonstrated marrow eosinophilia on aspirate as well as trephine biopsy, thereby confirming the clinical diagnosis. The least frequently encountered lesions were metastasis, storage disorders, and myelofibrosis and hypersplenism – 2/120 cases each – 1.66%. Of the 2 cases of metastasis one was secondary to neuroblastoma and the other secondary to PNET. 50% cases bone marrow aspirate and biopsy gave the diagnosis and in the other 50% it was only the biopsy that gave the diagnosis as the aspirate was a dry tap. In the study of Penchansky et al,<sup>10</sup> a similar result was obtained, in which half the number of cases required bone marrow aspiration and bone marrow biopsy for the diagnosis and the other half were diagnosed only by the bone marrow trephine biopsy, emphasizing the fact stressed in the literature that both these procedures are complimentary in the workup for metastasis-Penchansky et al.<sup>10</sup> This study also emphasizes that no single hematological parameter is predictive of bone marrow metastasis, but these authors found that the percentages of Hb and platelet count pancytopenia with a haemoglobin value of 6 gm% and the other one showed microcytic hypochromic anemia, with a haemoglobin value of 9.5 gm%.

There were 7 cases clinically suspected to be lymphoma but none showed bone marrow involvement. Bone marrow metastasis was also not detected in a clinically diagnosed case of soft tissue sarcoma. Thus out of the total 10 cases of non hematological malignancies only two (20%) showed bone marrow involvement. This figure is slightly higher than that of Valdes S. M. et al<sup>11</sup> who detected bone marrow involvement in 17.5% cases, of non hematological malignancies. The series of Penchansky et al<sup>10</sup> however found evidence of metastasis in a very high percentage of cases-45 percent in their series of non- hematological malignancies. We encountered two cases of storage disorders; the patients presented with hepatosplenomegaly and were clinically suspected to be having a storage disorder. The bone marrow aspirate in both the cases was dilute and it was the biopsy which confirmed the diagnosis. One case was diagnosed as Niemann-Pick and the other as Gaucher's. We also encountered two cases of myelofibrosis-one a known case of MDS and clinically suspected to have progressed to CML and the other secondary to lymphocytic depleted Hodgkin's Lymphoma. In both the cases aspirate was a dry tap and the biopsy gave the diagnosis. In the case of Hodgkin's lymphoma, the lymphoma cell however could not be detected as a result of extensive myelofibrosis, studies of bone marrow trephine biopsies in cases of Hodgkin's disease

(Mahoney et al)<sup>12</sup> indicate that patients with bone marrow disease have a stage IIIB disease, pre biopsy. Positive bone marrow results do not effect a change in therapy. The small number of positive cases does not allow any prediction as to prognosis and there is no role for bone marrow biopsy with a clinical stage of I-IIIA Hodgkin's disease.

Out of 10 cases of all malignancies that is hematological and non hematological that we encountered in our study. None showed evidence of myelonecrosis while the same is described by Pui CH et al<sup>13</sup> in 0.5% of their patients with malignant diseases. The percentage of leukemic patients showing myelonecrosis is quite high in the study of Prajapati N C et al<sup>14</sup> -6.66%. and they noticed that thrombocytopenia/leucopenia was the common presenting feature.

Out of 74 cases of anemias, the majority were due to dimorphic anemias- 60.81% i.e. a combination of iron deficiency and B12 deficiency anemia showing micronormoblastic and megaloblastic change, this figure is much higher than that of Hasenbegovic et al<sup>4</sup> who found it in only 9.3% of their cases. Pure iron deficiency anemia manifesting as micronormoblastic maturation in the marrow was seen in 13.51% cases, more than the percentage found by Farhi et al<sup>15</sup>-8% but much less than the percentage of Buhr T et al<sup>16</sup>-22.7% and Gomber et al<sup>17</sup> -68.92%, however this percentage includes both a pure and mixed type of iron deficiency anemia. The other group of deficiency anemias i.e. megaloblastic anemias constituted -4.05% of cases, this figure is similar to that of the study of Farhi et al<sup>18</sup> and Buhr T et al<sup>19</sup> who found pure megaloblastic anemia in 4% and 3% of their cases respectively, but higher than the figure of Hasenbegovic et al<sup>4</sup> who found in only 1.3% of his cases. The study of Gomber et al<sup>17</sup> however found a much higher percentage of 28.42% cases but this includes both pure and mixed type of B12 deficiency. We encountered 12.16% cases of hemolytic anemias, more than the percentage of Buhr T et al<sup>19</sup> -7.2%. The subgroups of hemolytic anemia being four cases of thalassemia, two cases of sickle cell disease, one case of elliptocytosis and unknown causes in the other biopsy. Aplastic / hypoplastic anemias constituted – 9.45% of anemias is higher than the – 6.8% found by Buhr et al.<sup>18</sup> The cases of aplastic/ hypoplastic anemias- showed evidence of pancytopenia on the peripheral smear, the aspirate showed a dry tap except in one case and it was the trephine which confirmed the diagnosis. This compares well with study of Gruppo et al<sup>19</sup> who found bone marrow trephine biopsy to be an important and reliable indicator of marrow cellularity as compared to aspiration in diagnosing aplastic anemias and leukemias.

Out of the 120 cases studied in 12 cases -10% the biopsy was inadequate for conclusive interpretation, this figure is much lower than that of Patricia et al 120 and Reid et al<sup>20</sup> 17% and 13% respectively.

A correlation of the clinical diagnosis and bone marrow biopsy diagnosis indicated that in the majority of cases 57/120- 47.5% the biopsy confirmed the clinical diagnosis. The biopsy alone gave the diagnosis in a significant number-51/120 cases-42.5% while it was non contributory in a smaller number of cases in 12/120 cases-10%. In these cases the biopsy was inadequate for reporting.

A comparative evaluation of bone marrow aspiration and biopsy showed that both the procedures were complimentary to each other and both gave the diagnosis in a high percentage of 72.5%

this is similar to the findings of Nanda et al<sup>18</sup> who made the diagnosis by aspirate and biopsy also in a high percentage of 88.6% cases. The bone marrow trephine biopsy alone gave the diagnosis in 17/120 cases- 14.16%, a figure slightly higher than that of Nanda et al<sup>21</sup> – 11.4. The bone marrow aspirate alone gave the diagnosis in 16/120 cases, out of these 16 cases, biopsy was inadequate in 12 cases, 2 cases were of malaria and 2 of kalaazar where the LD bodies and schizonts could not be detected on the trephine biopsy. Thus the bone marrow trephine biopsy should not be taken as a substitute but as a complimentary procedure to aspirate to enhance the yield of the diagnosis.

## CONCLUSIONS

Bone marrow Aspiration and BM Biopsy are confirmative for tissue diagnosis and plays important role in clinical diagnosis, prognosis and also to decide line of management.

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# Megalencephalic Leucoencephalopathy with Subcortical Cysts (VAN DER Knaap Disease) – A Rare Case Presentation

Sanjeev Suman<sup>1</sup>, Babita<sup>2</sup>, G. N. Singh<sup>3</sup>

## ABSTRACT

**Introduction:** Megalencephalic leucoencephalopathy with subcortical cysts (MLC) is a rare disease characterised by macrocephaly and early onset of white matter degeneration. This disease should be included in the differential diagnosis of macrocephaly with early onset leucoencephalopathy.

**Case report:** We report a case of 18 month old boy having diagnosed Megalencephalic Eucoencephalopathy with Subcortical Cyst (Van Der Knaap Disease). He had history of mild motor developmental delay seizures and also had megalencephaly during the first year of life. The diagnosis was made on the basis of characteristic finding in MRI.

**Conclusion:** So MLC should be included in the differentials of macrocephaly with early onset leucoencephalopathy.

**Keywords:** Vanderknaap disease, leucoencephalopathy.

## INTRODUCTION

Megalencephalic leucoencephalopathy with subcortical cysts (MLC) also called as van der knaap disease is a relatively new entity of neurodegenerative disorder with autosomal recessive inheritance, in which the affected patient's presents typically presents with megalencephaly during the first year of life and extremely slow course of functional deterioration associated with mild motor developmental delay and seizures. It is very rare disease first described by Vander knaap et al, in 1995.<sup>1,2</sup> No definite or curative treatment is available and the affected patients dies in their second or third decade but some may leaves up to fourth decade.<sup>3,4</sup>

We report a case of 18 months old boy diagnosed to have this rare disease.

## CASE REPORT

An 18 months old boy of non-consanguineous marriage from a Muslim community from Bihar presented with progressively increasing head size since last 6 months. The birth history was uneventful and the child was born full term with normal vaginal delivery. There was history of developmental delay and the child attained social smile at 4<sup>th</sup> month, neck holding at 7<sup>th</sup> month, sitting at 11<sup>th</sup> month. He was not able to stand or walk himself without support.

On examination the child was conscious and irritable. There was Macrocephaly and the head circumference measures 57 cm. He was not able to speak. Deep tendon reflexes were increased bilaterally. Chest, C.V.S. and abdominal examinations were within normal limits. Bladder and bowel habits were not affected.

### Imaging findings

Non contrast and contrast enhanced computed tomography (CT) scan was formed using a 16 slice CT scanner (Somatoform) from GE health care and it revealed extensive bilaterally symmetrical

white matter signal abnormalities which are hypodense and cystic lesions of C.S.F. densities affecting bilateral fronto-parietal and anterior temporal lobes. Both deep and subcortical u fibers were involved. There was no hydrocephalus seen. On post contrast study no abnormal enhancement seen.

A presumptive diagnosis of MLC was made and a non-contrast MRI of brain (T1W, T2W, FLAIR and MRS) was performed using 1.5 T MRI from SIEMENS. On T1W sequence- there is extensive white matter involvement as described in CT scan finding, which appears hypointense with multiple hypointense cysts in bilateral frontoparietal and anterior temporal lobes. (Figures 1-10).

{TE-59, TR-1920}- Echo time Repetition

On T2W sequence- the white matter and the cysts appears hyperintense as that of C.S.F. signal intensity. (Figures 11-14).

{TE-107, TR-3000}- Echo time Repetition

On FLAIR sequence- the white matter changes are still hyperintense suggestive of extensive demyelination but the cysts were suppressed and became hypointense confirming their cystic nature. (Figure 15-18).

{TE-102, TR-6000, TI-2500}- Echo time Repetition

On MRS- mild decrease in NAA/Ch and mild increase in ch/cr ratio is seen. The above MRI findings confirm the diagnosis of MLC. The child has an elder sister of 3 years old who was doing well and was asymptomatic for the disease. The child was discharged and put on physical therapy to improve the motor function.

## DISCUSSION

Vanderknaap disease (MLC) is a very rare inherited (autosomal recessive) neurodegenerative disorder is named after Marjo van der knaap, a Dutch physician.<sup>1</sup> The affected gene locus has been mapped as MLC 1 at chromosome 22q.

In India majority of the reported cases till now were from northern part (Agarwal community of Gujarat). Our case is from a Muslim community of Bihar. The diagnosis of MLC is highly suspected in patients with typical clinical and radiological features. The characteristic feature of this disease is relatively mild clinical course despite very abnormal findings on cranial MRI study.<sup>5,6</sup>

<sup>1</sup>Assistant Professor, <sup>3</sup>Professor and HOD, Department of Radiology, Patna Medical College Hospital, <sup>2</sup>Assistant Professor, Department of Microbiologyogy, Nalanda Medical College Hospital, India

**Corresponding author:** Dr Babita, Assistant Professor, Department of Microbiologyogy, Nalanda Medical College Hospital, India

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Figure-1: Skull photographs; Figure-2: Skull photograph

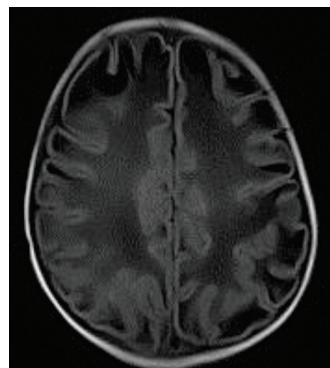


Figure-9: T1 W sequence; Figure-10: T1 W sequence

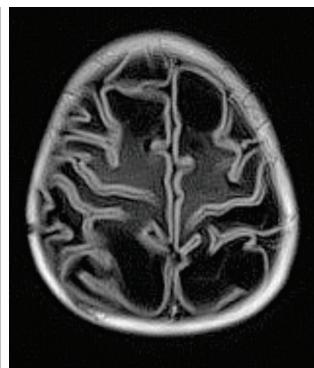


Figure-3: NCCT axial sections; Figure-4: NCCT axial sections

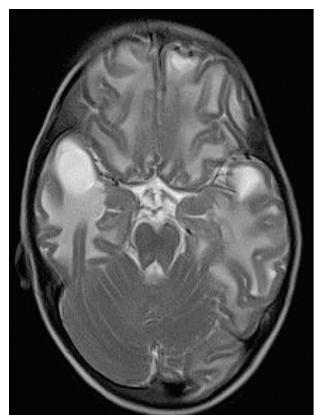
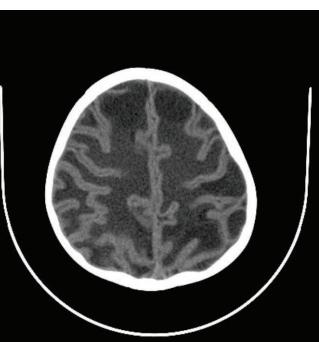


Figure-11: T2 W sequence; Figure-12: T2 W sequence

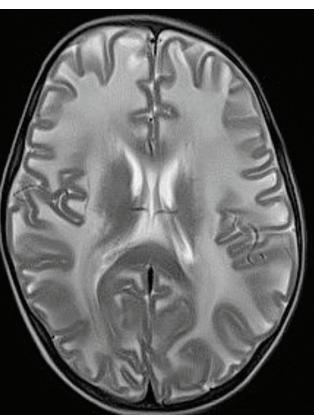


Figure-5: CECT axial sections; Figure-6: CECT axial sections

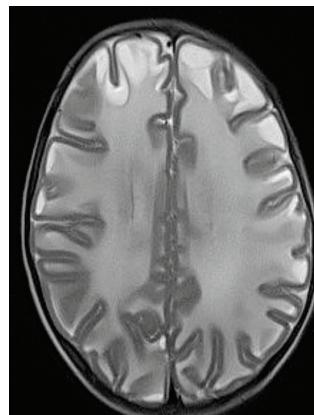
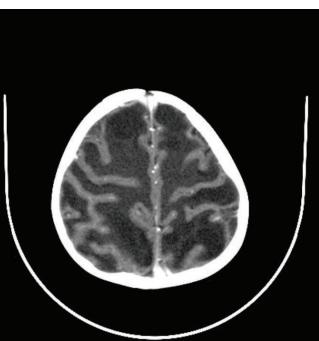


Figure-13: T2 W sequence; Figure-14: T2 W sequence

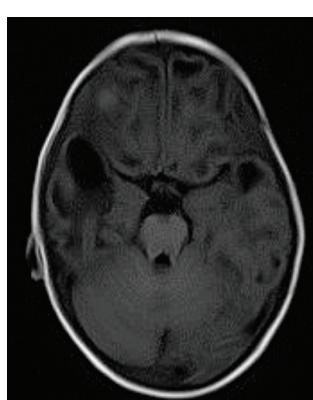
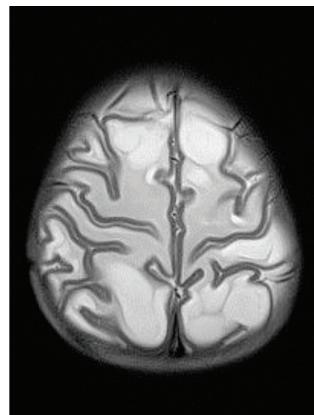


Figure-7: T1 W sequence; Figure-8: T1 W sequence

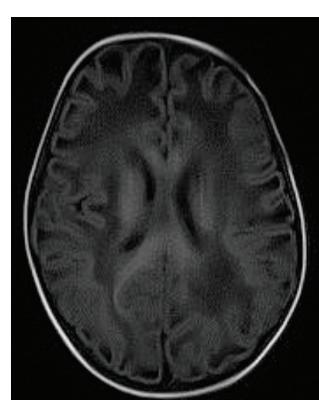
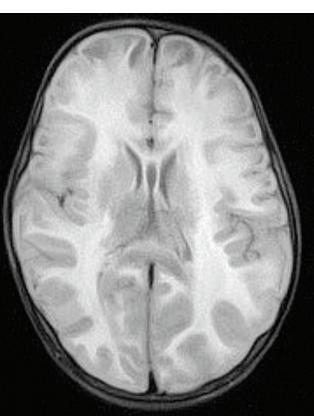
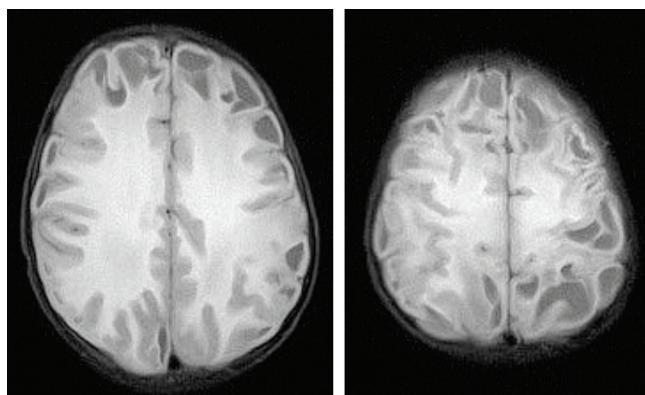


Figure-15: Flair sequence; Figure-16: Flair sequence

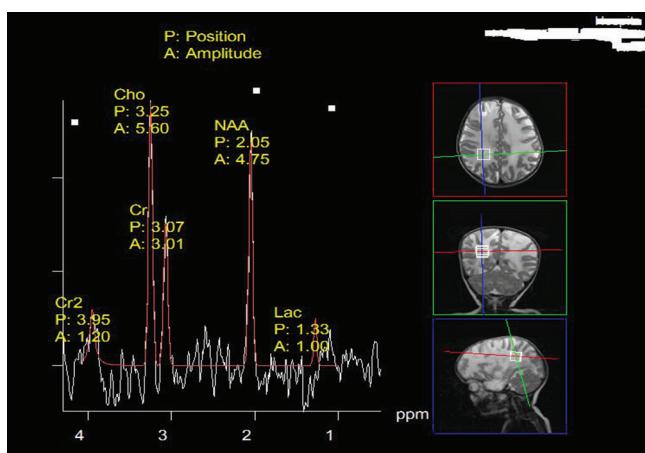


The typical clinical features are-

- Megalencephaly during the first year of life.
- Mild motor developmental delay.
- Gradual onset of ataxia and spasticity in early childhood and is slowly progressive.
- Most patients have seizures. Our patient had no history of



**Figure-17:** Flair sequence; **Figure-18:** Flair sequence



**Figure-19:** Magnetic resonance spectroscopy

seizure till now.

- e) Mental status is relatively preserved till late stages and when decline occurs is much milder as compared to motor functions.

The characteristic radiological findings are—

- a) On CT scan-bilaterally diffuse C.S.F. density hypodensities involving subcortical white matter and subcortical cysts.
- b) Cranial MRI is the best diagnostic radiological test and is characterised by diffuse bilateral leucoencephalopathy associated with cystic degeneration of white matter. Cysts are predominantly seen in anterior temporal and frontoparietal lobes. Cysts may increase in number and size with age.

On MRS-moderate decrease in NAA/cr and ch/cr have been previously reported but in our case mild decrease in NAA/Ch and mild increase in ch/cr ratio is seen. On serology-increase glycine is seen in C.S.F.<sup>2,7</sup>

Other causes of megalencephaly with subcortical white matter involvement includes—

1. Canavans disease- characterised by spongiform degeneration of white matter. Subcortical cysts are not seen and shows NAA peak on MRS.
2. Alexander's disease- bilateral frontal and temporal lobes are predominantly involved.
3. Vanishing white matter disease- characterised by childhood ataxia and hypomyelination. White matter gradually looks the same as C.S.F.

None of the above mentioned disorders have subcortical cysts. All of them have some degree of deep grey matter involvement

and are fatal in early childhood or in adolescence but MLC has relatively much better outcome as life expectancy up to third or fourth decade is expected.

Subcortical white matter involvement without macrocephaly includes galactosemia and Kearns sayre disease. Deep white matter disorders includes krabbe disease and infantile onset GM1 and GM2 gangliosidosis.

## CONCLUSION

So MLC should be included in the differentials of macrocephaly with early onset leucoencephalopathy and the diagnosis should be made with confidence in patients with characteristic findings on cranial MRI and typical relatively mild clinical course.<sup>6,7</sup>

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# A Comparative Study of 2% Lignocaine vs 50% Magnesium Sulphate for Attenuation of Stress Responses to Laryngoscopy and Endotracheal Intubation

Sachin Padmawar<sup>1</sup>, Manish Patil<sup>2</sup>

## ABSTRACT

**Introduction:** Laryngoscopy and endotracheal intubation are essential parts of induction of general anaesthesia. Present study was undertaken to evaluate and compare the efficacy of lignocaine and magnesium sulphate for attenuating the stress responses to laryngoscopy and endotracheal intubation.

**Material and Methods:** The study enrolling 100 patients of either sex, age between 18-50 years, ASA grade I and II were randomly allocated in two equal groups to receive either 2% lignocaine (1.5 mg/kg) or 50% magnesium sulphate (40 mg/kg) via intravenous route. Anesthesia was induced with intravenous thiopentone sodium 5 mg/kg followed by injection succinylcholine 1.5 mg/kg. The smooth gentle laryngoscopy and tracheal intubation was performed within 30 second. The haemodynamic parameters like HR, SBP, DBP, MAP and rate pressure product at various time intervals up to 5 minutes post-intubation were recorded and efficacy of both drugs to reduce haemodynamic responses was compared with Z test.

**Results:** In lignocaine group, there was significant rise in heart rate, blood pressure and rate pressure product in post intubation period which does not came to baseline value at 5 min after intubation. Rate pressure product crossed the angina limit of 12000 in more than 50% patients. In MgSO<sub>4</sub> group, heart rate, blood pressure and rate pressure product were increase significantly only at 1 min after intubation and which came to baseline up to 5 min after intubation. Rate pressure product did not cross the angina limit of 12000 significantly. There were no any complications observed in our study.

**Conclusion:** We concluded that magnesium sulphate is better alternative to lignocaine for attenuation of stress responses of laryngoscopy and intubation.

**Keywords:** Lignocaine, Magnesium Sulphate, Stress responses, Laryngoscopy and endotracheal intubation.

## INTRODUCTION

It is well recognized that the occurrence of haemodynamic responses in the form of rise in heart rate and BP during and after laryngoscopy and endotracheal intubation mediated by sympathetic response, is a well-known treat. Laryngoscopy and tracheal intubation stimulate somatic and visceral nociceptive afferents of the epiglottis, hypopharynx, peritracheal area, and vocal cords, which<sup>1</sup> leads to various cardiovascular changes like increase in heart rate, blood pressure, intracranial pressure, intra-ocular pressure, dysrhythmias, cardiac asystole and even sudden death.<sup>2-5</sup> These responses may prove to be detrimental especially in patients with ischemic heart disease, cerebral aneurysms, cerebrovascular disease, hypertension, old age and diabetes mellitus. Hence there is a constant search for an ideal drug to attenuate haemodynamic response. In 1951, King et al<sup>6</sup> highlighted this and since then, various methods including

nitroglycerine,<sup>7</sup> fentanyl,<sup>8</sup> esmolol,<sup>8</sup> calcium channel blockers,<sup>9</sup> magnesium,<sup>10</sup> lidocaine<sup>11</sup> and gabapentin<sup>12</sup> have been tried to attenuate ill desired haemodynamic response. In our institute, we are routinely using 2% lignocaine to attenuate the stress responses of laryngoscopy and endotracheal intubation.

Lignocaine is an aminoethylamide and prototype of amide local anesthetic group.<sup>13</sup> It is the most widely used local anesthetic drug having membrane stabilizing action, so it is commonly used as an anti-arrhythmic drug in patients with ventricular ectopics. In 1961, Bromage showed that its intravenous (IV) use blunted pressure response to intubation.<sup>14</sup> An IV dose of lignocaine 1.5mg/kg has been proved to attenuate stress responses during laryngoscopy and intubation when given prior to induction. Magnesium is the fourth most abundant cation in the body and the second most abundant intracellular cation. It activates many of the enzyme system. Magnesium sulfate inhibits the release of catecholamines from the adrenal medulla and adrenergic nerve endings and is effective in attenuating the blood pressure (BP) response to tracheal intubation.<sup>15</sup> Different doses of the drug have been used by different authors to attenuate this response to endotracheal intubation.<sup>16-18</sup> Puri et al<sup>18</sup> showed that MgSO<sub>4</sub> 50 mg/kg administered before laryngoscopy could attenuated the pressor response to tracheal intubation better than lidocaine. So here we have compared the effect of lignocaine 2% and magnesium sulphate 50% in attenuating the pressor response of laryngoscopy and intubation.

### Material and Method

After obtaining institutional ethical committee approval and a written informed consent, this prospective randomized study was carried out on 100 ASA grade I and II patients of both sex, aged between 18-50 years, scheduled for either elective or emergency surgery under general anesthesia. Patients with neuromuscular diseases, electrolyte imbalance, preeclampsia eclampsia patients who were already receiving MgSO<sub>4</sub>, patients with anticipated difficult intubation, heart disease like ischemic heart disease, arrhythmias, cerebrovascular disease, patient allergic to study drug, patients on whom required duration for laryngoscopy was more than 30 second and required multiple attempts were excluded from the study. Hundred selected

<sup>1</sup>Assistant Professor, <sup>2</sup>Assistant Professor, Department Of Anaesthesiology, B.Y.L. Nair Ch Hospital, India

**Corresponding author:** Dr. Sachin Padmawar, House No. 68, Priti Sadan Behind Sunita Building, Anand Nagar, Yavatmal, Maharashtra. 445001, India

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patients were randomly allocated into two groups of 50 patients in each group. Group I (Lignocaine group) received injection 2% lignocaine at a dose of 1.5 mg/kg intravenously and group II ( $MgSO_4$ ) received injection 50% magnesium sulphate in a dose of 40 mg/kg intravenously. A detailed pre-anaesthetic evaluation including history and a thorough general and systemic examination and all relevant investigations were done for all the patients.

On operation table, standard monitoring devices - ECG,  $SpO_2$ , non-invasive blood pressure were applied to the patient and baseline parameters like pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and rate pressure product were recorded. Intravenous access was established and preloading was done with ringers lactate solution. All patients were pre-medicated with injection midazolam 0.03 mg/kg, pentazocine 0.3 mg/kg, ranitidine 1 mg/kg and metoclopramide 0.2 mg/kg 10 minutes prior to induction. Also patients were pre-oxygenated with 100% oxygen for 3 minutes. Patients in group I received 1.5 mg/kg of lignocaine intravenously while patients in group II received 40 mg/kg of 50% magnesium sulphate before induction of anesthesia. Anesthesia was induced with thiopentone sodium (5-7 mg/kg) till loss of eye lash reflex followed by injection succinylcholine (1.5 mg/kg) to facilitate endotracheal intubation. Then patients were intubated with appropriate sized cuffed endotracheal tube and received oxygen: nitrous (50:50). All intubations were smooth and gentle and were done within 30 seconds. Anaesthesia was maintained with 0.4-0.6% halothane. Muscle relaxation was maintained with injection vecuronium bromide (0.008 mg/kg). Any surgical interventions like catheterization, nasogastric tube insertion, incision were requested to do 5 minutes after intubation to avoid disturbances in data recording. At the end of surgery patients received neostigmine 0.05 mg/kg and glycopyrrolate 0.008 mg/kg for reversal of the neuromuscular blockade. All patients were monitored throughout the surgery and observations were made with respective to HR, SBP, DBP, MAP and RPP at various intervals- before premedication, 10 min after premedication, 30 sec after administration of study

Parameters	Group I	Group II	P value
Age (years)	29.4	30.9	>0.05
Weight (Kg)	51.5	51.1	>0.05
Sex (Male:Female)	12:38	13:37	

Table-1: Demographics profile of the patients

Parameters	Groups	Before premedication	After premedication	After the drug	1 min after intubation	3 min after intubation	5 min after intubation
Heart Rate	Group I	85.6±6.8	79.8±7.1	81.1±8.1	108±7.6	103±7.9	95.5±7.4
	Group II	86.6±5.7	80±5.45	87.7±5.7	96.8±6.6	90±6.5	86.6±6.4
Systolic blood pressure	Group I	115±6.53	110±5.75	109±5.9	138±8.3	131±6.51	124±6.04
	Group II	117±8.73	112±8.34	110±8.7	124±8.8	115±8.6	115±8.6
Diastolic blood pressure	Group I	77.64±4.4	74.6±4.4	74.3±4.4	91.8±6.6	86.4±5.5	82.2±5.8
	Group II	78.28±5.5	74.9±6.2	73±5.6	84.5±6.2	78.7±6.1	78.7±6.1
Mean arterial pressure	Group I	90.2±3.37	86.4±3.9	86±3.84	107±6.21	101±4.64	96.09±4.91
	Group II	91.3±5.78	87.2±6.15	85.4±5.7	97.7±6.06	90.9±6.06	90.95±6.1
Rate pressure product	Group I	9883.6±1236	8786.8±1094	8880.7±1170	14959.9±1612	13447.8±1465	11853.1±1306
	Group II	10159±926	8931.4±834	9650.1±938	12021±136	10350±114	10001±1083

Table-2: Comparison of two groups in respect to all observed parameters (mean ± std. dev) at various points

drugs, 1, 3, 5 min after intubation. Any adverse effect due to either of drugs i.e. lignocaine and magnesium sulphate were noted. After extubation patients were shifted to the recovery room.

## STATISTICAL ANALYSIS

Mean and standard deviation for all values were calculated and compared within the group with baseline values as well as inter group comparison was done. Efficacy of both the drugs to reduce haemodynamic response was compared by Z test.

## RESULTS

Hundred patients who underwent elective or emergency surgery under general anesthesia were selected for the study; the demographic profiles of the patients in both the groups were comparable with regards to age, weight and sex and difference was not statistically significant (Table-1).

Table-2 show the comparison of two groups in respect to all observed parameters (mean ± std.dev) at different time intervals. In lignocaine group, there was significant rise in HR in post intubation period which does not came to baseline value at 5 min after intubation. Systolic blood pressure also elevated in post intubation period significantly from baseline and also not came to baseline at 5 minutes after intubation. Similar trends were seen with respect to parameters DBP and MAP, RPP also rise after intubation and it crossed the angina limit of 12000 in more than 50% patients. While in  $MgSO_4$  group, there was initial increase in HR after drug administration which elevated after intubation at 1 minute but it came to baseline up to 5 minutes after intubation. SBP also rises at 1 min interval post intubation but it also came to baseline up to 5 min after intubation. Similar trends were seen with respect to parameters DBP and MAP, RPP increases at 1 min post intubation but did not cross the angina limit of 12000 significantly.

There were no complications like nausea, vomiting, hypotension and arrhythmias observed in our study.

## DISCUSSION

Hypertension and tachycardia have been reported since 1950 during intubation under light anaesthesia.<sup>2,3</sup> Increase in blood pressure and heart rate occurs most commonly from reflex sympathetic discharge in response to laryngotracheal stimulation, which in turn leads to increased plasma norepinephrine concentration.<sup>19</sup> These changes may be fatal in patients with heart disease and high blood pressure.

During recovery from anaesthesia hypertension may occur provoking post operative complications like bleeding, increased intracranial and intraocular pressure. Therefore effective attenuation of the sympathoadrenal stress response to laryngoscopy and endotracheal intubation is an important goal, especially in high risk patients. Many attempts have been made to attenuate the pressure response e.g. deep anaesthesia, topical anaesthesia, use of ganglionic blockers, beta blockers and antihypertensive agents like phentolamine. Sodium nitroprusside and nitroglycerine, calcium channel blockers like sublingual and nifedepine, verapamil, diltiazem, magnesium sulphate, opioids, vasodilators etc. are effective but requires continuous intra arterial blood pressure monitoring.

Various studies have reviewed the effect of lignocaine to blunt the sympathoadrenal pressure response. Lev and Rosen<sup>20</sup> in their study using prophylactic lignocaine in a dose of 1.5 mg/kg intravenously prior to intubation produced optimal attenuation sympathoadrenal pressure response to laryngoscopy and intubation without any overt harmful effects. R. K. Stoepling<sup>21</sup> confirmed the protective use of IV lignocaine 1.5 mg/kg given 90 sec prior laryngoscopy but also reported topical anesthesia with viscous lignocaine would be more specific.

The methods and drugs used for attenuate stress responses of laryngoscopy and intubation have disadvantages related to either cardiovascular or respiratory depression; none directly inhibits the release of catecholamines. Among the therapeutic regimens useful in suppressing the hormonal stress response to tracheal intubation, magnesium may be a forerunner as it not only has direct vasodilator properties<sup>22</sup>, it also significantly suppresses the release of catecholamines.<sup>15</sup> Many studies have showed that MgSO<sub>4</sub> can attenuate cardiovascular responses to endotracheal intubation.<sup>15,18,23,24</sup> Allen RW. et al<sup>16</sup> showed its effectiveness in hypertensive proteinuric pregnant patients undergoing caesarean section. Also Puri GD. et al<sup>18</sup> showed magnesium sulphate attenuates pressure response in patients with coronary artery disease.

The present study was done in two groups, to evaluate and compare the effect of lignocaine and magnesium sulphate. In group I patients received 1.5 mg/kg lignocaine and in group II patients received magnesium sulphate 40 mg/kg. Variability in heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, rate pressure product and other complications was compared at different time intervals.

#### **Heart rate**

Heart rate in both groups after premedication show insignificant differences. In lignocaine group HR decreased after premedication, but it was not increased after lignocaine administration. However average rise in HR at 1 min after intubation was 22.58 beats. Majority (70%) of the patients show rise in HR in the range of 21-30 beats/min from baseline. this raised in HR did not come to baseline even at 5 minutes after intubation. While in magnesium sulphate group HR decreased after premedication, and it was increased after magnesium sulphate administration but rise in HR was insignificant. Average rise in HR at 1 min after intubation was 10.2 beats. Majority (68%) of the patients show rise in HR in the range of 0-10 beats/min from baseline and HR normalizes up to 5 min after intubation. On intergroup comparison between lignocaine and MgSO<sub>4</sub> group, it was noted that though MgSO<sub>4</sub>,

does not offer complete protection against HR, the difference between both the groups, in attenuating HR was significant at 1,3,5 minutes interval but HR came to base line towards 5 minutes after intubation in MgSO<sub>4</sub> group but that was not the case with lignocaine group. These findings correlate with other studies.<sup>15,16,18,25</sup>

#### **Systolic Blood Pressure**

Systolic blood pressure in both the groups after premedication and after study drug show insignificant differences. In lignocaine group SBP increase after intubation. Average rise was 22.84 mm Hg at 1 min interval. Majority (44%) of the patients show rise in the range of 21-30 mm Hg from baseline. This raised SBP did not come to baseline and remains significantly raised even 5 minutes after intubation. Similar findings were noted in 1990, by C.D. Miller and S.J. Warren.<sup>25</sup> In MgSO<sub>4</sub> group SBP increases significantly only at 1 min after intubation. Average rise was 6.64 mm Hg at 1 min interval and majority (90%) of the patients show rise in the range of 0-10 mm Hg from baseline. This rise in SBP came to baseline value towards 5 minutes and even 50% of the patients show decline in it from baseline. Similar findings were noted in 1989 by James FM.<sup>15</sup> On intergroup comparison, it was noted that SBP increase significantly in lignocaine group as compared with MgSO<sub>4</sub> group at 1,3,5 minutes after intubation. SBP rises in both the groups but it came towards baseline at 3 minutes after intubation in MgSO<sub>4</sub> group but that was not case with lignocaine group, this finding correlates with study of Allen et al.<sup>16</sup>

#### **Diastolic Blood Pressure**

Diastolic blood pressure in both the groups before and after premedication and after drug show insignificant differences. In lignocaine group DBP increases after intubation and average rise was 14.12 mm Hg at 1 min interval. The majority (56%) of the patients show rise in the range of 11-20 mm Hg from baseline. This raised in DBP does not come to baseline and remains significantly raised even 5 minutes after intubation. While in MgSO<sub>4</sub> group DBP increases significantly only at 1 min after intubation and average rise was 6.24 mmHg at 1 min interval. The majority (92%) of the patients show rise in the range of 0-10 mm Hg from baseline. This raised in DBP came to baseline value towards 3 minute and even 30% of the patients show decline in it from baseline. On intergroup comparison, it was noted that DBP increases significantly in lignocaine group as compared with MgSO<sub>4</sub> group at 1,3,5 minutes after intubation. DBP rises in both the groups but DBP came towards baseline at 3 minutes after intubation in MgSO<sub>4</sub> group but that was not the case with lignocaine group. Similar findings were noted in different studies.<sup>15,16,18,25</sup>

#### **Mean Arterial Pressure**

Mean arterial Pressure in both the groups before and after premedication and after drug show insignificant differences in lignocaine group MAP increases after intubation. Average rise was 17 mm Hg at 1 min interval. Majority (56%) of the patients show rise in the range of 11-20 mm Hg from baseline, this raised in MAP does not come to baseline and remains significantly raised even 5 minutes after intubation. In MgSO<sub>4</sub> group MAP increases significantly only at 1 min after intubation. Average rise was 6.4 mm Hg at 1 min interval. Majority (88%) of the patients show rise in the range of 0-10 mmHg from baseline,

this raised in MAP came to baseline value towards 3 minute and even 36% of the patients show decline in it from baseline. On intergroup comparison, it was noted that MAP increases significantly in lignocaine group as compared with MgSO<sub>4</sub> group at 1,3,5 minutes after intubation. MAP rises in both the groups but MAP came towards baseline at 3 minutes after intubation in MgSO<sub>4</sub> group but that was not the case with lignocaine group. These results were compared with various studies.<sup>16,18,25</sup>

### Rate Pressure Product

Rate pressure product in both the groups before and after premedication was show insignificant differences. In lignocaine group RPP increases after intubation and average rise was 5076.28 at 1 min after intubation. The maximum number of patients (44%) show rise in the range of 5001-6000 from baseline. This rise crosses angina limit of heart i.e. rate pressure product crosses level of 12000 at 1 and 3 minutes after intubation and it not came to baseline even 5 minutes after intubation. In MgSO<sub>4</sub> group RPP increases significantly only at 1 min after intubation. Average rise was 1863 at 1 min interval and maximum number of patients (46%) show rise in the range of 1000-2000 from baseline. 50% of the patients showed decline in their rate pressure product from baseline value. On intergroup comparison between lignocaine and MgSO<sub>4</sub> group, it was noted that RPP increases significantly in lignocaine group as compared with MgSO<sub>4</sub> group at 1,3,5 minutes after intubation. RPP rises in both the groups but RPP came towards baseline at 3 minutes after intubation in MgSO<sub>4</sub> group but that was not the case with lignocaine group.<sup>16,21,25</sup>

In this study magnesium sulphate was given diluted and slowly to avoid untoward side effects, hence no any complications observed in our study.

### CONCLUSION

The present study revealed that magnesium sulphate provide fairly good and sustained control over haemodynamic responses to the stress of laryngoscopy and intubation and is significantly better than lignocaine, so we conclude that magnesium sulphate is better alternative to lignocaine for attenuation of stress responses of laryngoscopy and intubation.

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# Comparision of Lung Functions among Males and Females with Sickle Cell Anaemia

Bageshree N Pande<sup>1</sup>, V.D.Tajne<sup>2</sup>

## ABSTRACT

**Introduction:** Sickle cell disorder has remained a neglected field of research in India and magnitude of problem has never been appreciated. Most of the reports spread a misconception that the sickle gene was confined to the tribal population. In India nearly 20 million people suffer from this disease. In it the red blood cells become deformed, rigid and obstruct the blood flow leading to tissue damage because of poor perfusion. The present study was undertaken to evaluate abnormalities in lung functions due to the disease.

**Material and Methods:** The study was carried out in department of Physiology in association with department of Medicine at Government Medical College. The study protocol was approved by the ethical committee. The study included 200 subjects, out of which 100 were sickle cell disease patients and 100 controls in the age group of 20-35 yrs. FVC, FEV1, FEV1/FVC%, FEF 25-75%, PEFR and MVV values were chosen. All the variables were compared among the cases and controls by performing unpaired 't' test. p value <0.05 was considered as statistically significant and <0.001 as highly significant.

**Results:** All the PFT parameters were highly significantly reduced in cases, decline in the pulmonary function tests parameters in study group is suggestive of both restrictive and obstructive changes in sickle cell disease, restrictive pattern been more common.

**Conclusion:** Most common abnormal pattern found was restrictive type. Pulmonary function testing can be used as routine test to predict respiratory dysfunction in these patients.

**Keywords:** Lung functions, restrictive pattern, obstructive pattern, sickle cell anemia

## INTRODUCTION

Red blood cells of adult healthy human individual consist of respiratory protein known as haemoglobin. Its major function is to transport oxygen from atmosphere to lungs and finally pass on to all vital organs. The property of combining reversibly with oxygen is unique wonder and interesting.

The Sickle cell disease is the first molecular disease known to man.<sup>1</sup> It was first described in a 20 year old dental student from Grenada in 1910 after he was admitted for anaemia by James Herrick<sup>2</sup> and his intern Ernest Edward Irons who found peculiar elongated sickle shaped cells in the blood. Sickle cell anaemia (also known as sickle cell disease) is the second most common haematological disorder next only to thalassemia. Sickle haemoglobin was first discovered from a tribal population of Nilgiri hills of South India in 1952.<sup>3</sup>

It has remained a neglected field of research in India and magnitude of problem has never been appreciated because most of the subsequent reports spread a misconception that the sickle

gene in India was confined to the tribal population and some scheduled castes only.

In this disease amino acid glutamic acid at position number 6 of  $\beta$  globin chain is replaced by valine. This happens due to change of nucleotide, adenine to thymine of codon 6 of  $\beta$  globin gene on chromosome 11. This changes the net charge of haemoglobin, oxygen affinity and three dimensional structure of haemoglobin which makes it an unstable one.

In India nearly 20 million people suffer from sickle cell anaemia. The belt extends from Assam, Orissa, Madhya Pradesh, Andhra Pradesh, Karnataka and Maharashtra. In Maharashtra, the reported prevalence of the disease varies from 1.9% to 33.5% in different communities.<sup>4</sup> The present study is undertaken to evaluate abnormalities in lung functions due to the disease.

## MATERIAL AND METHODS

The present study was carried out in department of Physiology in association with department of Medicine in Government Medical College, Nagpur for two years between 2012 to 2013. The study protocol was approved by the ethical committee of the college.

The cases were selected from the patients attending Sickle cell outpatient department (OPD). Before enrollment in the study, informed written consent was obtained from each subject. Sample size was 200, based on inclusion and exclusion criteria. Out of these, 100 were sickle cell anaemia patients and 100 served as controls.

### Inclusion criteria

1. Diagnosed cases of sickle cell disease (HbSS pattern) which was confirmed by cellulose acetate electrophoresis.
2. Patients attending OPD in a clinically steady state, in a symptom free interval, not in the crisis and not having acute chest syndrome.
3. Non smokers and non alcoholics.

### Exclusion criteria

1. Patients in crisis or having acute chest syndrome when performing the test.
2. Smokers and alcoholics.
3. History of any respiratory disease, cardiovascular disease, diabetes mellitus.

<sup>1</sup>Assistant Professor, Department of Physiology, Dr. D.Y. Patil Medical College and Research Centre, Pimpri, Pune, <sup>2</sup>Professor, Department of Physiology, Government Medical College, Nagpur, Maharashtra, India

**Corresponding author:** Dr. Bageshree Pande, 17/1, Rutambhara Niwas, Durga Colony, Ganesh Nagar, Thergaon, Pune, Maharashtra, India-411033.

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4. Patients engaged in occupation that can cause health hazard like dye industry, saw mill industry, etc.

#### Control group

1. Subjects with normal average height and weight for the same age and belonging to the same socio-economic status as that of the study group.
2. They had normal adult haemoglobin pattern (Hb AA) on electrophoresis.
3. They were non smokers and non alcoholics.
4. All subjects were free from cardiac and respiratory disease.

#### Method

The procedure was performed during morning OPD hours to avoid any diurnal variation. Before performing the pulmonary function tests, the following measurements were taken:-

1. Standing height
2. Weight
3. Body Mass Index (BMI)

#### Pulmonary Function Tests

The procedure of the pulmonary function tests was thoroughly explained. They were asked to sit comfortably and watch the demonstration.

The electronic computerized spirometer RMS Helios 401-version 1 was used.

In this procedure, each subject was asked to close the nostrils by the nose clip and execute fast forceful expiration as much as possible at the end of deep full inspiration into the mouthpiece. Three consecutive readings were obtained and best among the three was selected and noted.

After adequate rest, the test to obtain MVV was carried out. The subjects were asked to inhale and exhale as deep and as fast as possible for 12 seconds. The procedure was repeated for three consecutive times with adequate rest between each reading and best one was noted.

For each subject a sheet of predicted, pre i.e. observed and percentage predicted values of all the parameters was taken. The same procedure was followed for the control group. FVC, FEV1, FEV1/FVC%, FEF 25-75% and MVV values were chosen which are relevant to the study. The values obtained were in liters/min. Percent Predicted values were calculated by the instrument itself.

#### STATISTICAL ANALYSIS

All the variables were presented as mean  $\pm$  standard deviation (SD).

Continuous variables (age, PFT parameters) were compared among the cases and controls by unpaired t test. p value  $<0.05$  was considered as statistically significant and  $<0.001$  as highly significant. All the tests were two sided. Statistical software STATA version 10.0 was used for data analysis

#### Observations

#### RESULT

All the parameters are highly significantly reduced in study group when compared with controls. Table-1 shows comparison of anthropometric parameters between cases and controls. Mean BMI was significantly reduced in cases when compared with controls. Table-2 shows comparison of mean values of PFT parameters in study group and controls. All PFT parameters are

significantly reduced in study group as compared to controls. Table-3 shows age wise distribution of abnormal pattern of PFT in study group. Most common abnormal pattern found is restrictive type followed by obstructive followed by mixed pattern. Most common age group affected is 25-29 years.

#### DISCUSSION

The statistical analysis of the observations in the present study reveals that the patients of sickle cell disease show significant decrease in their Body Mass Index as compared to controls. Also there is statistically highly significant decrease in all the PFT parameters (% predicted) i.e. FVC, FEV1, FEF25-75%, PEFR and MVV in study group as compared to controls. These findings correlate with the findings of the previous studies. The finding that most of the SCD patients were below 30 years of age is in keeping with the notion that life expectancy of the SCD patients is reduced.<sup>5</sup> In the present study, Body Mass Index was highly significantly decreased in cases when compared with controls. This correlates with the findings of Modebe O et al.<sup>6</sup> H. S. Nikharet al has shown a significant decline in BMI in sickle cell disease children from rural areas as compared to urban areas.<sup>7</sup> In the present study, mean height was decreased though not significantly in cases as compared to controls, whereas weight was reduced significantly. It is stated that delayed skeletal maturation during adolescence may allow for a longer growth period in the long bones of the extremities, resulting in normal adult height among surviving adults with sickle cell disease.

Reduction in BMI might be reduced due to poor dietary intake because of appetite especially during vaso-occlusive crisis. It

Baseline characteristics	Cases (n=100)	Control (n=100)	p value
Age (year)	25.81 $\pm$ 3.20	25.56 $\pm$ 3.11	0.5766, NS
Height (cm)	156.95 $\pm$ 5.13	157.11 $\pm$ 4.14	0.808 NS
Weight (kg)	50.11 $\pm$ 3.89	52.72 $\pm$ 2.55	<0.001 HS
BMI (kg/m <sup>2</sup> )	20.36 $\pm$ 1.65	21.37 $\pm$ 1.20	<0.0001, HS

**Table-1:** Shows baseline characteristics in study group and controls

Parameters	Cases (n=100)	Controls (n=100)	p-value
FVC (% pred)	82.45 $\pm$ 9.83	91.33 $\pm$ 4.05	<0.0001, HS
FEV1 (% pred)	76.71 $\pm$ 10.5	88.25 $\pm$ 3.82	<0.0001, HS
FEV1/FV(%pred)	93.30 $\pm$ 8.63	96.64 $\pm$ 1.87	<0.0001, HS
FEF25-75(pred)	83.27 $\pm$ 8.66	93.07 $\pm$ 2.01	<0.0001, HS
PEFR (% pred)	84.38 $\pm$ 7.90	91.2 $\pm$ 2.97	<0.0001, HS
MVV (% pred)	86.62 $\pm$ 8.50	92.51 $\pm$ 2.20	<0.0001, HS

All values are expressed as mean $\pm$  S.D.

**Table-2:** Shows pulmonary function test parameters in study group and controls

Age (years)	Total cases	Restrictive Pattern	Obstructive pattern	Mixed pattern
20-24	29	10	3	0
25-29	62	20	3	4
$\geq$ 30	9	4	3	2
Total	100	34	9	6

**Table-3:** Shows age wise distribution of abnormal pattern of PFTs in study group

is believed that anaemia plays a major role in pathophysiology of sickle cell disease but it is not clear whether anaemia affects overall cell metabolism sufficient to result in growth retardation.

### Pulmonary Function Test Parameters

**Forced Vital Capacity (FVC):** In the present study FVC was highly significantly reduced in study group when compared to controls. The reason for decrease in FVC was anthropometric differences in these patients. The thorax is not only short relative to body stature in this disease, but the lateral chest diameter is also narrower than that of healthy individuals.<sup>8</sup>

FVC is usually decreased more than FEV1% in restrictive lung disease. The restrictive pathology may be due to the following reason -

In the sickle cell disease population, mechanism of restriction would be ineffective inspiration due to chest wall pain related to peripheral vasoocclusion, prior rib infarctions, or vertebral disease.<sup>9</sup>

**Forced expiratory volume in one second (FEV1):** In the present study FEV1 was highly significantly reduced in study group when compared with controls. FEV1 was also decreased in studies by Koumbourli et al, Hulke et al, Williams K et al.<sup>10</sup> FEV1 is usually considered as the marker of both central and peripheral airway obstruction. In some studies the obstructive pattern was accompanied by an increase in diffusing capacity and suggested that it might have been related to an increase in lung blood volume. Obstructive lung disease possibly precedes the development of restrictive lung disease and airway reactivity may be part of the pathogenic mechanism.

**FEF25-75%:** The present study shows highly significant decrease in mean FEF25-75% in study group. Koumbourlis et al<sup>11</sup> suggested that chronic inflammation initially affects the smaller airways. Long-standing inflammation causes lower airway obstruction in early phases, which might lead to fibrosis in later phases.

**Maximum Voluntary Ventilation (MVV):** Study had revealed highly significant reduction in MVV in study group. It is comparable with the finding noted by Young et al, S Hulke et al.<sup>10</sup>

The decrease in MVV can be explained on the basis of pathological finding suggestive of restrictive changes as demonstrated by decreased FVC and MVV, obstructive changes by decreased FEF 25-75%, PEFR and FEV1. Thus it provides an overall assessment of pulmonary compliance, pulmonary obstruction and restriction.

### CONCLUSION

Thus the study concludes that the decline in all the pulmonary function tests parameters in study group is suggestive of both restrictive and obstructive changes in sickle cell disease, restrictive pattern been more common. The highly significant decline in MVV is suggestive of increased airway resistance and lowered lung compliance. Cause of the restrictive lung disease may be vasculopathy, repeated episodes of acute chest syndrome, airway hypersensitivity, haemolysis and organ dysfunction associated with sickle cell disease.

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# Our Experience of Blood Transfusions in Patients with Moderate Anemia Undergoing Elective Cesarean Sections at Government Medical College, Ananthapuramu

J. Sandhya<sup>1</sup>, Shamshad Begum<sup>2</sup>, B. Renuka<sup>2</sup>, S. Syamala Devi<sup>3</sup>

## ABSTRACT

**Introduction:** Anemia during pregnancy increases the incidence of preterm labor, preeclampsia, sepsis. Anemia also effects fetal outcome in the form of preterm baby, IUGR, increased mortality rate. The aim of the present study was to evaluate the perioperative requirement of blood transfusions, complications and outcome of patients with Moderate anemia undergoing Elective Cesarean section.

**Material and Methods:** This retrospective study is conducted over a period of one year from Jan 2015 to Dec 2015, in pregnant women with moderate anemia undergoing elective cesarean section. Data regarding patient details, hemoglobin estimation, cross matching, need of transfusions, multiple blood transfusions, any intra operative or post operative complications and outcome was assessed.

**Results:** Number of patients with moderate anemia was 470 out of 557 elective LSCS patients. Out of 470 Elective LSCS cases with moderate anemia, 17 were in Group I(Hb <8 g/dl), 195 were in Group II (Hb 8-9 g/dl) and 258 were in Group III (Hb >9 g/dl). 45 out of 470 Elective LSCS women with moderate anemia received blood transfusions. There was significant reduction in blood transfusions in Group II and III patients.

**Conclusion:** It is safe always to cross match and preserve blood as there is a threat of ongoing blood loss per and post operatively; but restricted blood transfusion practices are advocated only in cases of hemodynamic instability perioperatively to avoid blood transfusion reactions and infection transmission (HBV, HIV).

**Keywords:** Blood transfusion, Elective LSCS, Moderate Anemia.

## INTRODUCTION

Anemia is defined as quantitative or qualitative deficiency of RBC or hemoglobin in circulation resulting in decreased oxygen carrying capacity of blood to organs and tissues. Anemia is major public health problem globally especially in developing countries like India and Africa. In India, anemia contributes to 10-15% of maternal deaths.<sup>1</sup> Nearly two billion people are suffering from anemia (iron deficiency anemia).<sup>2</sup>

WHO estimates that in India, prevalence of anemia in pregnant women is 65-75%.<sup>3</sup> Due to anemia, nearly half of the maternal deaths occur in South Asian countries.<sup>4</sup>

According to ICMR 1989 Anemia is classified as follows according to Hemoglobin levels<sup>5</sup>:

Very Severe anemia - <4g/dl

Severe anemia - 4-6.9 g/dl

Moderate anemia - 7-9.9 g/dl

Mild anemia - 10-10.9 g/dl.

Pregnant women with Hemoglobin level of 11% and hematocrit value of less than 33%<sup>6</sup> are consider as anemic according to WHO. WHO classification of Anemia based on Hb levels.

Mild anemia: 10-10.9 g/dl

Moderate anemia: 7-9.9 g/dl

Severe anemia: <7 g/dl

Mild anemia may not cause any significant effect on pregnancy and during labor. Moderate anemia can cause fatigue, poor work performance. Severe anemia in pregnant women is associated with poor outcome and may results in breathlessness, palpitations, tachycardia, post partum depression, cardiac failure.<sup>5,7,8</sup> Anemia during pregnancy increases the incidence of preterm labor, preeclampsia, sepsis. Anemia also effects fetal outcome in the form of preterm baby, IUGR, increased mortality rate.<sup>7</sup>

Anemia during pregnancy has to be corrected before labor for better outcome of mother and baby. By good antenatal care, anemia can be easily diagnosed and managed.<sup>5</sup> Treatment of anemia depends on Hemoglobin level. Mild anemia can be treated using oral iron preparations, whereas moderate and severe anemia may have to be managed by i.v iron preparations or blood transfusions. Decision has to be taken whether blood transfusion is necessary or not based on clinical findings. Transfusion threshold is the Hb value, and the Hb value should not fall below this threshold value during the perioperative period, particularly in the context of ongoing or anticipated blood loss.

Blood transfusion helps to save lives in critical conditions. But at the same time there can be adverse effects of blood transfusion that vary from milder headache, fever, rash, itching to major side effects like life threatening anaphylaxis as well as transmission of infection like HIV, HBV, HCV.<sup>9,10</sup> This morbidity and mortality of blood transfusion can be minimized by properly estimating the need of blood transfusion. So the decision of selecting patients for blood transfusion is done carefully to strike a balance between genuine indications versus adverse effects of blood transfusion.

When Hb concentration is >10g/dl transfusion is rarely indicated, when Hb concentration is <6 g/dl, transfusion is always indicated and if Hb concentration is 6-10 g/dl then decision of transfusion should be made based on patient risk for complications of inadequate oxygenation, as stated by ASA task

<sup>1</sup>Associate Professor, <sup>2</sup>Tutor, <sup>3</sup>Professor, Department of OBG, Government Medical College and General Hospital, Ananthapuramu, India

**Corresponding author:** Dr.J.Sandhya M.D., Associate Professor, Department of OBG, Government Medical College, Ananthapuramu - 515001, Andhra Pradesh, India

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force on blood component therapy (1994).<sup>11</sup>

Scanty literature is found regarding role of blood transfusion among patients with moderate anemia posted for elective LSCS. So we undertook this retrospective analysis to assess the incidence of blood transfusions in patients with moderate anemia and undergoing Elective LSCS.

The aim of the present study is to evaluate the requirement of blood transfusions, complications and outcome of patients with Moderate anemia undergoing Elective Cesarean section perioperatively at Government General Hospital, Ananthapuramu, A.P, India where blood bank facilities are restricted.

## MATERIAL AND METHODS

This retrospective study was done in a government general hospital (Government General Hospital attached to the Government Medical College, Ananthapuramu, Andhra Pradesh, India) a tertiary center catering primarily to the rural and low socioeconomic population of the district. Most of the patients were assessed in this study come to hospital nearer to Expected Date of Delivery without proper antenatal work up. The study was conducted over a period of one year from Jan 2015 to Dec 2015, in pregnant women with moderate anemia undergoing Elective Cesarean section after taking approval from ethical committee of the institute. The sample size was calculated by qualitative data by referring various previous literatures.

A total of 8047 deliveries were registered from our institute in 2015. Among those 557 underwent elective LSCS. All Elective LSCS sections were done under spinal anesthesia by monitoring blood pressure mean arterial pressure, heart rate, ECG and SpO<sub>2</sub>. Elective LSCS patients with moderate anemia were categorized in to three subgroups based on hemoglobin level: Group I - Hb <8 g/dl; Group II - Hb 8 - 9 g/dl; and Group III - Hb >9 g/dl. Cross matching was done and Compatible units of blood were preserved routinely for all the patients undergoing Elective LSCS. CT ratio (Cross match transfusion ratio) was calculated by dividing the number of units of blood cross matched to the number of units transfused. Data regarding patient details, hemoglobin estimation, cross matching, need of transfusions, multiple blood transfusions, any intra operative or post operative complications and outcome was assessed and entered into spread excel sheet.

## STATISTICAL ANALYSIS

Statistical analysis was done and expressed in the form of ratio, percentages and histograms.

## RESULTS

Total number of deliveries in 2015 at the institute was 8047. Among these, Elective LSCS was done in 557 patients (6.9% of total deliveries). Number of patients with moderate anemia was 470 out of 557 elective LSCS patients.

Patients with Moderate anemia undergoing Elective LSCS were subcategorized into three groups based on Hb levels. Out of 470 Elective LSCS cases with moderate anemia, 17 were in Group I, 195 were in Group II and 258 were in Group III (Figure-1).

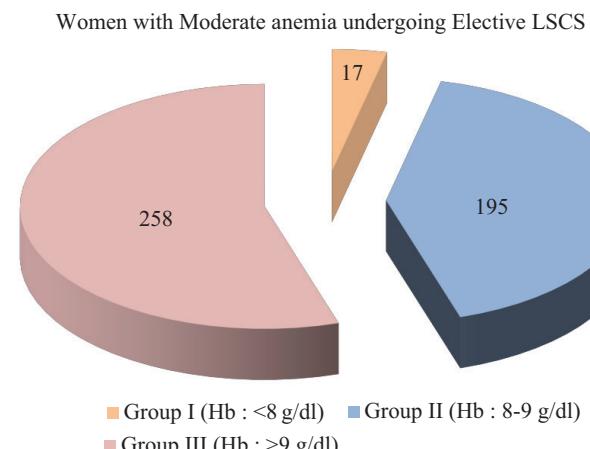
Out of 557 total Elective LSCS, 49 patients received blood transfusions. Number of patients receiving blood transfusion was 45 out of 470 Elective LSCS women with moderate anemia.

Total number of compatible blood units received by the studied population was 57 and varied from single bag to 5 bags per patient. Blood transfusion was given in 47% (8) of Group I; 14% (28) of Group II; 3.5% (9) of group III patients (Figure-2). 57 blood units or bags were transfused to 45 patients undergoing elective LSCS with moderate anemia. More number of blood bags were transfused to Group I moderate anemia patients (Hb < 8 g/dl), 18 blood units were transfused to 8 patients (Table-1). The ratio of number of patients typed and cross matched to patients transfused (CT ratio was 10:1) (Table-1). The ratio of units of blood typed and cross matched to units transfused was 11.8 (57 out of 482).

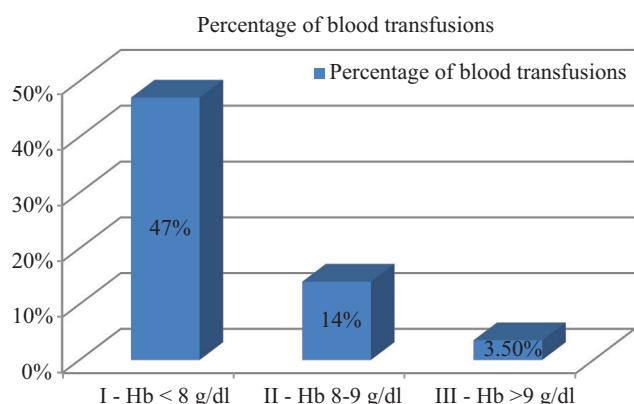
The ratio of total units transfused (n=57) to the total cesarean sections (n=470) was 0.12 unit per patient. In group I the blood transfusions were in 8 patients (47%) of which 4 patients received transfusions preoperatively; 2 patients post operatively and 2 patients both pre and post operatively. No intra operative transfusions in Group I (Figure-3).

In group II the number of transfusions came down significantly to 14% (28 out of 195) (Figure-2). 11 patients received transfusion preoperatively; 1 patient received intra operatively and 16 patients received postoperatively. None of them had multiple transfusions (Figure-3). In Group III patients, out of 258 patients only 9 (3.5%) received blood transfusions, all of them in postoperative period (Figure-3).

Among Group I patients breathlessness and wound gaping were observed in 4 and 2 patients respectively. Among Group



**Figure-1:** Pie chart showing distribution of women undergoing Elective LSCS with moderate anemia according to Hb levels



**Figure-2:** Bar diagram showing percentage of blood transfusions in different groups

Group	Total No. of Patients		No. of patients who received blood transfusions		No. of Transfused Blood bags	CT ratio
	No.	Percentage	No.	Percentage		
I	17	3.6%	8	47%	18	2:1
II	195	41.4%	28	14%	28	7:1
III	258	54.8%	9	3.5%	11	29:1
Total	470	100	45	9.5%	57	10:1

Table-1: Percentage of Blood transfusions among Elective LSCS patients with moderate anemia

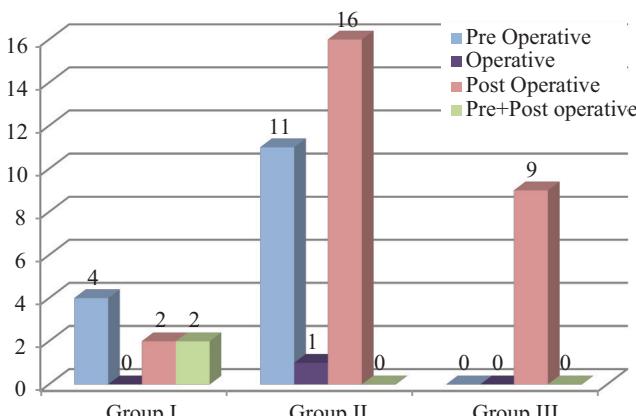


Figure-3: Bar diagram showing Number of blood transfusions occurred during perioperative period

II patient's breathlessness was observed in 4 members. No morbidity reported from group III patients. No Maternal death was observed in any of elective LSCS patients.

## DISCUSSION

Rural Indian women with moderate anemia present without any clinical signs and symptoms of anemia, as they can tolerate this chronic anemia without any ill effects. Cardiac output usually does not change until hemoglobin concentration falls to below 7 grams.<sup>12</sup> Without much significant maternal and fetal effects our obstetric patients usually tolerate moderate anemia. In our study this is reflected in the form of reduced need for blood transfusion in spite of moderate anemia undergoing surgery (LSCS).

Factors like hemoglobin level, blood volume, the volume of blood lost any consisting diseases and complications decide the ability of pregnant women with anemia to withstand blood loss at the time of delivery (LSCS).<sup>13</sup> Blood transfusion is used only when strictly needed for fear of transmission of diseases like HIV, HBV as well as blood transfusions reactions.<sup>14,15</sup>

For the safe conduct of anesthesia a minimum of hemoglobin of 10 grams was believed to be required by anesthetist since long time. No single index can be the basis of perioperative transfusion due to better means of understanding and monitoring the relationship between oxygen delivery and oxygen consumption.<sup>16</sup>

FDA drug bulletin 1989 states that "adequate oxygen carrying capacity can be met by as low as hemoglobin of 7 grams when intra vascular volume is adequate for perfusion".<sup>17</sup>

The factors deciding the individual patients transfusion trigger is to be based on clinical judgment in conjunction with monitoring of tissue oxygen delivery. Therefore the concept of an acceptable hemoglobin level varies with the underlying medical condition, extent of physiological compensation the threat of intra operative bleeding and ongoing blood losses post

operatively may be in the form of atonic PPH.

Clinical and hematological grounds will decide the blood transfusion. Transfusion is rarely indicated in stable patient when hemoglobin > 10 g and is almost always indicated when Hb < 6 grams.<sup>18,19</sup> In our study we found that there was a significant increase in blood transfusion in Group I (47%). If the hemoglobin is between 8 and 9 g/dl the decision of blood transfusion is to be made on the informed basis according to preexisting medical conditions, continuous bleeding and threat of blood loss.

In asymptomatic parturient there is little evidence of benefit of blood transfusion.<sup>19</sup> The present study also showed the same results as there was significant reduction in blood transfusions in Group II and III patients. Subramanyam KL et al<sup>16</sup> observed the same results as our study.

As per this study the CT ratio (Cross match transfusion ratio) was 11.8:1 (57 out of 482 in Moderate anemia). Fauzia A Khan et al<sup>20</sup> documented that the ratio of units of blood typed and cross matched to blood units transfused was 9.7:1.

In this study among Group I patients breathlessness and wound gaping were observed in 4 and 2 patients respectively. Among Group II patient's breathlessness was observed in 4 members. No morbidity reported from group III patients. No Maternal death was observed in any of elective LSCS. Subramanyam KL et al [16] documented that breathlessness was observed in all the groups.

No difference in mortality rates is established by Herbert in large RCT between liberal and restrictive transfusion strategies in non cardiac and non critically ill patients who can tolerate lower levels of hemoglobin.<sup>21</sup> In an attempt to increase tissue oxygen delivery the maintenance of higher hemoglobin concentration by blood transfusion is not associated with any clinical benefit according to the study by Reiles and Linden.<sup>22</sup>

It may be concluded that any particular single value of hemoglobin level is not a trigger to initiate transfusion after considering various clinical data. Pregnant women's physiological aspects like cardio vascular fitness, age, operative blood loss and disease status are more important than relying on single value of hemoglobin. The potential clinical benefits adverse effects and cost of blood component therapy may be considered for the decision of blood transfusion. After an internal audit on transfusion guidelines Mallet found a 43% decrease in blood transfusions.<sup>23</sup>

In our hospital acceptable hemoglobin from anesthetist point of view is concerned only for the maintenance of hemodynamics during Cesarean section. It is a general policy that we wait and watch in all asymptomatic parturient with hemoglobin of 8-9 g/dl in order to strike a balance between benefits of replenishing oxygen carrying capacity by transfusion versus transfusion associated reactions and infection transmission. But

obstetrician has to visualize perspectives of post op morbidity, wound healing, fatigue, lactation adequacy and quality of life of the women in post natal period. Hence the obstetrician has to consider maintenance of hemoglobin to normality by other means like IV iron sucrose infusion before the women is discharged from the institute. They can also be supplemented by other measures like deworming, good diet, oral iron proper, post natal follow up, advice on spacing etc., after the discharge.

## CONCLUSION

Cesarean section is the most common surgery done at district hospitals both in government and private setup where moderate anemia always poses a challenge of controversy of blood transfusion decision. It is safe always to cross match and preserve blood as there is a threat of ongoing blood loss per and post operatively; but restricted blood transfusion practices are advocated only when there is perioperative hemodynamic instability.

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# Speciation and Antimicrobial Susceptibility of Coagulase Negative Staphylococci, Isolated from the Anterior Nares of Health Care Workers, in A Tertiary Care Hospital in South India, with Special Reference to Methicillin Resistance

Ragini Ananth Kashid<sup>1</sup>, Kausalya Raghuraman<sup>2</sup>

## ABSTRACT

**Introduction:** Coagulase negative staphylococci (CoNS) are identified as emerging pathogens causing nosocomial infections, with significant morbidity and mortality. Speciation of CoNS helps in the understanding of their susceptibility patterns, the reservoirs and the epidemiology. CoNS are multidrug resistant and act as reservoirs for drug resistant genes. They are found in health care workers (HCWs), who act as reservoirs and help, in the spread of nosocomial infections. This study was undertaken to determine the occurrence, the species and susceptibility pattern of CoNS isolated from the anterior nares of HCWs working in our tertiary care hospital.

**Material and Methods:** Anterior nasal swabs were taken from a total of 310 HCWs. Speciation of CoNS was done by a practical scheme adopted from various references. Kirby Bauer disc diffusion method was performed as per CLSI guidelines. Statistical methodology: Percentage description of the data was given.

**Results:** The rate of isolation of CoNS was 55.8% (173/310). Among the 173 CoNS isolated in this study, 44%(76/173 ) were *S. haemolyticus*, 30% (52/173) were *S. warneri*, 14%(25/173) were *S. capitnis*, 5% (8/173) were *S. simulans*, 4%(7/173) were *S. epidermidis*, 2%(3/173) were *S. schleiferi* and 1%(2/173) were *S. lugdenensis*. 16.18% of the isolates were MRCoNS. Doctors had the highest number of MRCoNS (10/28, 35.7%). Methicillin resistance was highest in *S. lugdenensis* (50%). Multidrug resistance was seen in the CoNS isolates. All isolates were sensitive to vancomycin.

**Conclusion:** This study reiterates the need to screen HCWs for CoNS and to adopt simple, economical and user friendly tests for speciation. The species and its susceptibility pattern help to eliminate reservoirs and prevent nosocomial infections.

**Keywords:** anterior nares, antibiotic susceptibility, Coagulase negative Staphylococci (CoNS), health care workers(HCWs), methicillin resistant Coagulase negative Staphylococci (MRCoNS), multidrug resistant CoNS, speciation of CoNS.

## INTRODUCTION

Coagulase negative staphylococci (CoNS) are commonly found on human skin and several biotypes can be detected on a single individual.<sup>1</sup> In Microbiology laboratories, it is a common practice to identify coagulase negative Gram positive cocci as CoNS and the identification process stops there. It was also common to think that these organisms were not pathogenic and were dismissed as contaminants.<sup>2</sup> But in the last few years, various studies have demonstrated that CoNS are an emerging group of pathogens.<sup>2-4</sup> They are associated with nosocomial infections.<sup>2,3,5</sup> They are identified as the third commonest cause

of blood stream infections, which causes significant morbidity and mortality.<sup>5</sup> Several reports of CoNS infections, involving indwelling foreign bodies, catheters and artificial devices are on the rise.<sup>3</sup>

It is important to identify CoNS up to the species level, as the epidemiology, the pathogenicity and drug resistance varies from species to species.<sup>5</sup> Multidrug resistant strains have been reported from various studies.<sup>2,6</sup> The challenge with CoNS is that, not only are they multi drug resistant, but they are known to act as reservoirs for drug resistant genes.<sup>7</sup> The presence of such multidrug resistant strains and methicillin resistant strains in species of *Staphylococcus*, pose a challenge especially if they are found in the health care workers (HCWs). They act as reservoirs and help in nosocomial spread of infections. In addition, they cause problems for hospital infection control programmes in tertiary care hospitals.<sup>7</sup>

The data on the carriage rate of CoNS in HCWs is lacking.<sup>7</sup> Hence, we undertook this study, to determine the occurrence, the species and susceptibility pattern of CoNS isolated from the anterior nares of HCWs working in our tertiary care hospital.

## MATERIAL AND METHODS

This was a purposive sampling done on all health care workers (HCWs), for a duration of six months with an inclusion criteria being that all consenting HCWs working in our hospital to be included in the study. The exclusion criteria were: all non-consenting HCWs, HCWs who were on antibiotics, who had recent upper respiratory tract infection, who underwent recent nasal surgery and who had lesions in the nose, were to be excluded from the study.

We conducted a prospective study for 6 months duration among the health care workers (HCWs) in Raja Rajeswari Medical

<sup>1</sup>Associate Professor, <sup>2</sup>Post Graduate, Department of Microbiology, Raja Rajeswari Medical College and Hospital, Kambipura, Mysore Road, Bangalore-560074, India

**Corresponding author:** Dr. Ragini Ananth Kashid, M.B.B.S., M.D. (Microbiology), Flat no. A- 601, Ashwini Apartments, No. 14, Ring Road, Banashankari II stage, Bangalore 560070, India

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Group/species	Clump-ing factor	Tube co-agulase	Orni-thine decarbo-xylose	Urease	Novo-bio-cin (5 µg)	Mannose	Species/Subspecies	Trehalose growth	Mannitol	Acetoin	Lactose	Anaero-bic	Xylose
<i>S. epidermidis</i> group	-	-	+	S	+	<i>S. epidermidis</i>	-	-	-	-	-	-	-
<i>S. haemolyticus</i> group	-	-	-	S	-	<i>S. caprae</i>	+	-	-	-	-	-	-
<i>S. saprophyticus</i> group	-	-	-	R	-	<i>S. capitis</i>	-	-	-	-	-	-	-
<i>S. warneri</i> group	-	-	-	+	+	<i>S. ureolyticus</i>	-	-	-	-	-	-	-
<i>S. lugdenensis</i>	-	-	-	-	-	<i>S. haemolyticus</i>	-	-	-	-	-	-	-
<i>S. schleiferi</i>	-	-	-	-	-	<i>S. auricularis</i>	-	-	-	-	-	-	-
subsp. <i>schleiferi</i>	-	-	-	-	-	<i>S. caseolyticus</i>	-	-	-	-	-	-	-
<i>S. schleiferi</i>	-	-	-	-	-	<i>S. saprophyticus</i>	-	-	-	-	-	-	-
subsp. <i>coagulans</i>	-	-	-	-	-	<i>S. simulans</i>	-	-	-	-	-	-	-
<i>S. capitis</i> subsp. <i>capitis</i>	-	-	-	-	-	<i>S. xylosus</i>	-	-	-	-	-	-	-
<i>S. cohnii</i> subsp. <i>cohnii</i>	-	-	-	-	-	<i>S. cohnii</i>	-	-	-	-	-	-	-
<i>S. cohnii</i> group	-	-	-	-	-	subsp. <i>ureolyticum</i>	-	-	-	-	-	-	-

Table-1: Identification of CoNS by simple scheme and additional tests

College and Hospital. Doctors, nurses, technicians and class IV workers were included in the study. The institutional ethical committee approved the study. All health care workers who consented to give samples were included in the study. Prior to enrollment in the study, written consent was obtained from the health care workers. Two pre-moistened swabs were used to swab the anterior nares of health care workers. One swab was inoculated on to Mannitol salt agar and the other swab was inoculated into BHI broth, after overnight incubation at 37°C it was subcultured on to blood agar plates. The CoNS gave red coloured colonies on Mannitol salt agar. These red coloured colonies were identified as CoNS based on colony morphology, Gram stain, catalase test, slide coagulase and tube coagulase test. To exclude Micrococci and Stomatococcus species, bacitracin susceptibility test was performed.<sup>5</sup> To identify CoNS up to species level, we chose tests that were simple, user friendly and economical, from Kloos and Schleifer scheme, Mackie and Mc Cartney and Koneman et al.<sup>8-10</sup> (Table-1).

The tests mentioned in Table-1 were used to identify the common species of CoNS, which are as follows: the *S. haemolyticus* group (*S. haemolyticus*, *S. auricularis* and *S. caseolyticus*), the *S. saprophyticus* group (*S. saprophyticus* subsp. *saprophyticus* and *S. hominis* subsp. *novobiosepticus*), the *S. epidermidis* group (i.e., *S. epidermidis*, *S. capitis* subsp. *ureolyticus* and *S. caprae*), the *S. warneri* group (*S. warneri* and *S. hominis* subsp. *hominis*), *S. lugdenensis*, *S. schleiferi* subsp. *schleiferi*, *S. capitis* subsp. *capitis*, *S. simulans* and *S. cohnii* subsp. *cohnii*, the *S. cohnii* group (*S. xylosus* and *S. cohnii* subsp. *ureolyticum*).<sup>4</sup>

This scheme involved a two-step procedure (Table-1), first step aimed to identify species group and combined slide and tube coagulase with novobiocin resistance, test for urease activity, ornithine decarboxylase and aerobic acid from mannose. If identification required additional tests, a maximum of two tests were selected from Table-1:

- i. Trehalose and mannitol for the *S. epidermidis* group
- ii. Acetoin production and lactose for the *S. haemolyticus* group
- iii. Trehalose for the *S. saprophyticus* group
- iv. Anaerobic thioglycollate broth for the *S. warneri* group
- v. Xylose for the *S. cohnii* group.

Standard protocol was followed to perform the above tests.<sup>4,8-10</sup>

#### Antimicrobial susceptibility testing

Kirby Bauer disc diffusion method was performed for susceptibility testing. The following antibiotic discs were tested: amoxyclav (20 µg amoxicillin and 10 µg clavulanic acid), ciprofloxacin (5 µg), chloramphenicol (30 µg), clindamycin (2 µg), cotrimoxazole (1.25/23.75 µg), cefoxitin (30 µg), doxycycline (30 µg), erythromycin (15 µg), gentamicin (10 µg), linezolid (30 µg), oxacillin (1 µg) penicillin (10 units) and vancomycin (30 µg).

Methicillin resistance was screened using disc diffusion method. Four to five colonies from overnight growth were inoculated into peptone water. This was incubated at 35°C till it matched a turbidity standard of 0.5 McFarland. Cefoxitin (30 µg, Hi-Media, Mumbai, India) was used to identify methicillin resistant coagulase negative staphylococci (MRCoNS). Zone size of ≤ 24mm or less is considered as resistant to cefoxitin, for all CoNS, except for *S. lugdenensis*, for which zone diameter ≤ 21mm is considered resistant to cefoxitin.<sup>5,7,11</sup> Quality control was done using ATCC strain *Staphylococcus aureus* 25923.

#### STATISTICAL ANALYSIS

SPSS version 20 software was used for the statistical analysis. Descriptive analysis was given in terms of percentages to infer data.

#### RESULTS

Out of the 310 HCWs included in the study, 94(30.3%) were males and 216 (69.7%) were females. The anterior nares of 310 HCWs were swabbed. Of which, 105(33.8%) were attenders, 78 (25.2%) were doctors, 75 (24.2%) were technicians and 52 (16.8%) were nurses. Of the 310 HCWs who were included in this study, 60 % (186/310) were aware of health care associated infections. The various isolates that were isolated in this study are as follows: 55.8% (173/310) CONS, 25.5 % ( 79/310) Micrococcus species and 9% (28/310) *S.aureus*. 9.7 % (30/310) of the nasal swabs yielded no growth. Among the 173 CoNS isolated in this study, 44% (76/173) were *S. haemolyticus*, 30% (52/173) were *S. warneri*, 14%(25/173) were *S. capitis*, 5% (8/173) were *S. simulans*, 4% (7/173) were *S. epidermidis*, 2% (3/173) were *S. schleiferi* and 1% (2/173) were *S. lugdenensis* (Figure-1).

67.94% (53/78) of the doctors, 55.23% (58/105) of the attenders, 50% (26/52) of the nurses and 48% (36/75) of technicians were positive for CoNS (Table-2).The HCWs who tested positive for CoNS, were distributed in our hospital as follows: 19.7% (34/173) of CONS were isolated from Pharmacy, 11.6% (20/173) of CoNS were isolated from Laboratory, 11% (19/173) of CoNS were isolated from OBG ward, 9.8% (17/173) from Surgery ward, 9.2% (16/173) from Orthopaedics ward, 9.2% (16/173) from OT, 8.7% (15/173) from Paediatrics ward, 8.1% (14/173) from Medicine ward, 6.9% (12/173) from ICU, 2.3% (4/173) from ENT, 1.7% (3/173) from Psychiatry, 1.2% (2/173) from

Radiology and 0.6%(1/173)from Ophthalmology (Figure-2). *S. haemolyticus* showed resistance to the following antibiotics- 6.6% (5/76) resistance was seen to amoxicillin clavulanic acid, 5.3% (4/76) to chloramphenicol, 14.5% (11/76) to cefoxitin, 7.9% (6/76) each to ciprofloxacin and doxycycline, 32.9% (25/76) to clindamycin, 17.1% (13/76) to cotrimoxazole, 57.9% (44/76) to erythromycin, 3.9% (3/76) to gentamicin, 1.3% (1/76) to linezolid, 11.8% ( 9/76) to oxacillin and 61.8% (47/76) to penicillin. No resistance was seen to vancomycin (Table-3). *S. warneri* showed 7.7% (4/52) resistance to each of the following antibiotics: chloramphenicol, ciprofloxacin, doxycycline, gentamicin and oxacillin. It showed 11.5% (6/52) resistance to amoxicillin clavulanic acid, 13.5% (7/52) to cefoxitin, 26.9% (14/52)to clindamycin, 17.3% (9/52) to cotrimoxazole,

HCW group	Number screened	No. of CoNS isolated (Percentage %)	No. of MR-CoNS isolated (Percentage %)
Attenders	105	58(55.23)	9(32.2)
Doctors	78	53(67.94)	10(35.7)
Technicians	75	36(48)	6(21.4)
Nurses	52	26(50)	3(10.7)
Total	310	173(55.8)	28(100)

Table-2: Isolation of CoNS and MRCoNS in the various groups sampled

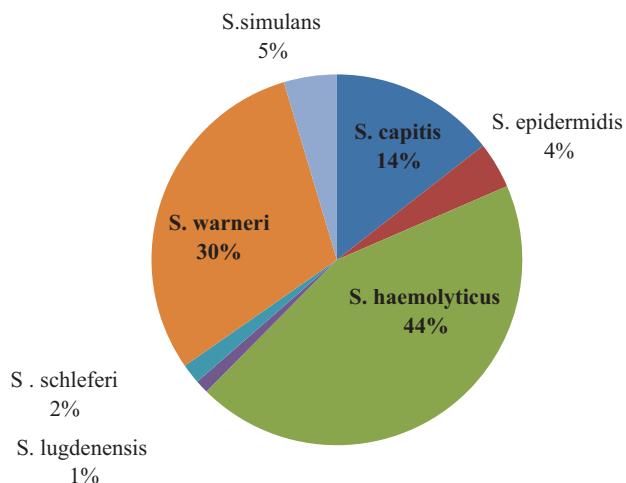


Figure-1: The various species of Coagulase negative Staphylococci isolated

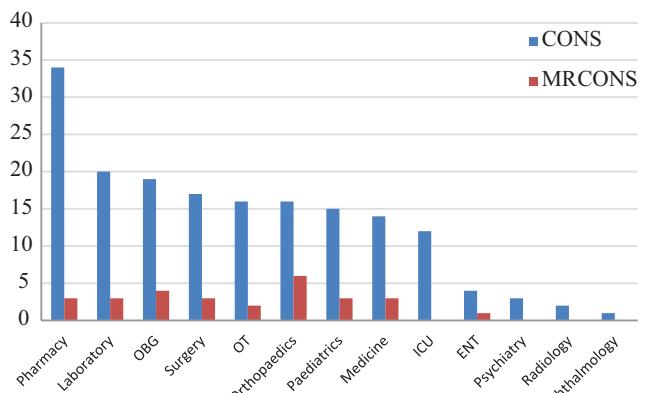


Figure-2: Distribution of HCWs who tested positive for CoNS and MRCNS in different areas of the hospital.

	Amoxicillin clavulanic acid	Cefoxitin	Chloramphenicol	Ciprofloxacin	Clindamycin	Cotrimoxazole	Doxycycline	Erythromycin	Gentamicin	Linezolid	Oxacillin	Penicillin	Vancomycin
	R	S	R	S	R	S	R	S	R	S	R	S	R
<i>S. haemolyticus</i> (76)	5	71	65	4	72	6	70	25	51	13	63	6	70
<i>S. warneri</i> (52)	6	46	45	4	48	14	38	9	43	4	48	27	25
<i>S. capitis</i> (25)	2	23	6	19	0	25	2	23	9	16	4	21	2
<i>S. simulans</i> (8)	1	7	1	7	1	7	1	7	2	6	1	7	3
<i>S. epidermidis</i> (7)	0	7	1	6	0	7	1	6	0	7	0	7	0
<i>S. schleiferi</i> (3)	1	2	1	2	0	3	0	3	1	2	1	2	1
<i>S. lugdenensis</i> (2)	1	1	1	1	1	1	1	1	1	1	1	1	1
Total	16	157	28	145	10	163	14	159	51	122	29	144	15
Percentage (%)	9.25	90.75	16.18	83.82	5.78	94.22	8.09	91.91	29.48	70.52	16.76	83.24	8.67

Table-3: Resistance pattern of the various species of CoNS.

51.9% (27/52) erythromycin, 1.9% (1/52) linezolid and 48.1% (25/52) to penicillin. No resistance was seen to vancomycin (Table-3).

*S. capitis* showed resistance to the following antibiotics - 8% (2/25) resistance was seen to amoxicillin clavulanic acid, 24% (6/25) to cefoxitin, 8% (2/25) to ciprofloxacin, 36% (9/25) to clindamycin, 16% (4/25) to cotrimoxazole, 8% (2/25) to doxycycline, 36% (9/25) to erythromycin, 4% (1/25) to gentamicin, 4% (1/25) to linezolid, 20% (5/25) to oxacillin, 44% (11/25) to penicillin. No resistance was seen to chloramphenicol and vancomycin (Table-3).

*S. simulans* showed 12.5% (1/8) resistance to each of the following antibiotics: Amoxicillin clavulanic acid, cefoxitin, chloramphenicol, ciprofloxacin, clindamycin, doxycycline, gentamicin, linezolid and oxacillin. It showed 25 % (2/8) resistance to cotrimoxazole, 37.5 % (3/8) to erythromycin and 62.5 % (5/8) to penicillin. No resistance was seen to vancomycin (Table-3).

*S. epidermidis* showed 14.3 % (1/7) resistance to clindamycin, cefoxitin and oxacillin, 28.57% (2/7) resistance to penicillin. No resistance was seen to amoxicillin - clavulanic acid, chloramphenicol, ciprofloxacin, cotrimoxazole, doxycycline, erythromycin, gentamicin, linezolid and vancomycin (Table-3).

*S. schleiferi* showed 33.3% (1/3) resistance each, to amoxicillin clavulanic acid, cefoxitin, doxycycline, erythromycin and oxacillin. 66.6 % (2/3) resistance was seen to penicillin. No resistance was seen to chloramphenicol, ciprofloxacin, clindamycin, cotrimoxazole, gentamicin, linezolid, and vancomycin (Table-3).

In *S. lugdenensis*, 50% (1/2) resistance was seen to each of the following: amoxicillin clavulanic acid, cefoxitin, chloramphenicol, ciprofloxacin, clindamycin, cotrimoxazole, doxycycline, erythromycin, oxacillin and penicillin. No resistance was seen to gentamicin, linezolid and vancomycin (Table-3).

Of the 28 MRCNs isolated, 10 (35.7%) were from doctors, 9 (32.2%) were from attenders, 6 (21.4%) were from technicians and 3 (10.7%) were from nurses (Table-3). The distribution of the HCWs in whom MRCNs were isolated is as follows: 21.4% (6/28) of MRCNs were isolated from Orthopaedics, 14.3% (4/28) of

MRCNs were isolated from OBG ward, 10.7% each (3/28) of MRCNs were isolated from Medicine ward, Surgery ward, Paediatrics, Laboratory and Pharmacy respectively. 7.2% (2/28) of MRCNs from OT and 3.6% (1/28) from ENT (Figure-2)

## DISCUSSION

In recent years CoNS have been identified as an important nosocomial pathogen. It is important that we identify them up to the species level, as it helps in identifying the reservoir, studying the distribution of CoNS implicated in the causation of nosocomial infections and in determining the etiological agent.<sup>4</sup> For species identification, tests that were simple, user friendly and economical were chosen (Table-1).

A total of 310 HCWs were included in the study. 69.7% of the HCWs included in this study were females, as more number of females were included in the study as compared to males. Of the 310 HCWs who were sampled, 173 HCWs yielded CoNS. The rate of isolation of CoNS was 55.8% (173/310). This correlates with the study conducted by Narayani et al. who reported a nasal carrier rate of 62% CoNS.<sup>12</sup> The percentage of isolation of CoNS was highest in the doctors (67.94%), followed by attenders (55.23%), nurses (50%) and technicians (48%). 57% of the HCWs, who participated in the study, were aware about health care associated infections. For the remaining 43% of HCWs, our hospital conducts several training and informative programmes to improve their knowledge about health care associated infections.

The various species of CoNS that were isolated are as follows: 44%(76/173) were *S. haemolyticus*, 30% (52/173) were *S. warneri*, 14% (25/173) *S. capitis*, 5% (8/173) were *S. simulans*, 4% (7/173) were *S. epidermidis*, 2%(3/173) were *S. schleiferi* and 1% (2/173) were *S. lugdenensis*. Studies conducted by, Mohan U (82.29%), Goyal R (41%), Shobha KL (49.23%) report *S. epidermidis* as their predominant isolate.<sup>1-3</sup> In our study, *S. haemolyticus* (44%) was the predominant isolate, followed by *S. warneri* (30%) and *S. capitis* (5%). *S. epidermidis* was the fifth highest isolate (4%) in this study.

Highest number of CoNS was isolated from the anterior nares of HCWs working in the Pharmacy (19.7%), followed by HCWs

working in the laboratory (11.6%) and in the OBG department (11%) (Figure-2). However, the highest number of MRCNs were isolated from the HCWs working in Orthopaedics (6/28, 21.4%), followed by those working in OBG (4/28, 14.3%) (Figure-2). Therefore, it is important to include all the hospital staff, working in all areas of the hospital for surveillance studies.

In a study conducted by KL Shobha 22.22% of MRCNs were reported from anterior nares.<sup>7</sup> In our study, 16.18% (28/173) of the isolates were MRCNs. Anterior nares of HCWs Doctors had the highest number of MRCNs (10/28, 35.7%). These findings reflect that doctors are important in the chain of transmission of nosocomial infections and have to upgrade their compliance with hospital infection control programmes.

With regards to susceptibility testing, multidrug resistance was seen in many isolates. This correlates with the studies conducted by Mohan U, Goel MM and Pathak J.<sup>1,13,14</sup> Maximum resistance was seen towards drugs like penicillin (53.76%), erythromycin (49.13%), clindamycin (29.48%), cotrimoxazole (16.76%), cefoxitin (16.18%) and amoxiclav (9.25%). *S. lugdenensis* was the only species which showed resistance to almost all the antibiotics on the testing panel except for gentamicin, linezolid and vancomycin. Methicillin resistance was observed in all the species of CoNS isolated in this study. The percentages are as follows: 50% methicillin resistance in *S. lugdenensis*, 33.3% in *S. schleiferi*, 24.5% in *S. capitis*, 14.5% in *S. haemolyticus*, 14.3% in *S. epidermidis*, 13.57 % in *S. warneri* and 12.5% in *S. simulans*.

There are reports of emerging vancomycin resistance among Methicillin resistant CoNS.<sup>16</sup> In our study, all isolates were sensitive to vancomycin. The variability in antibiotic susceptibility pattern is because, we have different species of CoNS as our predominant isolates, there is a geographical variation and, differences in the antibiotic panel used in every hospital.

Today there are several molecular tests, which detect genes like the *ica* gene ( intercellular adhesion – operon – *ica* ADBC ), *atlE* gene (encodes for the vitronectin – binding cell surface protein involved in primary attachment ) and the *mecA* gene (controls the synthesis of PBP2a).<sup>3</sup> Other tests like plasmid analysis, tests for slime production and adherence help in the better understanding of pathogenesis, diagnosis and epidemiology of CoNS.<sup>15</sup> These tests may not be economically viable for all hospitals to carry out.

## CONCLUSION

Therefore, this study, reiterates the need to speciate the CoNS with an easy, user friendly and economical tests. It is important to speciate the CoNS as this study has proved that the species reported in other hospitals (*S. epidermidis*) may not coincide with the species isolated in our hospital (*S. haemolyticus*). The study also presses the need to screen the HCWs for carriage of CoNS on a regular basis, as these HCWs act as reservoirs for CoNS. CoNS are identified as emerging pathogens and are known for multidrug resistance. CoNS could be potential roadblocks to hospital infection control programmes. The species and its corresponding sensitivity pattern have to be kept in mind so as to eliminate reservoirs and prevent the spread of nosocomial infections.

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# Clinical and Radiological Success Rates of Biodentine for Pulpotomy in Children

Mobeen Akhtar<sup>1</sup>, Sadiq Amin Ahmed Rana<sup>2</sup>, Muzammil Jamil Ahmed Rana<sup>3</sup>, Naghma Parveen<sup>4</sup>, Muhammad Kashif<sup>5</sup>

## ABSTRACT

**Introduction:** Formocresol pulpotomy in primary teeth is commonly accepted method in many countries. Current studies have reported limitations of formocresol technique for vital amputation and favour the use of biodentine for vital pulpotomy as it is a biocompatible material and its sealing ability is superior to other available alternatives. Study aimed to find out the clinical and radiological success rate of biodentine for pulpotomy in children visiting Nishtar Institute of Dentistry, Multan, Pakistan.

**Material and Methods:** 122 consecutive patients ranging in age from 4-12 years presenting in Nishtar Institute of Dentistry and fulfilling the inclusion and exclusion criteria were included in the study. Thorough history, clinical examination, periapical radiographs using standardized methods for children were performed. The whole procedure of pulpotomy was carried out. After achieving hemostasis, pulp stumps were covered with Biodentine™. Children were followed up for clinical and radiographic assessment at 3 months. The clinical success criteria in terms of absence of pain, pathologic mobility, swelling, sinus, pathological root resorption and radiographic success criteria in terms of periapical and furcal radiolucency were noted.

**Results:** Among 122 pediatric patients, males were 75/122 (61.47%) and females were 47/122 (38.52%). Mean age of the patients was  $7.67 \pm 1.3$  years. The clinical success of Biodentine™ was identified in 117/122 (95.90%) of the patients. Where as radiological success was identified in 115/122 (94.26%) patients.

**Conclusion:** Biodentine™ as a pulpotomy agent has a high success rate and should be routinely used in practice for the treatment of carious primary molars.

**Keywords:** Pulpotomy; Biodentine; Formocresol.

## INTRODUCTION

It is always a challenge for a dentist to manage a grossly carious primary molar tooth. Therefore, competency in selecting an appropriate restorative material and technique is required by the clinician for treating the deciduous molars.<sup>1</sup>

Pulpotomy is a clinical procedure which is performed upon accidental or carious exposure of dental pulp, if a tooth is free of any obvious periradicular pathology. In case of primary teeth, this procedure is indicated for reversible pulpitis or mechanical exposure of pulp.<sup>1</sup> After amputation of coronal tissue, it is assumed that remaining radicular tissue is vital. This tissue should be free of any necrosis and excessive hemorrhage.<sup>2</sup>

Different materials are used to treat remaining vital radicular pulpal tissue. These clinically successful medicaments include Buckley's Solution of formocresol, ferric sulfate, glutaraldehyde and calcium hydroxide.<sup>2</sup> Electrosurgery also has demonstrated success. However, since mid 1990s, Mineral Trioxide Aggregate (MTA) has been recognized as the reference material for the conservative pulp vitality treatments such as pulpotomy in temporary teeth. It has shown to stimulate the formation of dentin

bridge protecting the pulp markedly more than that observed with calcium hydroxide.<sup>3</sup> Biodentine is the latest development in this class of drugs. This new calcium silicate based material exhibits physical and chemical properties similar to those described for certain Portland cement derivatives.<sup>4,5</sup> On the biological level, it is perfectly reactionary dentin as it stimulates odontoblast activity and reparative dentin by induction of cell differentiation.<sup>6</sup> It is in effect a dentin substitute that can be used as a coronal restoration material and can be placed in contact with the pulp. Its faster setting time makes it directly functional intraorally without fear of the material deterioration.<sup>6,7</sup> Clinical trials show that biodentine performs equal to or better than formocresol, ferric sulfate or MTA and is now considered as the preferred pulpotomy agent for the future.<sup>8-11</sup>

The clinical and radiological success rate of Biodentine for pulpotomy are extensively being studied internationally in various ongoing large randomized controlled trials and cohort studies.<sup>9,10</sup> The published data mostly consists of its beneficial effects at a molecular level.<sup>4-6</sup> However, one published study states that Biodentine has success rates similar to that of mineral trioxide aggregate (MTA)<sup>11</sup> i.e. 94.7% with additional benefits of faster setting time and better odontoblastic activity. In another study, the reported clinical as well as radiological success rate of biodentine was 95%.<sup>12</sup> However, as this is currently an area of ongoing research and debate, we conducted this study to find out the success rate of this newly emerging pulpotomy agent in our local population too. This will add to our local database, and if its success rate found to be high will enable us to use this material in our patients more confidently.

## MATERIAL AND METHODS

After informed consent, 122 study subjects were selected consecutively by following non probability sampling technique for this Quasi experimental study. This study was approved and verified by Institutional Ethical Review Committee of NID, Multan. Patients visiting the Operative Dentistry Department, NID, Multan, fulfilling the inclusion and exclusion criteria were included in this study. The diagnosis of the vital pulps was determined by history, clinical examination, response to thermal and electrical pulp tests, and pre treatment radiographs of the

<sup>1</sup>Demonstrator, <sup>2</sup>Assistant Professor, <sup>4</sup>Associate Professor, NID, Multan, <sup>3</sup>Assistant Professor AFID, Rawalpindi, <sup>5</sup>Doctoral Research Fellow, University of Health Sciences, Lahore, Pakistan

**Corresponding author:** Muhammad Kashif, Doctoral Research Fellow, University of Health Sciences, Lahore, Pakistan

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affected teeth. All the patients were treated with biodentine pulpotomy. Medicaine injection with 1:100,000 epinephrine (Huons Co.Ltd, Korea) was administered as a local anesthetic in all patients. Cotton rolls and suction were used for maintenance of isolation in all patients (in order to standardize procedures), since some children under age 6 years did not tolerate a rubber dam. All caries were removed. Upon pulpal exposure during cavity preparation, the status of the exposure site and the amount and characteristics of bleeding were evaluated. If the bleeding was easily controlled and light red in color, the inflammatory process was assumed to be limited to the coronal pulp. Following this diagnosis, the pulp chamber roof was removed, and the coronal pulp was amputated using a high-speed instrument with a sterile diamond bur and continuous water spray (gentle technique). All remaining pulp tissue was excavated, and the chamber was irrigated with normal saline. Hemorrhaging was controlled by placing a sterile cotton pellet over the radicular pulp stump using light pressure. The pellet was removed within 5 minutes, and the hemorrhaging was re-evaluated. Amputation stumps were covered with biodentine paste (Septodont) for 3 minutes. Then intermediate restorative material paste was placed over the pulp stump, and the teeth were restored with Miracle Mix (GC). All the patients were followed up at 12 weeks to assess for clinical and radiological success / failure. All the data were entered in a specially designed proforma.

## STATISTICAL ANALYSIS

SPSS version 20.0 was used to analyze the data. Frequencies and percentages were calculated for the descriptive variables like gender, clinical success, radiological success. Mean  $\pm$  S.D were calculated for quantitative variables like age. Effect modifiers like age and gender were controlled through stratification. Chi-Square test was applied to see the effect of these on clinical and radiological success rate. When a P value was found to be  $\leq 0.05$ , it was considered as significant.

## RESULTS

In the present study 122 patients were treated for the pulpotomy with biodentine material. After treatment All patients were assessed clinically and radiologically. In 75 male patients participated with minimum age 4 years to maximum age 11 years. Mean age was  $7.06 \pm 1.58$ . When we applied Chi-Square test to observe the statistical association between gender and treatment success, it was found to be insignificant ( $p = 0.52$ ). All these descriptive statistics are tabulated in the Table-1 and 2. Out of total 75 male patients, 3 patients showed failure when assessed radiologically after 12 weeks. At the same time, among 47 female patients, 4 patients showed the radiological failure. Overall, out of 122 patients, 115 were radiologically successful (Table-3).

## DISCUSSION

Although many newer and advanced materials, e.g. MTA, are available in the market for pulpotomy but a longer time of setting, fairly complicated to use and low cost effectiveness, are the few factors which urge the scientists to formulate some more suitable materials. Biodentine has dentin-like mechanical properties, which may be considered a suitable material for clinical indications of dentin-pulp complex regeneration.<sup>13</sup>

In the current study, out of total 75 male patients, 1 patient

	Gender		Statistic
	Male (75)	Female (42)	
Age	Mean	7.0533	
	Std. Deviation	1.57595	
	Minimum	4.00	
	Maximum	11.00	
	Mean	7.6383	
	Std. Deviation	1.59381	
	Minimum	4.00	
	Maximum	12.00	

Table-1: Age and gender distribution of study participants

		Clinical success		Total
		Yes Clinical success	No Clinical success	
Gender	Male	74	1	75
		63.2%	20.0%	61.5%
	Female	43	4	47
		36.8%	80.0%	38.5%
Total		117	5	122
		100.0%	100.0%	100.0%

\*p = 0.052

Table-2: Association between gender distribution and clinical success rate

		Radiological success		Total
		Yes radiological success	No radio- logical success	
Gender	Male	72	3	75
		62.6%	42.9%	61.5%
	Female	43	4	47
		37.4%	57.1%	38.5%
Total		115	7	122
		100.0%	100.0%	100.0%

\*P = 0.297

Table-3: Association between gender distribution and radiological success rate

showed failure when assessed clinically after 12 weeks. At the same time, among 47 female patients, 4 patients showed the clinical failure. If we see the clinical success rate, it was highly successful, as among 122 patients, 117 were clinically successful.

A study was carried out on intact permanent premolars which were scheduled to be extracted for orthodontic reasons. The researchers electively exposed the pulp of 28 teeth and utilized Biodentine a pulp capping material. These teeth were extracted after six weeks and were stained with hematoxylin and eosin stains. Nowicka et al. found that majority of specimens showing a complete dentinal bridge formation and an absence of inflammatory pulp response. Layers of well-arranged odontoblast and odontoblast-like cells were found to form tubular dentin under the osteodentin. They also found no statistically significant differences between the Biodentine and MTA experimental groups.<sup>14</sup>

Another type of MTA (ProRoot) was compared with Biodentine in relation to silicon and calcium uptake in root dentine in a study by Han and Okiji. They observed that elemental uptake was more pronounced in roots treated with Biodentine as compared

to MTA.<sup>15</sup> Laurent *et al.* evaluated its genotoxicity, cytotoxicity, and effects on the target cells' specific functions and found that it did not affect the pulp fibroblast specific functions such as mineralization, as well as expression of collagen I, dentin sialoprotein, and Nestin.<sup>16</sup>

Regarding the biological effects of Biodentine on dental pulp, Perard and his colleagues conducted a study, they reported that COL-1A1 expression was slightly lower in cultured spheroids of odontoblasts treated with MTA but it was higher in case of Biodentine. This CO1A1 gene is responsible for matrix formation. Therefore, they were of the opinion that Biodentine is more suitable material for pulp capping as compared to MTA.<sup>17</sup> Similar beneficial effects of Biodentine had been reported by Ville and his coworkers. He demonstrated a rapid tissue response and the formation of a dentinal bridge in the root as well as coronal dentine over a period of 3-6 months after pulp capping with Biodentine. In another study, researchers had reported that blood contamination had no effects on a push out bond strength of Biodentine.<sup>17,18</sup>

Researchers studied the effect of etching with 35% phosphoric acid as compared to glass ionomer cement and light-cured glass ionomer cement and found that Biodentine exhibited a lower calcium to silicon ratio and a reduction in the chloride peak height when etched.<sup>19</sup> Biodentine performs well without any conditioning treatment as a dentin substitute. Hence, etching of Biodentine is not recommended and it is directly bonded to the resin composite. Use of self etch and total etch systems for bonding Biodentine to resin composites had no significant difference between both and suggested use of both self etch as well as total etch adhesives.<sup>20</sup>

## CONCLUSION

In current study this product (Bidentine) found very effective in terms of clinical and radiological aspect. Biodentine holds promise for clinical dental procedures as a biocompatible and easily handled product with short setting time. Therefore, Biodentine is an interesting alternative to MTA.

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# Ocular Manifestations in Road Traffic Accidents: A Study Done at A Medical College Hospital in South India

Parri Muralidhar<sup>1</sup>, N. Lakshmi Chowdary<sup>2</sup>

## ABSTRACT

**Introduction:** Ocular trauma due to road traffic accidents are increasing in number and are a cause of concern. This study aimed to evaluate the frequency of different types of ocular injuries in road traffic accidents and assess the visual outcome.

**Material and methods:** This was a cross sectional, non interventional, hospital based study done during a period of 6 months from December 1st 2015 to may 31st 2016 done at a Medical College Hospital from South India. A total of 40 patients who met with ocular injury were included in this study. Demographic data and other details were obtained and analyzed.

**Results:** Of 40 patients, male - 38, female - 2; most of the patients who sustained injuries were between 41 to 50 years (40%, 16/40). Right eye injury was more frequent (60%, 24 patients). The visual acuity immediately after the trauma ranged between 6/6 to perception of light (PL). Most common form of injury was sub conjunctival hemorrhage constituting 70% (28/40) followed by ecchymosis constituting 50% (20/40).

**Conclusion:** Immediate medical attention and appropriate surgical or nonsurgical conservative management will aid in quick visual rehabilitation of the patient.

**Key words:** ocular trauma, road traffic accidents

## INTRODUCTION

Road traffic accidents are common now a day. Trauma to eye can cause severe and permanent visual impairment owing to its delicate and complex architecture.<sup>1</sup> Motor vehicular crashes are one of the leading cause of ocular trauma in United States and form an unique risk factor for the same.<sup>2-4</sup> Ocular trauma due to road traffic accidents resulting in visual loss may cause enormous trauma to the person and to the society on the whole. Ocular trauma may involve the eye lids, lacrimal canaliculi, orbital wall, peri orbital structures, conjunctiva, cornea, sclera, extra ocular muscles. In some instances there may be prolapse of uveal tissue, vitreous hemorrhage, choroidal hemorrhage, globe rupture. This paper analyzes the spectrum of ocular injuries seen in road traffic accidents in a South Indian city and assesses the visual outcome by providing appropriate medical and surgical treatment

This study was performed to evaluate the frequency of different types of ocular injuries in road traffic accidents and assess the visual outcome along with the age and gender distribution of the study group.

## MATERIAL AND METHODS

This is a cross sectional, non interventional, hospital based study done during a period of 6 months from December 1<sup>st</sup> 2015 to May 31<sup>st</sup> 2016 done at NRI academy of medical sciences, Chinakakani, Guntur, Andhra Pradesh after obtaining the ethical clearance from the ethical board of the college.

## Inclusive criteria

- 1) Patients between 1 to 60 years of age.
- 2) Individuals who were driving or were in the vehicle during accident.
- 3) Patients who sustained ocular injuries during the road traffic accidents.

## Exclusive criteria

- 1) Patients who sustained ocular injuries due to domestic trauma.
- 2) Patients who sustained ocular injuries due to assault.
- 3) Patients who sustained ocular chemical injuries.

A total of 40 patients who sustained ocular injuries due to road traffic accidents (also fulfilled the inclusion and exclusion criteria) and attended the causality department & ophthalmology outpatient department of Medical college hospital during the study period were included in this study. Demographic data and details were obtained and analyzed. Bed side vision was recorded. Thorough slit lamp evaluation of anterior segment and fundus examination were done. X ray of orbit (AP and Lateral view) and computerized tomography (CT) scan were done in all suspected cases of orbital rim fractures and peri orbital trauma. The results were analyzed and conclusions were drawn.

## STATISTICAL ANALYSIS

Microsoft office 2007 excel sheet was used to tabulate data. Mean, ratio and percentages of the variables were calculated and the results were analyzed.

## RESULTS

### Age and gender distribution

In the study of 40 patients (male -38: female 2), the youngest patient was 12 years and eldest patient was 49 year old; the details are shown in Table-1. Most of the patients who sustained injuries were between 41 to 50 years (40%, 16/40), followed by second decade (30%, 12/40).

### Laterality

Right eye injury was more frequent (60%, 24 patients) than left eye (40%, 16 patients). One patient had bilateral eye injury.

### Consciousness

All except one patient were conscious and coherent when they

<sup>1</sup>Assistant Professor, <sup>2</sup>Professor and Head of the Department, Department of Ophthalmology, NRI Academy of Medical Sciences, Chinakakani, Guntur, Andhra Pradesh, India

**Corresponding author:** Dr. Parri Muralidhar DNB. DO, Assistant Professor, Department of Ophthalmology, NRI Academy of Medical Sciences, Chinakakani, Guntur, Andhra Pradesh, India

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were brought to OPD. One patient had altered sensorium.

#### **Visual acuity (VA)**

The visual acuity immediately after the trauma ranged between 6/6 (on Snellen chart) to perception of light (PL). The details are shown in Table-2.

#### **Type of injury**

Most common form of injury was subconjunctival hemorrhage constituting 70% (28/40), followed by ecchymosis constituting 50% (20/40). The frequencies of different types of injury are shown in Table-3. Extra ocular muscles were involved in 16 patients (40%); superior and inferior rectus muscles were involved in 8 patients each respectively (20%). Twenty patients had fracture of periorbital structures (fracture of maxillary sinus – 8, fracture of frontal bones -12); details are shown in table 3. One patient had blunt injury resulting in dislocation of lens with hyphaema. Vision was profoundly decreased in one person due to traumatic optic neuropathy exhibiting Relative Afferent Papillary Defect (RAPD) sign.

#### **Management**

Visual acuity was assessed and detailed examination of anterior segment and posterior segments was done with torch light and slit lamp biomicroscopy. The severity of injury was assessed. Vision improved with conservative treatment without any surgical procedure in ecchymosis, subconjunctival hemorrhages and periorbital trauma. Lid tears were repaired under local anesthesia. X ray of orbit (AP and Lateral view) was taken to rule out any muscle entrapment in patients with fractures of orbital rim. Hyphaema was treated by non surgical medical management. Lens was removed in lens dislocation patient. Worsening grade of vision was found in patients with multiple eyes injuries. Vision was not recovered in a patient who presented with PL vision where optic nerve was damaged.

#### **DISCUSSION**

Ocular trauma is one of the main causes of blindness and ocular morbidity. Ocular trauma has profound effect on both professional and personal life of the patient influencing his family as well as the society. Especially in our study where the peak age group was between 41 to 50 years who are the main bread winners of the family. Peak age in this study is higher than that reported in literature; Ezegwui IR<sup>1</sup> had reported peak age between 16 to 30 years in his study. Armstrong GW et al<sup>2</sup> and Arora AS et al<sup>3</sup> have also reported similar results.

In this study, male patients were more commonly affected than female patients with M: F ratio of 19:1. Shtewi M EL et al<sup>4</sup> have done a two year study from an Eye hospital in Libya on road traffic accidents and ocular trauma; they reported that out of 248 patients included in their study, 186 (75%) were male and 62 (25%) were female. Similarly Johnston PB<sup>5</sup> from Northern Ireland reported the incidence as 72.20% in males and 27.80% in females after seatbelt legislation. Arora AS et al<sup>3</sup> have done a similar study from India, Rajasthan and reported the M: F ratio to be 2.5:1.

Right eye injury was more frequent (60%, 24 patients) than left eye (40%, 16 patients), in this study similar to other studies.<sup>3,4,6</sup> The visual acuity immediately after the trauma ranged between 6/6 to PL. Most of the patients had VA between 6/9 to 6/36,

Age group	Number (percentage) n=40
10-20	4 ( 10% )
21-30	12 ( 30% )
31-40	8( 20% )
41-50	16( 40% )

**Table-1:** Age distribution

Visual acuity	No. of Patients( n=40)
6/6-6/9	8 ( 20% )
>6/9-6/18	12 ( 30% )
>6/18-6/36	12( 30% )
>6/36-6/60	6(15%)
Hand movements	1(2.5%)
PL+	1(2.5%)

**Table-2:** Visual acuity at presentation

Type of injury	No. of Patients( n=40)
Lid tear	4 ( 10% )
Lid abrasion	8 ( 20% )
Ecchymosis	20 ( 50% )
Extra ocular muscle paralysis	
Superior rectus	8 ( 20% )
Inferior rectus	8 ( 20% )
Medial rectus	0
Lateral rectus	0
Fracture of orbital rim	
Lateral wall	4( 10% )
Medial wall	4( 10% )
Floor	4 ( 10% )
Peri orbital structures	
Fracture of maxillary sinus	8 ( 20% )
Fracture of ethmoidal sinus	0
Fracture of frontal bones	12 ( 30% )
Subconjunctival hemorrhage	28 ( 70% )
Corneal abrasion	4 ( 10% )
Hyphaema	4 ( 10% )
Lens dislocation	1(2.5%)
Traumatic optic neuropathy	1(2.5%)

**Table-3:** Type of injury

who had sustained ocular adnexal injury, periorbital fracture, subconjunctival hemorrhage, and ecchymosis. Drastic fall of VA to hand movements and perception of light had occurred in two patients who sustained dislocation of lens and posterior segment involvement mainly traumatic optic neuropathy. After treatment there is regain of VA to 6/9 in patients who sustained ocular adnexal injury and periorbital fracture.

Most of the patients had sustained subconjunctival hemorrhages, ecchymoses and ocular adnexal injuries rather than penetrating globe injuries involving posterior segment of the eye. Oum BS<sup>7</sup> and Kulkarni AR et al<sup>8</sup> had also made similar observations in their respective studies. Closed globe injuries were more common in our study than open globe injuries similar to that reported by Mittal G<sup>9</sup> Arora AS el al<sup>3</sup> and Gully CM el al.<sup>10</sup> The eye ball is protected by bony socket and periorbital structures, which are the first structures to take the impact of the injury during road traffic accidents, so they are more frequently injured rather than posterior segment; this might be the probable explanation for the type and distribution of injuries seen in our study.

## CONCLUSION

Ocular injuries due to road traffic accidents are on rise, due to increasing vehicular traffic. They cause profound effect on the vision of the patient leading to significant burden on their families and to the society as a whole. Strict implementation of the existing traffic rules by the governments and adherence to the same by the civilians can reduce the impact of injury. Immediate medical attention and appropriate surgical or nonsurgical conservative medical management will aid in quick visual rehabilitation of the patients.

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# Correlation Between Transcutaneous and Serum Bilirubin Measurements in Neonates in a Tertiary Neonatal Care Center

Arasar Seeralar. A. T<sup>1</sup>, Ganesh. J<sup>2</sup>, Suganya. M<sup>3</sup>, Narayana Babu. R<sup>1</sup>, Sathyamoorthi. B<sup>1</sup>, Padmanaban. S<sup>4</sup>

## ABSTRACT

**Introduction:** Hyperbilirubinemia is one of the common problem in Neonates. An estimation of the bilirubin value is essential for decision making in jaundiced babies. Transcutaneous bilirubin screening is a quick, noninvasive technique to measure bilirubin level in neonates. The objective of this study was to evaluate the Transcutaneous bilirubin and analyse the correlation with serum bilirubin values and find out whether Transcutaneous bilirubin measurement could avoid invasive serum bilirubin measurement.

**Materials and Methods:** Retrospective study was conducted in the neonatal unit of Kilpauk Medical college. All newborns with history of Jaundice and neonates in nursery who were clinically diagnosed to have jaundice during the period November 2015 to January 2016 were included in the study. 267 babies who met the inclusion criteria were enrolled in the study. Transcutaneous bilirubin measurement was done using the Transcutaneous Jaundice Meter and simultaneously a serum sample serum bilirubin estimation done. Babies who had received prior phototherapy, exchange transfusion and unstable babies in shock were excluded from the study.

**Results:** There seems to be a close correlation between Transcutaneous bilirubin measurement and Total serum bilirubin measurement. The overall mean difference between the two values was only 1.35mg/dl. The mean difference seems to correlate very closely when the bilirubin values are low.

**Conclusion:** The study demonstrates clearly that there is good correlation between the Transcutaneous bilirubin measurement and Total serum bilirubin measurement. The Transcutaneous bilirubin values were higher than the Total serum bilirubin values.

**Keywords:** Transcutaneous bilirubin, Total serum bilirubin, Transcutaneous jaundice meter

## INTRODUCTION

Hyperbilirubinemia is one of the common problems in Neonates. An estimation of the bilirubin value is essential for decision making in jaundiced babies. TcB screening is a quick, noninvasive technique to measure bilirubin level in Neonates.<sup>1</sup> Many previous studies have shown that transcutaneous bilirubin measurement provides a close estimate of total serum bilirubin levels.<sup>1-6</sup> Each study has used a different Transcutaneous Jaundice meter for estimation of TcB.<sup>1</sup> The test is easy to perform and obviates the need for pricking the baby for blood sample for TSB measurement and sending to lab and waiting for the report. We used the M and B Electronic Instruments Co., Ltd Transcutaneous Jaundice Detector model MBJ-20 to evaluate the Transcutaneous Bilirubin. Jaundice is one of the most common condition in newborn. Serum bilirubin estimation is one of the essential investigation done to assess the severity of Jaundice. Serum bilirubin estimation is traditionally done on serum sample drawn by venipuncture which is invasive and painful.<sup>2,3</sup> Hence there was need for a non invasive, reliable method to assess the bilirubin level. The objective of the study

was to find out whether Transcutaneous bilirubin measurement could be reliably used to assess jaundice and avoid veni puncture for serum bilirubin measurement.

## MATERIAL AND METHODS

The study was conducted in the neonatal unit of Kilpauk Medical college and Hospital as Prospective cross sectional study. All newborns referred to the neonatal unit with history of Jaundice and neonates in nursery who were clinically diagnosed to have jaundice were included in the study. 267 neonates who met the inclusion criteria during the period November 2015 to January 2016 were enrolled in the study. Informed consent was obtained from the parents of the newborns. TcB measurement was done using the Transcutaneous Bilirubinometer. Measurement was obtained over the sternum. Simultaneously a serum sample was collected and sent to biochemistry lab for serum bilirubin estimation. Babies who had received prior phototherapy, exchange transfusion and unstable babies in shock were excluded from the study.

The Transcutaneous bilirubin measurement was done using the MBJ 20 Transcutaneous Jaundice detector. MBJ20 Transcutaneous jaundice detector is developed with advanced electronics and optics, adopting Filter optics, spectrum splitter, controlled spectrum filter, NFM switching and information processing techniques. It uses dual wavelengths 450nm and 550nm which reach different layers of the skin. Serum bilirubin was estimated in the biochemistry lab using the Diazo method. The study was approved by institutional Ethics committee.

## STATISTICAL ANALYSIS

SPSS version 21 was used for statistical analysis. Correlation, regression, paired t test, intra class correlation, ROC curve and Bland and Altman plot were done to infer the data.

## RESULTS

Paired sample statistics of 267 neonates for TcB and TSB was analysed. The mean for TcB was 13.08 mg /dl and the mean of TSB was 11.73 mg /dl. The overall mean difference between the TSB and TcB values was only 1.35mg/dl with a correlation

<sup>1</sup>Professor of Paediatrics, <sup>3</sup>Assistant Professor of Paediatrics, Department of Paediatrics, <sup>4</sup>Scientist B(Statistics), NIRRH Field Unit, ICMR, Kilpauk Medical College Hospital, Chennai, <sup>2</sup>Professor of Paediatrics, Department of Paediatrics, Stanley Medical College, Tamilnadu, India

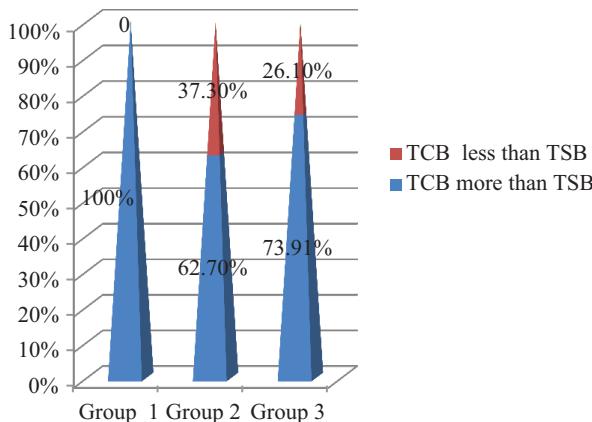
**Corresponding author:** Dr. Arasar Seralar A. T., 53, Amirjan street, Choolaimedu, Chennai, Pin- 600094, India

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	No	Paired Mean Differences	P value and Significance	Correlation	Intra Correlation		Regression Coefficient
					Single Measures	Average Measures	
Total group	267	1.3461	<0.0001	0.7351	0.7229	0.83914	0.5465
Group 1 (TSB < 9.9)	60	1.9500	<0.001	0.9586	0.8694	0.9301	0.9189
Group 2 (TSB 10-14.9)	161	1.314	<0.001	0.3491	0.2530	0.4039	0.1219
Group 3 (TSB 15 and above)	46	0.6696	0.06	-0.2708	-0.2204	-0.5655	0.07332
ROC	267	Sensitivity	Specificity	Criterion	Area Under curve		
		100	70.9	>14.4	0.915969		

**Table-1:** Statistical Analysis- consolidated.

TSB VS TCB Difference	Level 1 TSB ≤ 9.9	Level 2 TSB 10-14.9	Level 3 TSB ≥ 15
TCB More than TSB	60(100%)	101 (62.73%)	34 (73.91%)
TCB Less than TSB	0	60 (37.27%)	12 (26.1%)
Total	60(100%)	161 (100%)	46 (100%)

**Table-2:** TCB AND TSB Relationship**Figure-1:** TCB AND TSB relationship

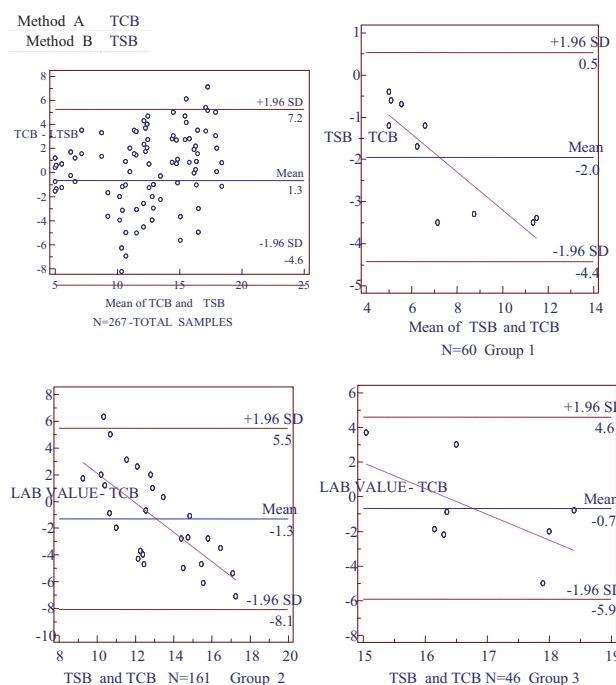
coefficient of 0.7351 with a 95 % confidence interval of 0.6746 to 0.7858 with significant  $P < 0.0001$  (Table-1).

Out of 267 neonates with jaundice for clinical convenience they were divided in to three groups based on TSB values. Group I - 5 - 9.9 mg/dl (60 in numbers), Group II – 10 – 14.9mg/dl, (161 in numbers) Group III 15 and more( 46 in numbers) for analysis. Statistical analysis showed paired mean difference between the group I, II and III. Mean difference was 1.950 ( $P < 0.001$ ), 1.314 ( $P < 0.001$ ) and 0.670 ( $P = 0.06$ ) respectively (Table-1).

The correlation coefficient for Group I was 0.9586 with a 95% confidence interval of 0.9314 to 0.9752 with a significant  $P$  value of  $< 0.0001$ . The correlation coefficient for Group II was 0.3491 with a 95% confidence interval of 0.2055 to 0.4780 with a significant  $P$  value of  $< 0.0001$ . The correlation coefficient for Group III was 0.2708 with a 95% confidence interval of 0.5202 to 0.02119 with  $P$  value of 0.06 which was statistically non significant (Table-1).

The bland Altman plot was drawn for both TSB and TCB values. The plot reveals that difference between two rater more than 7.2 and lesser than-4.6 are out layers, which are bad sectors. Using this bad sector and good sector were classified. The ROC curve was plotted to find out the optimum cut off value of TSB with respect to badly correlated difference values (Figure-2).

The Intra class correlation between TSB and TCB were good

**Figure-2:** Bland-Altman plot

for all 267 patients. The analysis between TSB and TCB of all the three groups were done using intra class correlation, paired T test and Bland Altman plot. Of all the three groups group 1 is having very good correlation, linear regression coefficients and good Altman plot.

## DISCUSSION

Our study primary outcome was to assess the TSB - TcB difference between paired values. In 195 paired values out of 267 TcB value was greater than the corresponding TSB level and only in 72 paired values TcB measurement was less than the paired TSB level. The correlation between linked TcB and TSB levels was calculated.<sup>1,2</sup> Under estimation of TSB values would miss cases needing intervention and high TcB may lead few more serum sampling for appropriate management. The magnitude of the TcB – TSB difference would tend to vary based on the TSB level, TSB was included in all regression models.

Across all the three groups the TcB values were more than the TSB values (in 73 % of paired values) (Table-2, Figure-1). This indicates TcB can be used as a screening tool without falsely underestimating serum bilirubin values.<sup>3-5</sup> Racial differences in population was presumed to affect the transcutaneous estimation of bilirubin. Engle et al has done a study predominantly in a Hispanic Neonates.<sup>6</sup> It shows that the TcB measurement were underestimating TSB values when serum bilirubin was high. Our study done on Asian neonates also shows a similar trend. Our study was done using

MBJ 20 Transcutaneous jaundice detector and compares well with results obtained by using Bilicheck bilirubinometer done by Ebbesen et al.<sup>7</sup>

The optimum cut off value of TSB was more than 14.4mg/dl, with a sensitivity of 100 and specificity of 70.9 (Table 1). This very much correlated with the study by James A Taylor et al.<sup>2</sup> Overall, the findings in this study suggest that TcB measurements can be used effectively to screen newborn infants for hyperbilirubinemia, with TSB measurements reserved for those newborns whose TcB level is above a certain cutoff value. The limitation of the study was that it did not take in to account the differences that may exist between Preterm and Term babies in assessment of TcB.

## CONCLUSION

The study demonstrates clearly that there is good correlation between the TcB measurement and TSB measurement using the Transcutaneous Jaundice meter MBJ20. The TcB values were higher than the TSB values in 73% of our samples. We suggest that TcB measurements can be used effectively to screen newborn infants for hyperbilirubinemia, with TSB measurements reserved for those newborns whose TcB level is above a certain cutoff value.

## ETHICAL APPROVAL

Approved by institutional Ethical committee

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# Untreated Severe Dental Decay- A Neglected Determinant of Child's Oral Health

Pai Tanvi<sup>1</sup>, Priya Nagar<sup>2</sup>, Mayuri Borse<sup>1</sup>, Jessy P<sup>1</sup>

## ABSTRACT

**Introduction:** Oral health is an integral component of general health. Dental caries, one of the most widespread diseases in the world affecting 60-90% of school children, goes untreated with significant impacts on their general health, quality of life, development and educational performance. This study was done to evaluate the prevalence and experience of clinical consequences of untreated dental caries in 6 and 12 year old school children, using DMFT and PUFA index from Bengaluru North; and to assess the quality and reliability of the PUFA index in the Indian population.

**Material and Methods:** The study sample included 150 children, aged 6 and 12 years from randomly selected schools of rural region of Bengaluru North. Caries experience in primary and mixed dentition period was evaluated according to WHO criteria (DMFT/dmft index). The clinical consequences of untreated dental caries were assessed by PUFA/pufa index. Data were analysed to express the experience and distribution of caries and PUFA scores of the sample population.

**Results:** The combined mean dmft scores for 6 and 12 year old school children was 1.787 whereas combined DMFT score was 0.333. Mean pufa scores for 6 and 12 year old population was 0.1 whereas mean PUFA scores was 0.773. Untreated caries, PUFA ratio was 61% and 65.33% of 6 year old population needed urgent or emergency treatment due to pain/infection or dental trauma whereas the same value for 12 year population was 18.66%.

**Conclusion:** PUFA/pufa index is relevant in addressing the neglected problem of untreated caries and its consequences. The index helps us to show the amount of untreated caries that has progressed to infection, clearly demonstrating the limited and often misleading explanatory power of the DMFT. PUFA/pufa can also be used to plan, monitor and evaluate access to treatment

**Keywords:** Untreated caries, DMFT, PUFA/pufa

## INTRODUCTION

Oral health is an integral component of general health.<sup>1</sup> Dental caries is one of the most widespread diseases in the world affecting 60-90% of school children.<sup>2</sup> Most of the dental decay remains untreated with significant impacts on general health, quality of life, development and educational performance of the children.

For the last 70 years, the prevalence of dental caries has been shown using the Decayed, Missing, Filled Teeth (DMFT/dmft) index.<sup>2</sup> During last decade, DMFT came in for criticism to be a not enough valid tool to diagnose all stages of caries. DMFT only omits early non-cavitated lesions, but also fails to provide information on the clinical consequences of untreated dental caries.

To overcome this problem, Monse et al devised the PUFA/pufa index in 2010, which assesses and quantifies caries complications; named from the first letters of four oral conditions resulting from untreated caries viz. visible pulpal involvement

(P/p), ulceration caused by dislocated tooth fragments (U/u), fistula (F/f) and abscess (A/a). It is easy, safe to use, evaluation is short and does not require additional tools.<sup>3</sup>

The purpose of this study was to evaluate the prevalence and experience of clinical consequences of untreated dental caries in 6 and 12 year old school children, using DMFT, PUFA and PRS index, from Bengaluru North and to assess the quality and reliability of the PUFA and PRS indices in the Indian population.

## MATERIAL AND METHODS

### Study Population

The study was conducted across selected government schools in the rural region of North Bengaluru. One hundred fifty 6 and 12 year old school children were selected, using random sampling, amongst these schools and examined after taking consent from the parents, school authorities. The 6 year old and 12 year old group consisted of 75 children each. Table-1 presents the distribution of the population based on age and gender.

### Oral examination

Informed consent was taken from the parents of all the children who participated in the study along with necessary permissions from the school authorities to conduct the study. Dental examination was done following WHO guidelines using mouth mirror and periodontal (WHO) probe. WHO oral health assessment form for children was modified to suit our needs for this study. Both deciduous teeth and permanent teeth were checked and evaluated for DMFT/dmft index and Intervention urgency.<sup>4</sup>

Monse et al. developed an index to measure the clinical consequences of untreated dental caries, which he called the PUFA/pufa index. The capital letter scores the permanent dentition whereas the lowercase scores the primary dentition. In this index "P/p" stands for pulp involvement, e.g. tooth with an open pulp chamber or with excessive destruction of coronal part with only roots left, "U/u" stands for ulceration of oral mucosa because of sharp edges on the tooth surface with involvement of the pulp, "F/f" stands for an active fistula and "A/a" stands for an abscess. Each tooth will be given a single score with the gradient established as follows: ulceration will be a more advanced stage than pulp involvement, next level being fistula,

<sup>1</sup>PG Student, <sup>2</sup>Professor and Head, Department of Pedodontics and Preventive Dentistry, Krishnadevaraya College of Dental Sciences and Hospital, Hunasamaranahalli, Yelahanka, Bangalore- 562157, India

**Corresponding author:** Pai Tanvi Anandraya, G4, Sri Ganapathy Residency, 8th Cross, Munireddy Layout, Maruthi Nagar Main Road, Madivala, Bangalore-560068, India

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and an abscess would be scored as the most advanced stage of the index. The teeth without pulp involvement would not be recorded. The assessment of pufa scores was based only on the visual examination without the use of any instruments.<sup>3</sup>

## STATISTICAL ANALYSIS

The sample size and collected data were analysed using SPSS version 17 software. Mean and standard deviations were calculated to express the mean PUFA/pufa and DMFT/dmft scores.

Data were analysed using T-test, 95% confidence intervals (CI) were calculated and level of statistical significance (p-value) was set at 5%.

## RESULTS

A total of 150 children were examined, among whom 67 (44.66%) were girls and 83 (55.33%) were boys (Table-2). There was a significant difference observed in the sample size of boys and girls ( $p<0.05$ ).

The mean dmft scores of the deciduous dentition for the 6 year olds was 3.08 and 12 year olds was 0.68. The combined mean dmft scores for deciduous dentition in 6 and 12 year olds was 1.78. The mean DMFT scores of the permanent dentition for the 6 year olds was 0.26 and 12 year olds was 0.66. The combined mean DMFT scores for permanent dentition in 6 and 12 year olds was 0.33 (Figure-1).

Mean pufa scores for deciduous teeth for 6 year olds was 0, 12 year olds was 0.2 and the combined mean pufa scores for 6 and 12 year olds was 0.1. Mean PUFA scores for permanent teeth for 6 years olds was 1.25, 12 year olds was 0.29 and combined mean PUFA scores for 6 and 12 year olds was 0.773 (Figure-2). The untreated caries/PUFA ratio was 61% through which we can conclude and say that almost 2/3<sup>rd</sup> of the untreated decay progressed to pulpal involvement (Figure-3). Intervention urgency code given by WHO showed that 65.33% of the 6 year olds and 18.66% of 12 year olds needed Immediate/urgent treatment due to pain/infection of dental and/or oral origin falling under Code 3 of the intervention urgency criteria (Figure-4).

## DISCUSSION

In our study, we assessed 150 children aged 6 and 12 years for their oral hygiene status and the consequence of untreated dental caries. We emphasized on these two age groups as it is the time of eruption of the permanent first and second molars respectively, at the same time covering the deciduous teeth through their time in the oral cavity. WHO has also recommended the age groups 5 and 12 years in their survey methods.<sup>4</sup> As the school going age in Indian government schools is 6 years, we modified the sample to suit our need.

In our study, the overall untreated caries/PUFA ratio was 61%, which was found to be higher compared to the study done by Monse et al<sup>3</sup>, where the untreated caries/PUFA ratio was 41%.

The intervention urgency scores have also not been assessed in relation to PUFA/pufa index in the past. In our study, there was a positive correlation between intervention urgency and PUFA/pufa index, which shows the consequences of dental caries if left untreated.

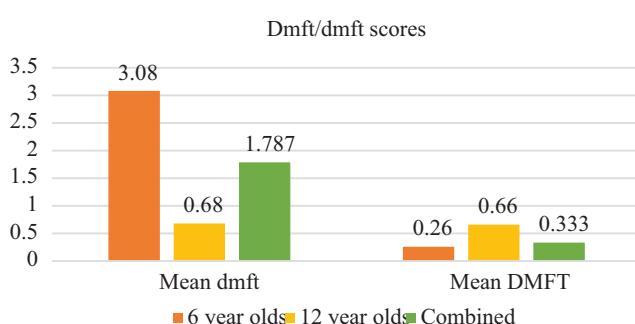
Frencken et al. proposed a new index termed as Caries Assessment Spectrum and Treatment (CAST) index in order to

	Gender		Total
	Boys	Girls	
6 year old	37	38	75
12 year old	46	29	75
Total	83	67	150

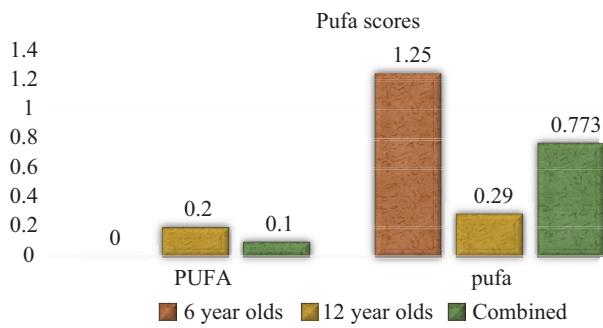
**Table-1:** Distribution of sample population based on age and gender

Age (in years)	Total (n=150)
6	75
12	75
Gender*	
Girls	67 (44.66%)
Boys	83 (55.33%)

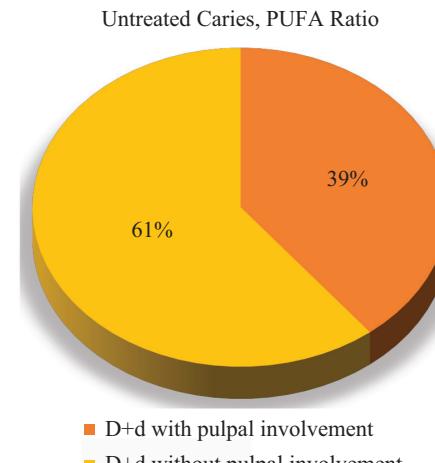
**Table-2:** Distribution of sample according to age and gender



**Figure-1:** Mean DMFT/dmft scores

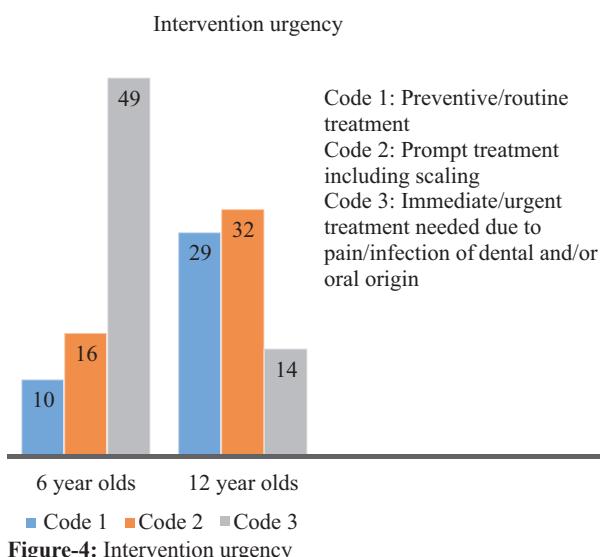


**Figure-2:** Mean PUFA/pufa scores



**Figure-3:** Untreated caries, PUFA ratio

find a reliable, concise, and easy-to-read scoring system, based on the strengths of PUFA and ICDAS-II indices and to provide a link to the widely used DMF index (M and F components).



**Figure-4:** Intervention urgency

It showed promising results for use in epidemiological studies where the DMF scores could easily be obtained from the CAST scores.<sup>5</sup>

Benzian et al. conducted a study on 11-13 year old Filipino school children and assessed the correlation between untreated dental decay and their Body Mass Index (BMI). He found a strong association between caries and BMI, particularly between odontogenic infections and below normal BMI; which shows us that dental caries is a largely neglected determinant of child's overall health.<sup>6</sup>

Shanbhog R et al. conducted a study among 12-14 year old orphan children to assess the relation between period of institutional stay, oral hygiene practice and diet of orphan children to untreated dental caries using PUFA index. His results showed that oral health amongst orphan children was neglected showing a high prevalence of dental caries with low dental care utilisation; and PUFA was an effective index in evaluating clinical consequences of untreated dental decay.<sup>7</sup>

Baginska et al. conducted a study on 5 and 7 year old school children from North-east Poland to study the correlation between pufa and dmft indices. He found negligence in the dental treatment of children from this area with the children found to be having a high prevalence and experience of pufa index in the primary dentition. He later described a modification of PUFA/pufa index to pulpal involvement-roots-sepsis (PRS/prs) index, as the PUFA/pufa index lacked in providing sufficient information on presentation of treatment needs. He concluded saying that the PRS instrument could be a good alternative to the PUFA index.<sup>8,9</sup>

Mehta A et al. studied the relationship between prevalence and severity of consequences of untreated dental decay using pufa index among 5-6 year old school children and found that more than one-third of the children with developed carious lesions caused adverse effects.<sup>10</sup>

Dua et al. investigated the effect of dental caries and its consequences on age-specific Body Mass Index (BMI) and socio-economic status (SES) of 4-14 year old rural children. He found that younger children with a lower SES have a higher mean PUFA/pufa score and below normal BMI compared to older children.<sup>11</sup>

## CONCLUSION

PUFA/pufa index is relevant in addressing the neglected problem of untreated caries and its consequences. The index helps us to show the amount of untreated caries that has progressed to infection, clearly demonstrating the limited and often misleading explanatory power of the DMFT. PUFA/pufa can also be used to plan, monitor and evaluate access to treatment.

However, further studies need to be conducted and newer indices need to be formulated as PUFA/pufa lacks in its ability to provide the concept of treatment need.

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# Spectrum of Disorders of Sex Development: Our Experience

N. Anil Kumar<sup>1</sup>, S. R. Sree Gouri<sup>2</sup>, S. Venkata Chaitanya<sup>3</sup>, Satish Bezawada<sup>3</sup>, Prasad Pulla<sup>3</sup>

## ABSTRACT

**Introduction:** Disorders of Sex Development (DSD) are defined as congenital conditions associated with atypical development of chromosomal, gonadal or anatomical sex. In this study we evaluate our experience with DSD with focus on profile, management and its challenges, and outcome of treatment.

**Material and methods:** The case notes which include prenatal and maternal history, sex of rearing, genital phenotypic appearance, general physical examination, karyotype, imaging studies of gonads and internal genitalia, laboratory investigations and management (surgery and gender assignment) were reviewed retrospectively for patients diagnosed as DSD between 2010 - 2015 at Sri Venkateswara Institute of Medical Sciences.

**Results:** Among the 14 patients, 2 patients had 46,XX DSD - congenital adrenal hyperplasia, 10 patients had 46,XY DSD which included a case of bilateral vanishing testis, 2 cases of mixed gonadal dysgenesis, 2 cases of testosterone biosynthesis defects, 3 cases of 5 alpha reductase deficiency and 2 cases of complete androgen insensitivity syndrome and the remaining 2 had sex chromosome DSD which were 46 XX males. Median age of presentation was 9 years ranging from 2 to 23 yrs. Gender reassignment was done in a case of 5 alpha reductase deficiency and in a case of testicular biosynthesis defect (from female to male). Surgical management was required in all cases.

**Conclusion:** DSD is a rare disorder requiring prompt investigation and early gender assignment logically based on a sound knowledge of normal sex determination and differentiation. Focused education of healthcare personnel, public awareness programs and improvement of diagnostic facilities and personnel through enhanced funding and international collaboration may improve outcome and minimize psychological morbidity.

**Keywords:** 5 alpha reductase deficiency, Disorders of Sex Development, Gonadal dysgenesis,

## INTRODUCTION

The Jost paradigm states that four steps must occur during sexual differentiation: establishment of chromosomal sex at fertilization, formation of undifferentiated gonads, gonadal differentiation into testes or ovaries and development of the internal and external genitalia.<sup>1</sup> Disorders of sex development (DSD) refer to a spectrum of congenital conditions in which there is biological discrepancy between chromosomal, gonadal, and phenotypical sex.<sup>2</sup> Currently the disorders are broadly classified as 46, XX DSD, 46, XY DSD and sex chromosome DSD.<sup>2,3</sup> DSD commonly manifest as ambiguity of the genitalia and has been shown to vary in frequency depending on their aetiology.<sup>2,4</sup>

Individuals with DSD have variable phenotypes ranging from completely female external genitalia to male appearing genitalia with hypospadias, bifid scrotum and descended gonads. The cornerstone of management of DSD is thorough investigations to adequately elucidate the nature of the genetic sex, the gonad and the phenotype and based on this, proper gender is

assigned and appropriate genital reconstruction undertaken.<sup>5</sup> This is best achieved with early diagnosis, multidisciplinary team management and communication between the surgeon and the patients and families. Recent studies show that though significant improvement of outcome has been observed with advances in diagnostic testing and genital repair, controversies still exist in the timing for gender assignment and definitive genital reconstruction.<sup>2,5,6</sup> Despite these, the management of DSD is challenging and remains a traumatic experience in some cases.<sup>2,3,7</sup> This study was conducted to review our experience with DSD with focus on clinical evaluation, diagnosis, medical, surgical, and psychological management and challenges encountered in management of these disorders.

## MATERIAL AND METHODS

This is a retrospective study conducted at Department of urology, Sri Venkateswara Institute of Medical Sciences and all patients who were diagnosed as DSD between January 2010 to January 2015 were included in study.

At our institute patients with DSD are managed by the department of Urology. The patients were managed in conjunction with the Endocrinologist, Gynaecologists, Radiologists and Clinical Psychologists. The initial evaluation of these patients was geared towards defining the anatomy of the internal genitalia and the gonad, and the likely genetic sex. For the former we used abdominopelvic ultrasonography, MRI pelvis (where required) and when this is inconclusive we resorted to diagnostic laparoscopy. The genetic sex was determined with karyotyping. Serum studies for ketosteroids were obtained as appropriate. Decision on gender assignment and gender reconstruction was based on the findings of the investigations and the appearance of the external genitalia and with aid of psychiatric counseling. Patients with congenital adrenal hyperplasia after evaluation were given long-term oral prednisolone 2 mg/m<sup>2</sup> /day to suppress excess adrenocorticotropin hormone production (ACTH). Hormonal therapy was given as appropriate based on final gender assignment. Surgical management was required in all cases either in form of hypospadias repair/ gonadectomy/ clitoroplasty/scrotoplasty/hysterectomy depending upon gender assignment.

<sup>1</sup>Associate Professor, <sup>3</sup>Post Graduate, Department of Urology,

<sup>2</sup>Assistant Professor, Department of Obstetrics and Gynaecology, Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, India

**Corresponding author:** Dr. Nallabothula Anil Kumar, Associate professor, Dept of Urology, SVIMS, D.No.5/346, 1st floor 2nd house, Near Sneha Hospital, Sarojini Devi Layout, Tirupati, Andhra Pradesh State, India, PIN: 517501.

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The case notes which includes prenatal and maternal history, sex of rearing, genital phenotypic appearance, karyotype, imaging studies of gonads and Mullerian/Wolfian structures, laboratory investigations for hormonal activity of steroidogenesis and associated disorders and imaging studies and management with surgery and gender assignment were reviewed retrospectively after obtaining ethical clearance from institutional ethics committee for patients diagnosed as DSD between 2010 - 2015 at Sri Venkateswara Institute of Medical Sciences.

#### Inclusion criteria

All patients who were diagnosed as DSD between January 2010 – January 2015 at Sri Venkateswara Institute of Medical Sciences were included in study.

#### STATASTIC ANALYSIS

These patients data was coded into a Microsoft Excel (Redmond, WA) spreadsheet and results were expressed as percentages, median or mean.

#### RESULTS

Overall, 8 (57.14 %) of the 14 cases were reared as female and 6 (42.8 %) reared as male at presentation. Median age of presentation in our series was 9 years ranging from 2 to 23 years. Table-1 summarizes the age and gender distribution of the cases at presentation.

#### External Genitalia at Presentation

A total of 8 (57.14 %) of the patients presented with enlarged phallus with unfused labia with perineal urethral meatus and vagina (TYPE A); 2 (14.2%)cases presented with proximal penile hypospadias with small testis (TYPE B) ; 4 cases (28.4%) presented with small phallus with empty labioscrotum and urethral meatus on perineum (Type C). Overall, cases with type A clinical finding were reared as female while the type B and Type C patients were reared as male prior to presentation (Table-2).

#### Investigations

Abdominopelvic ultrasonography did not demonstrate adrenal enlargement in any of the 14 patients. However, ultrasound demonstrated inguinal gonads in 4 (28.4%); but was inconclusive in 2 (14.2%) patients. MRI pelvis demonstrated utricle in 1 case

Age at Presentation	Gender at Presentation		Total
	Female	Male	
< 4 years	-	3	3
5 – 8 years	3	1	4
9 – 12 years	1	-	1
13 – 16 years	3	1	4
> 17 years	1	1	2
Total	8	6	14

Table-1: Age and gender distribution

Mode of Presentation	Gender at presentation		Total
	Female	Male	
Enlarged phallus with unfused labia with perineal urethral meatus and inguinal/nonpalpable gonads with vagina/vagina dimple(TYPE A)	8	-	8
Proximal penile hypospadias with small testis (TYPE B)	-	2	2
Small phallus with fused labia and urethral meatus on perineum inguinal/nonpalpable gonads (Type C)	-	4	4
Total	8	6	14

Table-2: External genitalia at presentation

at age of 9 years with bilateral undescended testis, perineal hypospadias and underwent Bilateral orchidopexy with scrotoplasty with hernia repair and staged hypospadias repair and sex was reassigned to male while another case presented at age of 16 years with cliteromegaly and bilateral inguinal testis and was continued to be reared as female by reduction cliteroplasty, orchidectomy and vaginoplasty.

Among the two cases of testosterone biosynthesis defects the case that presented at 13 years of age with bilateral undescended testis with perineal hypospadias and underwent Bilateral orchidopexy with scrotoplasty with hernia repair and staged hypospadias repair and sex was reassigned to male while another case that presented at 8 years of age continued to rear as female with reduction cliteroplasty, orchidectomy and vaginoplasty.

Both cases of complete androgen insensitivity underwent bilateral orchidectomy and reduction cliteroplasty and were continued to rear as female.

Both cases of Sex Chromosomal DSD were 46 XX Males who were reared as males presenting with penile hypospadias and underwent staged hypospadias repair and final gender reassignment was male.

After treatment male gender was assigned in 8 cases while female gender was assigned in 6 cases (Table-4). Overall Gender reassignment was done in 2 cases (14.2%) from female to male.

#### Treatment

Of the 8 cases that were assigned male gender, 6 cases (75%) required preoperative penile size augmentation with parenteral testosterone. Bilateral Gonadectomy was done in 3 cases

Age	Gender At Presentation	External Genitalia	Gonads	Internal Genitalia	Final Diagnosis	Surgery	Gender Assigned
2 years	Male	Type C	B/L Non-palpable Streak Gonads	Rudimentary Wolfian Duct Structures	Mixed Gonadal Dysgenesis	B/L Gonadectomy + Hypospadias Repair	Male
16 years	Male	Type C	B/L Non-palpable Streak Gonads	Rudimentary Wolfian Duct Structures And Uterus	Mixed Gonadal Dysgenesis	B/L Gonadectomy+ Hysterectomy+ Hypospadias Repair	Male
18 years	Male	Type C	B/L Vanishing Testis	B/L Blind Ending Cord Structures With Utricle Cyst	Bilateral Vanishing Testis	Utricular Cyst Excision + Hypospadias Repair	Male
16 years	Female	Type A	Rt Inguinal Testis And Left Iliac Fossa Testis	B/L Vas Deferens With Vagina	5 Alpha Reductase Deficiency	Cliteroplasty + B/L Orchidectomy + Vaginoplasty	Female
9 years	Female	Type A	B/L Inguinal Testes	B/L Vas Deferens With Seminal Vesicle S Rudimentary Prostate, Vaginal Dimple	5 Alpha Reductase Deficiency	B/L Hernia Repair + B/L Orchidopexy + Scrotoplasty + Hypospadias Repair	Male
13 years	Female	Type A	B/L Inguinal Testes	B/L Vas Deferens With Seminal Vesicles	Testosterone Biosynthesis Defect	B/L Hernia Repair + B/L Orchidopexy + Scrotoplasty + Hypospadias Repair	Male
8 years	Female	Type A	B/L Illiac Testis	B/L Vas Deferens With Vaginal Pouch	Testosterone Biosynthesis Defect	Cliteroplasty + B/L Orchidectomy + Vaginoplasty	Female
14 years	Female	Type A	B/L Inguinal Testis	B/L Vas Deferens With Vaginal Pouch	Complete Androgen Insensitivity Syndrome	Cliteroplasty + B/L Orchidectomy + Vaginoplasty	Female
3 years	Male	Type C	B/L Non-palpable Streak Gonads	Rudimentary Wolfian Duct And Mullerian Duct Structures	Mixed Gonadal Dysgenesis	B/L Gonadectomy+ Hypospadias Repair	Male
19 years	Female	Type A	Rt Inguinal Testis And Lt Iliac Testis	B/L Vas Deferens With Rudimentary Vagina	Complete Androgen Insensitivity Syndrome	Cliteroplasty + B/L Orchidectomy + Vaginoplasty	Female

Table-3: Spectrum of 46 XY DSD

Gender at presentation	Total	Definitive gender	
		Female	Male
Female	8	6	2
Male	6	-	6
Total	14	6	8

**Table-4:** Gender assignment

(37.5%) while bilateral orchidopexy with scrotoplasty was done in 2 cases (25%). Staged Hypospadias repair was done in all cases.

Among the 6 patients that were assigned female gender, 2 cases (33.33%) had reduction clitoroplasty, 3 cases (50%) had reduction clitoroplasty, vaginoplasty with bilateral orchidectomy while one case (16.6%) had bilateral orchidectomy only. Histology of the removed gonads did not show neoplastic changes.

### Outcome

Duration of follow-up ranged from 1 month to 4 years. A total of 3 (21.42%) developed procedure-related complications which include meatal stenosis (n=2) and urethrocutaneous fistula (n = 1). The cases with meatal stenosis responded to dilatation. Urethrocutaneous fistula was managed by operative closure. There were no gender assignment issues. However fertility remained a concern in 10 of 14 patients.

### DISCUSSION

DSD are congenital conditions in which the development of chromosomal, gonadal or anatomical sex is atypical or ambiguous.<sup>3</sup> In the newborn period, virilisation or over-virilisation of the external genitalia in girls and under-virilisation in boys, presenting as micropenis, hypospadias and undescended testes are the most common presentations. However, there are more complex situations in which the determination of rearing might not be possible. In such cases, gonadal structure and the anatomy of the internal genitalia should also be considered and an appropriate laboratory delineation is required. These disorders are now classified into three major categories: sex chromosome DSD, 46,XX DSD and 46,XY DSD.

Disorders of sexual development (DSDs) are estimated to be prevalent in 0.1 to 2 % of the global population.<sup>8</sup> In the past decades, important advances have refined the diagnosis and management of these disorders.<sup>2,3</sup> This notwithstanding, the affected patients, their parents and the medical staff are still confronted with challenges in areas of gender assignment, genital surgery and lifelong care, functional outcome and psychosexual adjustments.<sup>2,3,8</sup> This study has shown that the types of DSD, definitive treatment and short-term outcomes in our setting may be comparable to what has been previously reported.

In most of the reported large series, 46, XX DSD was indicated as the commonest type of DSD.<sup>9-11</sup> However, in some reports,<sup>4,12,13</sup> cases of 46, XY DSD outnumbered the other types of DSD as in our study. These variations may reflect deficiencies of representative patient sampling or more likely it may be the result of the new DSD classification system leading to expanded clinical spectrum of the disease with a change in the distribution of etiological diagnoses of DSDs.<sup>4</sup>

Historically, the management of DSD has focused on gender assignation and surgical/medical treatment to ensure congruent bodily appearance. Though this emphasis has not changed

over the years, the current protocol of treatment highlights the need to dispel the traditional binary concept of sexes, ethical considerations, informed consent and appropriately timed genital repair with the ultimate goal of achieving results that are in the best interest of the patients.<sup>2,3,14</sup> In the light of this, it is evident that the management of DSD in our setting may be imbued with challenges. Similar observations have been reported in studies from some other developing countries.<sup>15-17</sup> The challenges are mostly in the areas of delayed diagnosis, inadequate facilities and trained personnel, and high proportion of cases that need gender reassignment. Training and retraining of these personnel to recognize features of these disorders and the need for early referral to appropriate health facility may improve time to diagnosis.

In this study a total of 2 cases were wrongly reared as female prior to presentation. In these select cases, positive parental support, social support, medical support, and counseling may be needed for adjustment.<sup>18</sup> Studies have shown that thorough investigation is critical in the management of DSD.<sup>2-4,19</sup> The operative procedures undertaken on our cases did not differ from the procedures reported elsewhere.<sup>3,6,20</sup>

In patients assigned female gender the procedure involves removal of all testicular tissues, and depending on the degree of virilization staged genital repair is undertaken. For cases with isolated clitoromegaly, clitoroplasty will suffice.<sup>21</sup> If there is associated labial fusion, vulvoplasty is usually undertaken in the same procedure to improve cosmesis. However, cases with single urogenital orifice will require vaginoplasty the extent of which depends on the length of the urogenital sinus. Cutback vaginoplasty may be sufficient for vagina entering at the level of anterior urethra, but for patients with vagina entering at the level of posterior urethra, substitution or pull-through vaginoplasty may be undertaken. In cases with “penile” clitoris, phalloplasty may be required for optimal cosmetic result. In this procedure, the glans is mobilized with its neurovascular bundle, the corpora cavernosa is reduced symmetrically in length and diameter, and the volume of the glans reduced as appropriate.<sup>22</sup>

DSD assigned male gender undergoes masculinizing genitoplasty. The present report and some previous studies have shown that a significant number of these cases will require penile size augmentation with either parenteral or topical testosterone prior to genital repair.<sup>23,24</sup> For patients with mullerian duct remnant and/or ovarian tissue, salping-oophorectomy is undertaken. Orchidopexy is also carried out for cases with undescended testes. Definitive genital repair involves single or staged hypospadias repair and scrotoplasty as required.<sup>23-25</sup>

The outcome of treatment of DSD can be defined in shortterm and long-term. The short-term outcomes relate mostly to the physical appearance and functionality of the genitalia to the patient, the parents, and the surgeon.<sup>3,9,13,14</sup> In this aspect the outcome in the present report compares with the results of treatment previously reported.<sup>9,13,25</sup> Some complications of treatment like vaginal stenosis and meatal stenosis if mild may respond to dilatation, but severe stenosis may require revision of the vaginoplasty, and meatotomy respectively.<sup>24</sup> On the other hand persistent urethrocutaneous fistula following hypospadias repair will require operative closure.<sup>24,25</sup> Long-term follow-up of DSD patients is invariable to monitor for long-term outcomes such as personal satisfaction, gender

satisfaction, social adaptation, quality of life, sexual function, and other psychosexual parameters.<sup>2,3,9,24</sup> These underscore the importance of psychological, social, and family support in the treatment of children with DSD.

## CONCLUSION

DSD is a rare disorder requiring prompt investigation and early gender assignment that is logically based on a sound knowledge of normal sex determination and differentiation. Despite the significant advances that have been achieved, much remains to be clarified in terms of the accurate evaluation and optimal management of patients with DSD. Affected patients and the parents should be provided with full information to make an appropriate choice for gender assignment. Focused education of healthcare personnel, public awareness programmes, and improvement of diagnostic facilities and personnel through enhanced funding and international collaboration may improve outcome and minimize psychological morbidity.

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# Aloe Vera: An Ancient Option for Modern Day Dental Problems - A Review

Rajashekhar Sangur<sup>1</sup>, Wakinder Bajwa<sup>2</sup>, Tanu Mahajan<sup>3</sup>, Animesh Banerjea<sup>2</sup>

## ABSTRACT

The magical properties of Aloe Vera have been known to the world since time immemorial. It has inherent properties which help in enhancing the health and well-being of an individual in the most natural way possible. Its medicinal properties like anti-viral, anti-bacterial and wound healing capacity has led to the curiosity of using Aloe Vera in the treatment of various dental problems. This paper presents an overview explaining the use of Aloe Vera in the field of dentistry.

**Keywords:** Aloe Vera, wound healing, dentistry, herb, anti inflammatory.

## INTRODUCTION

Aloevera is in use since past 2000 years. The medicinal properties of Aloe Vera are well recognized and is also called as the Universal Panacea in Greek. History of using Aloe Vera to treat the wounded soldiers of Alexander and Christopher Columbus is also there.<sup>1</sup>

The word “Alloe” is an Arabic word which means “shining bitter substance” while the “vera” means “true” in latin. Aloe Vera (Aloe barbadensis miller) belongs to the family Liliaceae and is a bright green, shrubby, juicy, xerophytic, continuously growing plant mostly seen in the dry areas of Asia, America, Europe and Africa.<sup>2</sup>

## ALOE VERA: THE PLANT

The plant consists of two different parts, each producing different substances with completely different compositions and therapeutic properties. The innermost part of the aloe leaves produces the Aloe Vera gel which is transparent, thin, has no taste, has jelly-like consistency and the exudates consisting of bitter yellow latex are produced from other part of the plant.<sup>3</sup>

Aloe Vera is not only a powerful detoxifier, antiseptic and tonic for the nervous system but it also possesses immune-boosting and anti-viral properties. Aloe Vera gel (mucilaginous tissue) is formed in the centre of the plant and is responsible for the various cosmetic and medicinal products available in the market today.<sup>4</sup>

The pharmacological actions of Aloe Vera include anti-inflammatory, anti-arthritis, antibacterial and hypoglycemic effects.<sup>5</sup>

## Composition of Aloe Vera gel

**Nutrients:** 75 nutrients have been identified in stabilized Aloe Vera gel. The most important are:

- Cellulose like material known as Lignin provides the ability to penetrate the human skin when added in the topical aloe preparations.
- Approximately 3% of Aloe Vera Gel contains Saponins (soapy substances) and have antiseptics and cleansing

properties.

**Vitamins:** Aloe Vera contains many vitamins, including Vitamin A, C, E, B<sub>1</sub>, B<sub>2</sub>, B<sub>3</sub> (niacin), B<sub>6</sub>, choline, folic acid, alpha-tocopherol, beta-carotene. Aloe Vera is one of the few plants that contain vitamin B<sub>12</sub>. Vitamins A, C and E are important antioxidant vitamins, essential to fight against damaging free radicals. Vitamin C not only assists in wound healing but also helps in the formation of collagen thereby maintains the health of bone, skin and joints. Vitamin A is an important vitamin for the maintenance of night vision. Vitamin E is one such vitamin which possesses anti-coagulant properties thereby preventing thrombosis and as well as atherosclerosis and also improves wound healing and fertility.

**Anti-Inflammatories:** Aloe Vera is composed of many antiinflammatories. Bradykinasean enzyme found in Aloe Vera, reduces skin inflammation. There are about 12 anthraquinones, commonly known as laxatives. It possesses fatty acids, salicylic acid and hormones called auxins and gibberellins, all of which act as anti-inflammatories. The mechanism of action of these anti-inflammatories is either by stimulating the function of immune system function or by inhibiting the paths of irritants.

**Amino Acids:** The human body requires 20 amino acids to maintain good health, out of which only eight can be formed in the body. The other essential amino acids are taken from the outside source. Aloe Vera has the potential to provide nineteen of the twenty required amino acids.

**Enzymes:** Aloe Vera is a source of multiple enzymes, which can be categorized into two groups,

- Enzymes that help in digestion, like amylase, break down starch and sugar, while others, such as lipase, help break down fats.
- Enzymes that act as anti inflammatory.

**Sugars:** Glucose, a monosaccharide and glucomannose, often called as the Acemannan, a polysaccharide are present in Aloe Vera.

Acemannan is responsible for many actions such as;

- a. It boosts the level of antibodies thus provide immunomodulatory actions.
- b. It acts as an Antiviral specially against tumor producing

<sup>1</sup>Professor and Head, <sup>2</sup>Post Graduate Student, <sup>3</sup>Professor, Department of Prosthodontics, Rama Dental College-Hospital and Research Centre, Kanpur, India

**Corresponding author:** Dr. Rajashekhar Sangur, Professor and Head, Department of Prosthodontics, Rama Dental College-Hospital and Research Centre, Kanpur -208024 (Uttar Pradesh), India

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Chemical Composition			
Anthraquinones	Inorganic	Saccharides	Enzymes
1. Aloin 2. Barnaloin 3. Iaobarnaloin 4. Anthranol 5. Aloetic acid 6. Anthracene 7. Ester of cinnamic acid 8. Aloe-emodin 9. Emodin 10. Chrysophanic acid 11. Ethereal oil 12. Resistannol	1. Calcium 2. Sodium 3. Chlorine 4. Manganese 5. Magnesium 6. Zinc 7. Copper 8. Chromium 9. Potassium 10. Sorbate	1. Cellulose 2. Glucose 3. Mannose 4. L-Rhamnose 5. Aldopentose	1. Oxidase 2. Amylase 3. Catalase 4. Lipase 5. Alkaline phosphatase
Vitamins	Essential amino acids	Nonessential amino acids	Miscellaneous
1. Vitamin B1 2. Vitamin B2 3. Vitamin B6 4. Choline 5. Folic acid 6. Vitamin C 7. Alpha-tocopherol 8. Beta carotene	1. Lysine 2. Threonine 3. Valine 4. Methionine 5. Leucine 6. Isoleucine 7. Phenylalanine	1. Histidine 2. Arginine 3. Hydroxyproline 4. Aspartic acid 5. Glutamic acid 6. Proline 7. Glycerine 8. Alanine 9. Tyrosine	1. Cholesterol 2. Triglycerides 3. Steroids 4. Beta- sitosterol 5. Lignins 6. Uric acid 7. Gibberellins 8. Lectin like substance 9. Salicylic acid

viruses, such as feline leukemia.

- c. Reduces the occurrence of secondary infections.
- d. Increases the activity of T-lymphocytes by up to 50%.
- e. Increases the activity of macrophages thereby improving the wound healing properties.

**Sterols:** Lupeol a sterol present in Aloe Vera acts as an antiseptic and analgesic agent.

**Salicylic Acid:** Salicylic acid present in Aloe Vera together with lupeol acts as painkiller.

## ALOE VERA AND DENTISTRY

There are eight main uses of Aloe Vera in dental practice<sup>7</sup>

1. Directly at the sites of periodontal surgery.
2. Used on the traumatized gum tissues. Trauma may be due to toothbrush abrasion, sharp foods, dental floss or toothpick injuries.
3. Chemical burns
4. Application at extraction sockets immediately after extraction.
5. Acute oral lesions.Example: aphthous stomatitis, angular chelitis or herpetic lesions.
6. Chronic oral lesions. Example: Lichen Planus, Pemphigus.
7. Patients suffering with denture stomatitis, or ill fitting dentures.
8. Application around dental implants to control inflammation.

## ENDODONTICS

**Intracanal medicament<sup>8</sup>:** Aloe Vera has an antimicrobial effect against resistant microorganisms like Enterococcus faecalis and Candida albicans found in pulp space. The extracts of Aloe Vera like water, alcohol and chloroform also show anti microbial efficacy and can be used as an intracanal medicament.

**Can be used in root canals as sedative dressing and as file lubricant:** Aloe Vera helps reduce the sensitivity of the highly sensitive nerve ends present in the root canal by placing the gel

inside the pulp chambers and broaching alongside.

**Canal lubricant material:** Aloe Vera can also be used in lubrication of canal. Camphorated mono-chlorophenol with a drop of aloe Vera gel can be given in closed dressing and then sealed with temporary restorations.<sup>8</sup>

**Decontamination of Gutta-Percha points:** The importance of gutta-percha decontamination to prevent contamination of the root canal with bacteria during the obturation procedure is widely recognized in endodontic practice. Aloe Vera gel is proven to be a potent decontaminant of guttapercha points thereby helping in removal of bactaria within a minute.<sup>9</sup>

**Obturative material:** Aloe Vera has proved to be an effective obturative material for primary teeth.<sup>10</sup>

## PERIODONTICS

**Mouthwash:** Aloe Vera due to its wound healing and anti-inflammatory mechanism prevents radiation induced mucositis. It also reduces the incidence of oral thrush in patients undergoing radiotherapy due to its anti-fungal and immunomodulatory properties.<sup>10</sup> As a mouthwash, 1-3 table spoon of Aloe Vera should be used followed by swallowing it. This should be done at least three times a day. When compared with chlorhexidine mouth wash, Aloe Vera has shown to be equally effective anti-plaque agent and can become a potent herbal substitute with the necessary refinement of taste and shelf life at an affordable price.<sup>11</sup>

In order to improve the periodontal condition, Aloe Vera gel can be administered sub-gingivally. It helps in reduction of pocket depth by filling the pockets with Aloe Vera gel and placing coe-pack over it. Aloe Vera helps control bleeding of gums due to its soothing and healing properties thereby reducing swelling and soft tissue edema and hence restore the gum health along with reducing plaque and calculus formation.<sup>8</sup>

**Bad Breath:** *A. vera* naturally possesses anti-fungal and

antibacterial properties. It not only protects the sensitive tissue of the mouth but also kills bacteria and fights tooth decay. It Boosts body's ability to form collagen thereby strengthening weak and swollen gums. Mixing 1/4 cup of pure Aloe Vera gel with 1/2 cup of water or apple juice helps soothe acid digestion, which is a very common etiological factor of halitosis.<sup>8</sup> It is also used directly at the site of periodontal surgeries, as an adjunct to scaling and root planning.

## ORAL SURGERY: HEALING OF EXTRACTION SOCKETS

**Acemannan hydrogel**, a component of the Aloe Vera, when used immediately after extraction at the extraction site has proved to reduce the incidence of alveolar osteitis.<sup>12</sup>

**SaliCept Patch**, a freeze-dried pledge containing Acemannan Hydrogel when placed in socket after extraction has proved to fasten the process of healing and clot formation.<sup>2</sup>

## PROSTHODONTICS

**Denture Adhesive:** Acemannan, a complex mannose carbohydrate, an important component of the Aloe Vera gel has an inherent property of stickiness/ viscosity. This property of Aloe Vera led to the production of prototype acemannan denture adhesives. These denture adhesive formulations were evaluated for pH changes, cytotoxicity to human gingival fibroblasts and adhesive strength in both dry and wet conditions. A pH value of 6.0 or more in Acemannan denture adhesive formulation was found to be a herbal substitute for traditional denture adhesives.<sup>13</sup>

**Denture Care:** Applying Aloe Vera gel onto the denture once or twice a day helps prevent denture stomatitis and other fungal infections. It can also be used in combination with soft liners.<sup>8</sup>

## DENTAL IMPLANTS

Aloe Vera gel when placed around dental implants is found to be effective in reducing inflammation due to its antimicrobial and anti-inflammatory effects.<sup>8</sup>

## MISCELLANEOUS

**Oral Lichen Planus:** The topical application of Aloe Vera, three times a day controls the pain and improves the overall oral quality of life of patients suffering from oral lichen planus.<sup>14</sup> As shown by other studies, Aloe Vera can also be used in dosages of two ounces of Aloe Vera juice three times a day for a period of three months.<sup>15</sup> When compared with steroids like triamcinolone, topical use of Aloe Vera has shown better and effective results in treating oral lichen planus.<sup>10</sup>

**Aphthous Ulcers:** Acemannan hydrogel not only heals the aphthous ulcers but also helps reduce the pain associated with it. Acemannan has been used for the treatment of oral aphthous stomatitis in patients who don't wish to use steroids. Aloe Vera derivative is also an effective treatment option in the treatment of oral ulcers according to U.S Food and Drug Administratin.<sup>10</sup>

**Oral Sub Mucous Fibrosis:** A preliminary study to compare the effectiveness of Aloe Vera and that of antioxidants in the treatment of oral submucous fibrosis (OSMF) was carried out by Sudarshan et al. He concluded that Aloe Vera when applied topically, three times a day for three months was much more effective in reducing the burning sensation and improving

mouth opening in cases with OSMF when compared with antioxidant therapy.<sup>16</sup>

## CONTRAINDICATIONS TO USE ALOE VERA

1. Diabetics: it decreases the blood sugar levels and, thus, may interact with oral hypoglycaemic drugs and insulin.<sup>2</sup>
2. Pregnancy and Lactation.
3. Patients allergic to Liliaceae Family plants.
4. Children under 10 years of age.

## SIDE -EFFECTS<sup>2</sup>

When used topically, it may cause redness, burning sensation and rarely generalized dermatitis in sensitive individuals. It is thus advised to test for any possible allergy before starting its use.

When used orally, there may occur abdominal cramps, diarrhoea, red urine, hepatitis or constipation. Prolonged oral use of Aloe Vera has been reported to increase the risk of colorectal cancer. Laxative effect may cause imbalances in the levels of electrolytes.

## CONCLUSION

Aloe Vera is most definitely a promising herb in the field of dentistry and does require a lot of research in order to prove its worth. It is important to compare and evaluate the various properties of Aloe Vera to use it to its fullest. Aloe Vera being economical and easily available can prove to have a future in modern dentistry.

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# Pityriasis Versicolor: Therapeutic Efficacy of Various Regimes of Topical 2% Clotrimazole Cream, Oral Flucanazole and Ketoconazole

S Ravindranath<sup>1</sup>

## ABSTRACT

**Introduction:** Pityriasis versicolor is chronic superficial fungal infection caused by the organism *Malessezia furfur*. Pityriasis versicolor can be treated by various regimes of clotrimazole, Flucanazole and Ketoconazole. The therapeutic efficacy of these three drugs has been compared less. The study is aimed to evaluate the therapeutic efficacy of various regimes of clotrimazole cream, oral fluconazole and ketoconazole in the treatment of pityriasis versicolor.

**Material and methods:** A total of 75 patients were included in the study and were divided into 5 groups with 15 patients each and treated with various regimes consisting of topical clotrimazole cream, oral fluconazole and ketoconazole. The results were recorded after a period of one month and analysed.

**Results:** In the group treated with topical clotrimazole cream for one month and fluconazole 400mg single dose the clinical cure was 86% on an average. In the second group treated with topical clotrimazole cream for one month and fluconazole 150mg weekly for a period of 4 weeks the average clinical cure was 73%. In the third group treated with topical clotrimazole cream alone for one month the average clinical cure was 73%. In the fourth group treated with fluconazole 400mg single dose alone showed a clinical cure of 36% on an average. The fifth group ketoconazole 400mg single dose alone the average clinical cure was 32% only.

**Conclusion:** Fluconazole 400mg single dose with topical clotrimazole cream therapy for one month is the most effective regime followed by topical clotrimazole cream clotrimazole and fluconazole 150mg weekly.

**Keywords:** Pityriasis Versicolor, Clotrimazole Cream, Oral Flucanazole, Ketoconazole

## INTRODUCTION

Pityriasis versicolor is a cutaneous superficial fungal infection characterized by skin pigmentary changes due to colonization of stratum corneum by dermophilic lipophilic fungus in the normal flora of skin known as *Malessezia furfur*.<sup>1,2</sup> It is one of the most common disorders of pigmentation in the world.<sup>3</sup> Pityriasis versicolor is also known as tinea versicolor and less commonly as dermatomycosis furfuraceus, achromia parasitica and tinea flava.<sup>3</sup> Though world wide in distribution it is more common in tropics because of high temperature and humidity. The age distribution of the disease is variable with majority of cases occurring during adolescence.<sup>4</sup> Hormonal changes or increase in sebum secretion may be the cause.<sup>5</sup> This disease is most prevalently seen in tropics with an incidents as high as 40% in these regions.<sup>6</sup> In temperate areas it is more common during summer months.<sup>7,8</sup>

Pityriasis versicolor is caused by *pitrosporum ovale* and *pitrosporum orbiculare*, normal lipophilic and lipid dependent human flora that transformed into mycelial phase as *Malessezia furfur*.<sup>3</sup> *P.Orbiculare* and *P.Ovale* are identical in macromorphology but the difference lies in micromorphology,

*p.orbiculare* having a tendency to produce simple spherical buds on narrow base, while *p.ovale* produces single oval to cylindrical buds on broadbase.<sup>9</sup>

Pityriasis versicolor is a constituent of normal flora in 90 to 100% of populations.<sup>10,11</sup> Pityriasis versicolor occurs when yeast converts to mycelial phase as result of certain predisposing factors. The development of Pityriasis versicolor may be related to altered immune response to the organism<sup>12,13</sup>

The predisposing factors influencing Pityriasis versicolor may be classified as exogenous and endogenous. The exogenous factors are heat and moisture, occlusion of skin by clothing. Occlusion leads to altered microbial flora and altered PH range.<sup>3</sup> In temperate climate endogenous factors account for the prevalence of the disease. The endogenous factors are seborrhoeic dermatitis, cushing's syndrome, immunosuppressive therapy, malnutrition and hyperhidrosis(flexural).<sup>14,15</sup>

Pityriasis versicolor is generally rare among children although cases are more commonly seen in tropical climates.<sup>16</sup> Facial involvement may be more common in children than in adult.<sup>17,18</sup> Pityriasis versicolor is uncommon in adult (old people).<sup>19</sup> This is due to reduction in sebum production with advancing age.

The present study aims at evaluating the therapeutic efficacy of various agents both topical and systemic in the treatment of pityriasis versicolor. These agents include oral flucanazole, ketoconazole and topical clotrimazole cream.

## MATERIAL AND METHODS

The study was conducted in Dermatology department of Mahatma Gandhi Hospital/ Kakatiya Medical College, Warangal, over a period of 1 year. The permission of local research ethical committee was obtained. There were 75 patients in the study group. A detailed clinical history was taken with regard to age, sex, family history, occupation, cytotoxic and immuno suppressive therapy and history of similar episodes in the path along with details of treatment for the same. Patients with hypopigmented lesion with following diagnostic criteria were selected for study. As the lesions were situated on private parts of the body like chest, young women who were not willing to undergo examination were not taken into study. Children below 10 years, pregnant women and people with history of

<sup>1</sup>Assistant Professor of Dermatology, Department of Dermatology, Incharge Professor of Dermatology MGM Hospital / Kakatiya Medical College Warangal, India

**Corresponding author:** S Ravindranath, Assistant Professor of Dermatology, Department of Dermatology, Incharge Professor of Dermatology MGM Hospital / Kakatiya Medical College Warangal, India

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therapy for other disorders like malignancy and renal failure were excluded from the study. Patients who were already on treatment, and lactating woman were also excluded from the study.

The diagnosis of pityriasis versicolor was based on clinical features. The diagnostic criteria included hypopigmented or brown coloured macules which become augmented on scraping with a glass slide or blunt scalpel (Coup de ongle Beissner's sign). This was supported by bright yellow or gold coloured fluorescence under Wood's lamp examination.

The differential diagnosis includes vitiligo (particularly in dark skinned patients with hypopigmented lesion.), Cloasma, Tenia corporis, Seborrhoeic dermatitis, pityriasis rosea, pityriasis alba, erythrasma, pityriasis rotunda, secondary syphilis, confluent reticulate papillomatosis of Gougerot and Carteaud and pinta. Whenever necessary skin scrapings were sent for mycological examination for detection of *Malassezia furfur*. All routine laboratory tests were done. Liver function tests were conducted in patients who were administered oral ketoconazole drug.

The patients were divided into 5 clinical groups each group consisting of 15 patients.

*One group* of patients were administered with single dose of flucanazole 400mg and were asked to apply topical clotrimazole cream for a period of one month. *Second group* patients were given flucanazole 150mg weekly for a period of 4 weeks along with simultaneous topical therapy with clotrimazole cream for a period of 1 month. *Third group* patients were given topical therapy with clotrimazole cream alone for a period of one month. *Fourth group* patients were administered with single starting dose of flucanazole 400mg only. *Fifth group* of patients were given single starting dose of 400mg of ketoconazole alone.

All the patients were followed up after a period of 7 days, 2 weeks, and one month and the results were recorded.

## STATISTICAL ANALYSIS

Age and Sex incidence details, the site of the occurrence of the lesions in patients in the study groups, the therapeutic efficacy of various regimes in the study groups were analyzed descriptively and tabulated with the help of Microsoft office 2007.

## RESULTS

Majority of patients were young adults the youngest patient was 14 years old boy and the old age patient 45 years old adult male (Table-1). The most commonly effected sites were chest – (Figure-1), neck, shoulders (Figure-2), upper arms (Figure-3) and face in order of frequency (Table-2). 80% of the patients had hypopigmented brownish yellow coloured macules. Rest of the patients had a combination of yellowish brown hypopigmented and dark brownish hyperpigmented macules. Majority patients were young adolescent and adult males. As the lesion were situated on chest, neck and shoulders, these parts being concerned with privacy of an individual most of the young females were not willing to be a part of the study group. Hence they were not included in the study. As a result no comment can be made on the sex ratio of affected individuals with Pityriasis versicolor.

Among 15 patients who were administered with flucanazole 400mg single dose along with topical application of clotrimazole cream for a period of 1 month. 5 patients reported with 100% clinical cure, 4 patients reported with 90% clinical cure, 5

Age	Male	Female	Total
10 - 20	35	5	40
21 - 30	20	3	23
31 - 40	8	2	10
41 - 50	2	0	2
51 - 60	0	0	0
Total	65	10	75

Table-1: Age and sex incidence

Sl no	Site of Lesion	No.of Patients	Percentage
1	chest	40	53.4
2	Neck	12	16
3	Shoulders	10	13.4
4	Upper arm	8	10.6
5	Face	5	6.6
Total		75	100

Table-2: Site and frequency of lesion



Figure-1: Patient with pityriasis versicolor lesions on chest



Figure-2: Patient with pityriasis versicolor lesions on shoulder; Figure-3: Patient with pityriasis versicolor lesions on upper arm

patients reported with 80% clearance of the lesion and only 1 patient reported with 30% clinical cure. On an average there was 86 % clinical cure in this group (Table-3).

Within the group of 15 patients who were given flucanazole 150mg weekly for 4 weeks along with topical therapy of clotrimazole cream for a period of 1 month, 4 patients reported with 100 % clinical cure, 3 patients reported with 70 and 5 patients reported with 80% clearance of the lesions while 3 patients reported with 30% clearance of the lesions. On the whole the average clinical cure among this group is 73% (Table-4).

In the group of 15 patients who were treated with topical therapy of clotrimazole cream alone for a period of one month. 4 patients reported with 100% clinical cure, 3 patients reported with 70 and 3 patients reported with 80% clearance of the lesions while 5 patients reported with 50% clinical cure. There is an average clinical cure of 73% in this group (Table-5).

The other group of 15 patients who have received single starting dose of flucanazole 400 mg only, 3 patients reported with 70% clinical cure, 3 patients reported with 50% clearance of the lesions, 5 patients reported with 30% clinical cure while remaining 4 patients displayed only 10% clearance of the lesions. On the whole there is an average clinical cure of 36% in this group (Table-6), (Figure-4).

The last group of 15 patients who were administered with single dose of ketoconazole 400mg alone, 3 patients reported with 60% clearance of the lesions, 3 patients reported with 50% clinical cure, 3 patients reported with 30% clearance of

the lesion while remaining 6 patients reported with only 10% clinical cure.(Figures-5 and 6). There is an average clinical cure of 32% in this group (Table-7).

## DISCUSSION

Varied number of therapeutic options are available for the treatment of pityriasis versicolor. The anti fungal medications used are both topical and systemic. Topical therapy is the preferred mode in children as it is less expensive.<sup>20</sup> Low compliance due to reasons like odour and difficulty in applying over the back have led to the advent of oral medications like Fluconazole and ketoconazole which has got a clearance rate of as high as 97%<sup>21</sup> for the treatment of pityriasis versicolor. Systemic therapy is preferred in patients with extensive disease, frequent relapses and in whom topical drugs therapy have proved ineffective.<sup>22</sup>

The present study aims at the evaluation of various commonly

Sl no	Patients	Clearance rate at the end of one month
1	M 20	100
2	M 20	100
3	M 18	100
4	M 17	100
5	M 20	100
6	M 22	90
7	F 26	90
8	F 17	90
9	M 20	90
10	M 30	80
11	M 36	80
12	M 35	80
13	M 22	80
14	M 23	80
15	M 45	30

M-Male, F- Female; Average clinical cure = Percentage of total sum of clearance of all patients / No. of total patients in the concerned regime of therapy

**Table-3:** Clotramazole cream and Single dose Flucanazole 400mg

sl no	Patients	clearance rate at the end of one month
1	M 17	100
2	F 22	100
3	M 21	100
4	M 32	100
5	M 22	70
6	M 20	70
7	M 26	70
8	F 20	80
9	F 32	80
10	M 18	80
11	M 31	50
12	M 16	50
13	M 42	50
14	M 17	50
15	M 34	50

M-Male, F- Female; Average clinical cure = Percentage of total sum of clearance of all patients / No. of total patients in the concerned regime of therapy

**Table-5:** Clotramazole cream therapy alone for one month

sl no	Patients	clearance rate at the end of one month
1	M 17	100
2	M 16	100
3	M 22	100
4	M 25	100
5	M 20	80
6	M 19	80
7	M 25	80
8	M 22	80
9	M 19	80
10	M 20	70
11	M 16	70
12	M 20	70
13	M 28	30
14	M 32	30
15	M 30	30

M-Male, F- Female; Average clinical cure = Percentage of total sum of clearance of all patients / No. of total patients in the concerned regime of therapy

**Table-4:** Clotramazole cream and Flucanazole 150mg weekly for 4 weeks

Sl no	Patients	clearance rate at the end of One month
1	M 18	70
2	M 22	70
3	M 17	70
4	F 21	50
5	M 19	50
6	F 33	50
7	M 20	30
8	M 21	30
9	F 20	30
10	M 22	30
11	M 20	30
12	M 21	10
13	M 16	10
14	M 14	10
15	M 19	10

M-Male, F- Female; Average clinical cure 36 %; Average clinical cure = Percentage of total sum of clearance of all patients / No. of total patients in the concerned regime of therapy

**Table-6:** Flucanazole oral 400mg single dose

sl no	Patients	clearance rate at the end of one month
1	M 20	60
2	M 22	60
3	F 18	60
4	M 16	50
5	M 32	50
6	M 17	50
7	M 21	30
8	M 19	30
9	M 18	30
10	F 20	10
11	M 31	10
12	M 18	10
13	M 21	10
14	M 17	10
15	M 18	10

M-Male, F-Female; Average clinical cure 32 %; Average clinical cure = Percentage of total sum of clearance of all patients / No. of total patients in the concerned regime of therapy

**Table-7:** Oral Ketoconazole 400mg single dose

used therapeutic agent like clotrimazole cream, oral flucanazole and oral ketoconazole.

Clotromazole belongs to azole group of drugs. These have fungistatic effect inhibiting the biosynthesis of ergoseryl and thus disrupting the formation of fungal cellwall. HIV patients with pityriasis versicolor respond to topical azole as well as ketoconazole.<sup>23,24</sup> Clotromazole is a broad spectrum imidazoles reported to be effective against the pityriasis versicolor in both open<sup>25,26</sup> and controlled double blind trials.<sup>27,28</sup>

Flucanazole is a triazole. It has been investigated for its effective use in treatment of pityriasis versicolor. Various studies have suggested that flucanazole is an effective treatment option for therapy of pityriasis versicolor.

With ketoconazole, an imidazole, a number of regimens have been devised for therapy of pityriasis versicolor. The most common regimen is 200mg per day for 10 days. In a recent study comparing this regimen with a 400mg single dose of ketoconazole did not show any significant difference in outcome.<sup>29</sup> Ketoconazole affects the metabolism of many drugs by inhibiting mammalian cytochrome 450 in addition to fungal cytochrome 450.<sup>3</sup> There is risk of elevation of serum transaminases on long term ketoconazole therapy.<sup>30</sup>

Systemic ketoconazole hepatotoxicity appears to be idiosyncratic, more commonly seen in women above 40 years of age and is unlikely in one week such as in case of pityriasis versicolor.<sup>31</sup>

In the present study the first group of patients who were administered single dose of 400 mg flucanazole along with topical therapy of clotramazole for one month 33% of the group patients showed 100% clinical cure, 33% reported with 80% clearance while 27% showed 90% clinical cure whereas only one patient (7%) reported with 30% clinical cure after a period of one month.

This is the most effective regimen in the treatment of pityriasis versicolor in the present study with a clinical cure of 86%.

In the second group where the patients were given flucanazole 150mg per week for 4 weeks along with topical therapy with clotramazole cream for 1 month. 27% patient reported with 100% clinical cure, 20% patients reported with 70% clinical cure, 33% patient showed 80% clearance of the lesion while



**Figure-4:** A patient 15 days after therapy with oral flucanazole 400mg single dose



**Figure-5:** A patient 15 days after therapy with oral ketoconazole 400mg single dose



**Figure-6:** A patient after one month of therapy with ketoconazole 200mg single dose. only 10% of clearance of lesion

20% of patients showed 30% clinical cure. This regimen with a clinical cure of 73% has got slightly lower efficacy than the above regimen.

In another group of 15 patients who were treated with topical therapy with clotrimazole cream alone for a period of one month, 27% patients reported with 100% clearance of the lesions, 20% reported with 70% clinical cure, another 20% reported with 80% clinical cure while remaining 33% of patients in these group showed 50% clearance of lesions.

In the present study topical therapy with clotrimazole cream

alone also proved to be effective with a clinical cure of 73%. In the fourth group of patients with administration of single dose of flucanazole 400mg 20% reported with 70% clinical cure, another 20% reported with 50% clearance of lesion while 33% showed 30% clinical cure and the remaining 27% of patients of this group reported with only 10% clinical cure. Thus clinical cure of this group is 36% on an average. Faergeman is his open controlled trial reported a clinical cure of 74% at the end of 3 weeks with single dose of 400mg flucanazole<sup>32</sup> but in the present study the average clinical cure rate is only 36%. Mantego Gel et al in their open control trial with single dose of 450mg flucanazole showed a mycological cure of 70% at the end of one month.<sup>33</sup>

In the last group of the patients who were given single dose of ketoconazole 400mg only 20% reported with 60% clinical cure, other 20% reported with 50% clearance of lesion, another 20% reported with 30% clinical cure while remaining 40% of this group reported with only 10% of clearance of lesions. Thus this group showed a clinical cure of 32% only at the end of one month of therapy. Fernandez Nova et al in there open control trial have shown mycological cure of 42% at the end of one month.<sup>29</sup>

In the present study single dose of 400mg of oral flucanazole along with topical clotrimazole cream for one month proved to be most effective therapy with a clinical cure 86%.

The drug flucanazole given as 400 mg single oral dose achieves high serum concentration and has got better fungistatic effect due to its longer half life. This effect of single dose oral flucanazole is potentiated by regular topical application clotrimazole cream leading to synergistic additive effect of both oral and topical therapy. Slightly lower results achieved by weekly oral flucanazole 150mg along with clotrimazole topical therapy for one month might be due to lower serum concentrations achieved by weekly dose of 150mg flucanazole which might have lead to lower fungistatic effect compared to single dose of flucanazole 400mg.

The fact that in the present study topical clotrimazole cream alone for one month has also achieved a clinical cure of 73% indicates that topical clotrimazole therapy plays a better role than a single dose or weekly dose of oral flucanazole and single dose therapy with ketoconazole as well.

In the present study single dose of oral flucanazole 400mg has achieved slightly better therapeutic results than single dose of oral ketoconazole 400mg. In a study by Bhogal C.S. et al revealed that one oral dose of flucanazole 400mg might be better than one oral dose of 400mg ketoconazole.<sup>34</sup>

## CONCLUSION

Fluconazole 400mg single dose with topical clotrimazole cream therapy for one month came out to be the most effective regime with 86% clinical cure followed by topical clotrimazole cream for one month and fluconazole 150mg weekly for a period of 4 weeks with a clinical cure of 73% and topical therapy with clotrimazole therapy for one month which had also achieved 73% clinical cure. Single dose of 400mg oral flucanazole with 36% clinical cure is better than single dose of oral 400mg ketoconazole which has got 32% clinical cure. Further studies on large scale are required in this regard.

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# Non Ampullary Primary Duodenal Tumor (Villous Tumor of Duodenum) A Rare Case Report

Jigar V Shah<sup>1</sup>, Ronak D Vyas<sup>2</sup>

## ABSTRACT

**Introduction:** Solitary duodenal tumors are very rare. Majority of them (75%) are periampullary, sized less than 1 cm, 10 % are in the non periampullary region in 2nd part, 10 % in the 3rd part and only 5% are in the first part of duodenum. Majority of patients are asymptomatic or the complaints are non specific.

**Case report:** We present a case of 46 year old male, without any co-morbidity who on evaluation found to have a large ulcerated mass at d1/d2 junction.

**Conclusion:** Surgical management of VTD is selective, based on clinical presentation, information from pre-op diagnostic evaluation, presence of polyposis syndrome and intra op findings.

**Keywords:** Villous tumors of duodenum, duodenal tumors, local resection, pancreaticoduodenectomy.

## INTRODUCTION

Small bowel tumors are rare and account for less than 10% of the GI neoplasm.(1-3) Most of the time they are identified incidentally while upper GI endoscopy is done for some other purpose. Majority of patients present with small bowel obstruction, bleeding, or anemia. Small intestine makes about 75 % of the length and 90% of the surface area of the GI tract, but it is unique in being highly resistant to tumor formation. Bacteriological factors and the rapid passage of its liquid contents are the most obvious reasons.

With the use of upper GI endoscopy Villous Tumors of Duodenum (VTD) are being recognized with increasing frequency. Association of colonic polyps with duodenal tumors has increased awareness. 20 % have an associated polyposis Syndrome.

## CASE REPORT

The patient was a 46 year old male without any co-morbidity, presented in October 2015, with complains of pain abdomen and vomiting for 6 months, decrease appetite, and weight loss for 4-5 months. Clinical examination was within normal limit and further evaluation with upper GI endoscopy revealed a large ulcerated mass about 6x4x3 cms at d1/d2 junction and biopsy revealed tubulovillous adenoma (Figure-1).

**Blood investigations:** HB – 7.4, TLC – 8100, Platelets - 413000, INR - 1.10, Bilirubin - 0.58, SGOT - 19, SGPT - 12, SAP - 71, TP - 6.61, Albumin - 3.65, Cr - 0.91, Na - 139, K - 4.11

**Chest X-Ray:** No Abnormality Detected

## SPECIAL INVESTIGATIONS

**CT Abdomen:** Suggestive of large, relatively ill defined heterogeneously enhancing, hypo dense mass lesion within the

lumen of 2<sup>nd</sup> and 3<sup>rd</sup> part of duodenum causing luminal distention. The mass showed ill defined planes with the distal common bile duct, head and uncinate process of pancreas which appeared bulky and heterogeneous in attenuation – signs of invasion into the surrounding structures, with few sub centimeter size loco-regional lymph nodes which suggested possibility of mitotic etiology likely from duodenum with extension (Figures-2,3).

**CT – Angiography:** Enhanced mass lesion was seen in d2 and d3.

**CancerAntigen:** 19-9 – 2.09, Carcino Emroyonic Antigen – 0.75.

After preoperative clearance he was taken up for surgery with intent to do frozen section biopsy and proceed. He was operated for Vertical duodenal enterotomy, cholecystectomy, cannulation of lower bile duct and ampulla of vater by placing infant feeding tube through cystic duct stump, mass excision and frozen section biopsy, billroth 2 distal gastrectomy with duodenal enterotomy closure, with loop gastrojejunostomy with feeding jejunostomy (Figure-4).

## Operative findings

1. Large pedunculated mass arising from the mesenteric border of d1 and d2 junction around 6x4x3 cms. On cannulation of the ampulla of vater through cystic duct stump, it was found 2 to 3 cm proximal to it.2.Intraoperative frozen section: tubulovillous adenoma.3.Liver and other viscera normal.

**Hospital Course:** Postoperatively patient was kept in ICU for observation for one day. Post op day 2, Ryle's tube was removed and patient was started with oral sips. He was started with FJ trial feed on post op day 3 with oral liquid diet which was gradually increased and was discharged in a stable condition on post op day 6.

**No. of complications:** No complications.

**Clavien's grade:** 0.

**Charlson's Co-morbidity index score:** 1.

**Histopathology:** Section from the mass showed a polypoidal tumor composed of tubules which were closely packed and irregular. The cells lining them showed focal stratification,

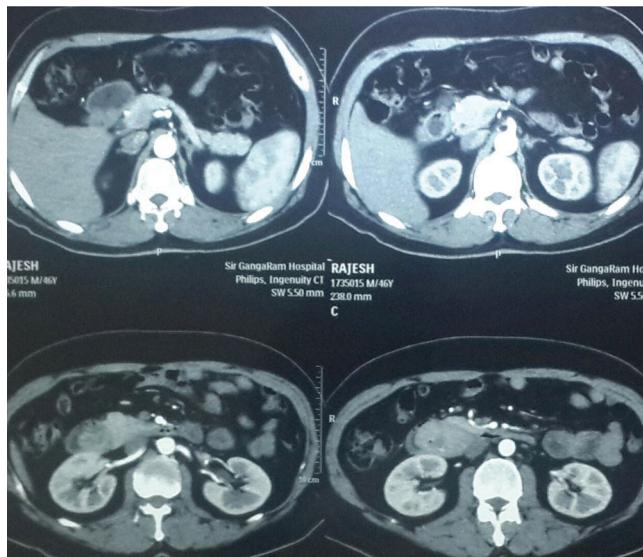
<sup>1</sup>Associate Professor, Department of Surgery SBKSMIRC, Sumandeep University, <sup>2</sup>Assistant Professor, Department of Surgery MP Shah Medical College Jamnagar, India

**Corresponding author:** Dr Jigar V Shah, 4, Keya Duplex, Near Radhika Society, Behind Devnagar, Makrand Desai Road, Vadodara, 390007, India

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**Figure-1** Endoscopy pictures showing tumour in the second part of duodenum.



**Figure-2:** CT Scan picture of Duodenal adenoma

nuclear hyperchromasia and a few mitosis, but there was no loss of polarity and no invasion into the underlying muscularis mucosa. Mild chronic inflammatory infiltrate was present in the stroma. The stalk and resected base were free of tumor. Section from the base of the stalk showed patchy ulceration. No residual tumor was seen. The duodenal mucosa on either side showed brunner gland hyperplasia. The proximal margin showed normal gastric mucosa.

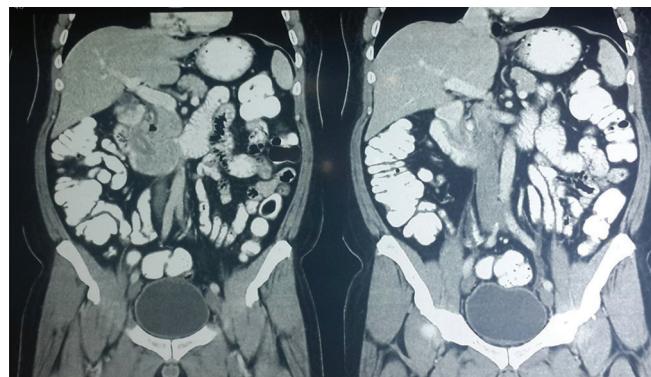
**Final Impression:** Tubular adenoma.

## DISCUSSION

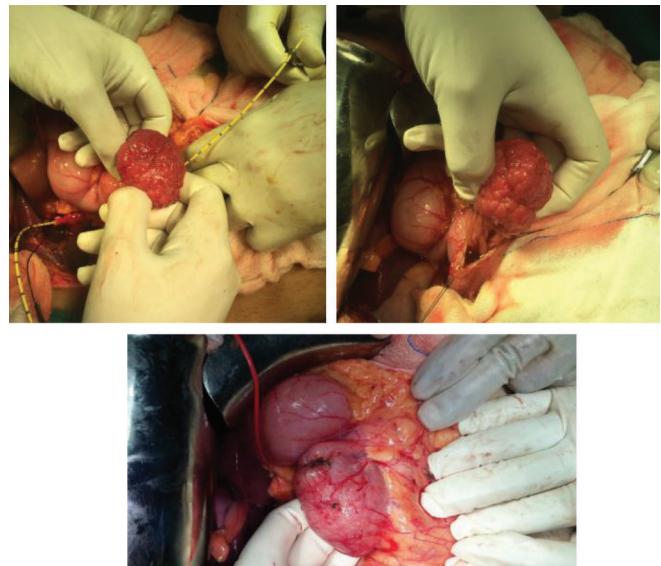
Cruveilhier described the 1<sup>st</sup> case of benign duodenal Brunner's gland adenoma in 1835.<sup>2</sup> In 1928, golden published the first definitive report for the treatment of duodenum adenoma. Duodenum is the common site for villous tumors of duodenum, and account for less than 1% of the total gastrointestinal tumors and only 16% of all benign tumors of intestine.<sup>3,4</sup>

Villous tumors of duodenum can behave in a manner similar to adenomas of the colon and rectum.<sup>5</sup> About 25% harbors invasive malignancy at the time of surgical excision. Size ranged from 0.5 to 9 cms. 75% are benign, 90% are solitary while 10% are multiple.<sup>6</sup>

Most common symptoms are abdominal pain, nausea and symptoms of pancreatitis.<sup>6</sup> They also present as anemia, obstructive jaundice and weight loss in patients containing invasive malignancy. VTD are asymptomatic in one third of patients.<sup>6</sup> They may cause GI bleed and small intestinal



**Figure-3:** CT Scan picture of Duodenal adenoma



**Figure-4:** Intra-op: showing duodenal adenoma and cannulation of cystic duct

obstruction.<sup>7-10</sup> Malignant changes occur in 30% to 60% of duodenal villous adenomas and much less in tubulovillous and tubular adenomas.<sup>11</sup> Most of the cases of VTD are sporadic. They are also found to be associated with Familial Adenomatous polyposis, Gardner's syndrome, and Peutz Jegher syndrome.<sup>6,12</sup> Patients with sporadic duodenal adenomas may be associated with colonic neoplasia and should be offered colonoscopy.<sup>13</sup> Extended Fiber-optic endoscopy with full visualization of duodenum is the most useful and accurate tool for VTD. Endoscopy allows both visualization and biopsy. ALL lesions at ampulla are within reach of side viewing duodenoscope.<sup>6</sup> There are controversies regarding the most appropriate treatment of VTD. Treatment depends on their location, size, and degree of dysplasia. Rapid growth, polyp induration, severe dysplasia or villous change makes intervention necessary.<sup>14</sup> Various treatment options are available as endoscopic snare removal or ablation, endoscopic mucosal resection, endoscopic submucosal resection, pancreas sparing duodenectomy and pancreaticoduodenectomy.<sup>6,12</sup> Many a times it is not possible to reach a accurate pre-op diagnosis because sample taken by endoscopic forceps are very small. Frozen section is sometimes associated with false negative results. There have been reports of recurrence after local resection.

For benign tumors which are less than 1 cm in size, endoscopic resection by an experienced endoscopist is considered

appropriate,<sup>6</sup> however endoscopic removal of lesions more than 1 cm has also been reported. For lesions larger than 2 cms, piecemeal resection may be required.<sup>13</sup> The lesion should be assessed carefully to determine size, involvement of mucosal fold, proportion of the circumference involved and the relationship with the ampulla of vater. Assessment focuses on endoscopic respectability of the lesion and detection of any feature predicting sub mucosal invasion.<sup>13</sup> Endoscopic treatment includes endoscopic mucosal resection (EMR) and endoscopic sub mucosal dissection (ESD). The procedural risks of EMR increases with the size of the lesion. Prior submucosal injection reduces the risk of duodenal perforation. Most common in use are 0.9% saline. ESD involves a sub mucosal injection to lift the lesion in similar fashion to EMR. Submucosal plane meticulously dissected to remove the lesion en bloc. The rates of enblock resection are high but at the risk of perforation and increase duration of procedure.<sup>14</sup> It is recommended that all the patients who have undergone endoscopic resection should be considered for surveillance endoscopy for the detection and treatment of recurrence.<sup>15</sup>

### Surgical Treatment

For benign lesions more than 1 cm, transduodenal local excision versus PD pancreaticoduodenectomy. Whipples in proved cases of carcinoma, advanced disease and carcinoma in situ. It is also an option for benign VTD in selected fit patient, especially for large or multicentric VTD to avoid recurrence. Factors like hard areas on palpation, an ulcerated tumour, dilatation or obstruction of common bile duct or pancreatic duct, pre-op biopsy showing severe dysplasia or villous lesions extending into bile or pancreatic duct should be considered as malignant lesions. In presence of these factors PD pancreaticoduodenectomy should be strongly recommended. In absence of these factors local resection is advised.<sup>5</sup>

For benign VTD, without the above mentioned factors in the lateral wall of 2<sup>nd</sup> part, 1<sup>st</sup> part, distal 3<sup>rd</sup> or 4<sup>th</sup> part segmental resections are reasonable options. For VTD, harboring invasive malignancy in 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> part, PD is the treatment of choice. Pancreatic fistula, anastomotic leakage and pancreatitis are serious complications after PD. Although the morbidity and mortality rates following PD have decreased drastically now, the procedure still results in considerable operative stress. For lesions in the distal 3<sup>rd</sup> or 4<sup>th</sup> portion, pancreas sparing duodenectomy with extended resection, because PD does not remove primary LN basins of these distal duodenal cancers. Previous studies had shown a recurrence rate of 32 % at 5 yrs after transduodenal local excision and 24% recurrences were cancer. Transduodenal local excision, wedge resection, segmental partial, full thickness and pancreas sparing duodenectomy are suitable for patients with premalignant or early malignant duodenal lesions. For early non ampullary duodenal cancer located in the distal third and 4<sup>th</sup> part of duodenum segmental resection is associated with reduced morbidity and mortality, while allowing for satisfactory clear margins and adequate lymph node dissection.

### CONCLUSION

Surgical management of VTD is selective, based on clinical presentation, information from pre-op diagnostic evaluation, presence of polyposis syndrome and intra op findings. For VTD treated by local excision and endoscopic method, regular,

frequent, and longterm endoscopic surveillance is mandatory. In our patient, the tumor was at D1/D2 junction, away from ampula of vater with benign histology, so one time surgical procedure was curative.

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# Autografts in Middle Ear Reconstruction: A Study of 30 Cases

Reema Rai<sup>1</sup>, Sanjay Chhabria<sup>2</sup>

## ABSTRACT

**Introduction:** Chronic suppurative otitis media is an inflammation of the middle ear cleft with ossicular destruction. Restoration of a sound transfer mechanism is the goal of modern ossiculoplasty using a variety of allogenic and autograft materials.

**Material and Methods:** A retrospective analysis of 30 cases of ossiculoplasty using autografts was done. Patients with sensorineural hearing loss, tuberculosis and other complications were excluded from the study.

**Results:** Thirty cases were analysed for various factors. Majority of cases were from 21 – 30 years age group (36.7%). Males were predominantly affected in a ratio of 3:1. Nine cases (30%) presented with otorrhoea for a duration of 1 – 5 years. Equal number of patients presented with unilateral and bilateral deafness. Moderate degree of hearing loss was present in maximum cases (47%). In 7 patients (24%) there was otalgia, while 4 patients (14%) had tinnitus. 18 cases (60%) had tubotympanic type of disease. Intra-operatively, necrosis of lenticular process of incus was seen in a majority of 24 cases.

**Conclusion:** Ossicular reconstruction with significant improvement of conductive hearing loss remains a surgical challenge. Autologous ossicles have been preferred because of easy availability, low cost of preparation, good sound conduction and biocompatibility.

**Keywords:** Autografts, Ear Reconstruction

## INTRODUCTION

Chronic suppurative otitis media is an inflammation of the middle ear cleft. It is of insidious onset, intermittent or progressive in nature, with the potential severe destruction and irreversible sequelae. The middle ear ossicles often have to be removed because of pathological destruction. The replacement of these ossicles has always been a challenge in middle ear surgery.

With the advent of the operating microscope, Halland Rytzner performed the first ossicular chain reconstruction using autologous ossicular bone and a sculptured autologous malleus, interposed between the tympanic membrane and stapes footplate.<sup>1</sup> Portmann reported various interposition techniques using a sculptured autologous incus or malleus.<sup>2</sup> Guilford found better hearing gains with malleus to stapes head or footplate interposition.<sup>3</sup>

Austin described various types of ossicular defects and reconstructive interposition techniques labeled as the ‘malleus-stapes assembly’.<sup>4</sup> Incus interposition for reconstruction of the ossicular chain has also been described by several other authors (Pennington<sup>5</sup>; Smyth<sup>6</sup>; Glasscock<sup>7</sup>; Mawson<sup>8</sup>).

Zollner and Wullstein laid down the requirements for a functioning middle ear in the 1950s: an intact elastic tympanic membrane, a ventilated middle ear space, a mobile and unobstructed oval and round window and a mechanism to link the tympanic membrane to the oval window.

Each technique has its own pros and cons, and there is currently

no universally effective way of correcting conductive hearing losses under these circumstances. Farrior reported that many transposition operations failed due to ossicular fixation.<sup>10</sup>

Incus is most commonly reshaped and placed between malleus and stapes. Allografts are used in cases when autograft materials are not available, or – as in patients with cholesteatoma - an ossicle may not be suitable because of osteitis, adherence to surrounding walls, resorption and loss of rigidity. The use of allogenic ossicles was first introduced by House et al in 1966.<sup>11</sup> Modern ossiculoplasty aims to restore stable sound transfer mechanism in middle ear.

In this study of 30 cases of ossiculoplasty with autografts, we aim to explore and correlate the importance of presenting symptoms and clinical signs of the disease with the investigations, intraoperative findings, various ossicular assemblies and post-operative follow up, finally to gauge hearing improvement in the patients.

## MATERIAL AND METHODS

We conducted a retrospective analysis of 30 cases of ossiculoplasty using incus/malleus/cartilage as autograft in patients who came for the treatment in our hospital over a period of two years. These cases, 16 to 60 years of age, presented with chronic suppurative otitis media (safe and unsafe) with or without previous surgery and with an air-bone gap (in pure tone audiogram). Patients with sensorineural hearing loss, bone diseases like tuberculosis, no follow-up for a period of 6 months after previous surgery, stapes fixation, congenital atresia, presence of any allergic or septic foci, other metabolic conditions like diabetes mellitus, hypertension, etc. and other complications of chronic suppurative otitis media like facial nerve dehiscence, labyrinthine fistula, etc. were excluded. We included 30 cases with the help of simple random sampling method after matching inclusion and exclusion criteria. Informed consent was taken. Institutional ethics committee approval was taken before the start of the study.

Following general physical and detailed ENT examination, the cases were prepared for surgery. Tuning fork tests, pure-tone audiometry and blood tests were carried out.

The following reconstruction options were used:

### 1. A malleus stapes assembly using incus

In patients who did not need a mastoidectomy, incus was used as the ossicle. Hearing results were better in such cases. As incus can be reshaped easily and its length can be adjusted, it can be used in different types of reconstruction.

<sup>1</sup>Resident, <sup>2</sup>Assistant Professor, Department of Ear, Nose and Throat, B. Y. L. Nair Ch. Hospital, Mumbai Central 400008, India

**Corresponding author:** Dr. Sanjay Chhabria, A703/704, Veenasur Mahavir Nagar, Kandivali (W), Mumbai – 67, India

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## 2. Ossicle on the stapes head – using incus/malleus

Here, either incus or malleus were used. The results were better with malleus autografts probably due to shape of malleus. The malleus when shaped is barrel like and having a broad base is a stable assembly. Hence it sits comfortably on the head of stapes. This also augments the stapes head in a modified radical mastoidectomy.

## 3. Ossicles on stapes footplate (incus/malleus/cartilage)

Incus, malleus or cartilage was used in certain cases. The results were good with incus, malleus and tragal cartilage, probably because it helps in creating a middle ear space. Malleus is adaptable to both stapes superstructure – present and stapes superstructure – absent situations as well as in the presence of a fixed footplate and can be used with all type of middle ear autografts.

All cases were followed post-operatively for a minimum period of 6 months. All cases were subjected to post-operative pure tone audiogram for 6 months following surgery.

## STATISTICAL ANALYSIS

Statistical Analysis was done with the help of SPSS version 21. Descriptive statistics like mean and percentages were used to infer data.

## RESULTS

Majority of cases were from second decade of life forming 36.7%, followed by third decade forming 30%. Males were predominantly affected as compared to females in a ratio of 3:1. 9 cases (30%) presented with otorrhoea for a duration of 1 – 5 years. Seven cases (23.3%) had discharge for duration of 5 – 10 years. There were equal number of patients presenting with unilateral and bilateral deafness, 15 cases each.

Moderate degree of hearing loss (41 – 55 dB) was present in majority of cases (60%) patients followed by mild degree in 9 cases (30%) and severe hearing loss (56 – 70 dB) was present in 3 cases (10%).

In 7 patients (24%) there was presence of otalgia, while 4 patients (14%) had tinnitus. 18 cases (60%) had tubotympanic type of disease while 12 cases (40%) who were operated for ossiculoplasty had atticoantral type of disease. All patients had sclerotic mastoid on X-ray.

Intra-operatively amongst a majority of 24 cases, necrosis of lenticular process of Incus was seen, and 22 cases had necrosis of long process of Incus. Handle of Malleus was necrosed in 16 cases. 7 cases who had necrosis of stapes superstructure also had associated necrosis of malleus and incus.

Also it was observed intra-operatively that in 16 cases (54%) handle of Malleus was necrosed, while in 4 cases (13%) the same was foreshortened. 10 cases (33%) had normal handle of Malleus.

In most of our cases, body of Incus (64%) was used for reconstruction of ossicular chain after reshaping. In 7 cases (23%) tragal cartilage was used and in 4 cases (13%) head of malleus was used (Table-1).

Most of our patients underwent tympanoplasty followed by cortical mastoidectomy (Table-2)

9 patients had a hearing gain of 20 dB which formed 45% of study group. 30 dB hearing was achieved in 4 (20%) patients (Table-3). 10 patients showed a loss in hearing following

surgery, of which 60% showed loss of 10 dB. Only one patient had loss of 30 dB.

23 cases (77%) showed an intact tympanic membrane or a healed mastoid cavity post-operatively. 13 % showed a residual perforation and 10% showed retracted pars tensa.

## DISCUSSION

The aim of middle ear reconstructive surgery is to restore the ossicular chain as near to normal as possible. In the last three decades, various ossiculoplasty methods using different graft materials have evolved and good result have been obtained but ossiculoplasty is still evolving.

The challenge during ossiculoplasty has been how to achieve a stable, reliable connection between the tympanic membrane and mobile stapes footplate that will provide the best long term hearing results, without complications, in a chronically infected ear.

Out of several materials that are available for middle ear reconstruction we have studied tragal cartilage, autograft incus and malleus.

There are several variables in middle ear surgery that affects the results.

- a. Most significant variable is the function of Eustachian tube. It affects the long term survival of the various grafts in middle ear surgery.
- b. The second variable is the status of the middle ear mucosa. The presence of active infection, polypoidal changes, granulation tissue, or bare bone can affect the subsequent function of an implanted autograft.
- c. The condition of the tympanic membrane is the third variable. Ossicular reconstruction when the tympanic membrane is intact gives better results than when there is a perforation in tympanic membrane.
- d. The fourth variable is the status of the ossicular chain. The presence of stapes superstructure is very important to improve hearing in ossicular reconstruction.
- e. The underlying process itself (disease or trauma factor) that has caused a specific ossicular defect is a fifth variable. Congenital ossicular abnormalities, cholesteatoma cases and traumatic ossicular discontinuities are difficult to

Ossicles used for reconstruction	No of cases	Percentages (%)
Body of Incus	19	64
Head of Malleus	4	13
Tragal Cartilage	7	23

Table-1: Ossicles used for reconstruction (n=30)

Type of surgeries	No of cases	Percentages (%)
Tympanoplasty	13	44
Cortical Mastoidectomy	10	33
CWD Mastoidectomy	7	23

Table-2: Types of surgeries (n=30)

Range	Gain	Percentages (%)
0 to 10 dB	7	35
11 to 20 dB	9	45
21 to 30 dB	4	20

Table-3: Hearing improvement following surgery

manage.

Success of ossiculoplasty is measured by air-bone gap closure which is a good indicator of comparing different reconstructions. In the present study, we have included 30 patients who have undergone ossicular reconstruction with either a head of malleus, body of incus or tragal cartilage as autograft.

The pre-operative hearing disability (by air-bone gap), intraoperative findings, autografts used and post-operative improvement or loss in hearing have been studied. The findings of this study were then compared to earlier published series.

In our series the majority of cases were between 21 – 30 years of age (36.66%). Youngest being 10 years and oldest being 54 years. But age was not found as a predictor of underlying disease in ours as well as any other study referred. Males were predominantly affected, and the male to female ratio was 3:1. Out of 30 patients, 23 were males (77%) and 7 females (23%). 60% had tubotympanic type of disease while 40% had attico-antral type of disease.

Moderate degree of hearing loss was present in majority of cases. Intra-operatively in 22 cases which formed majority had necrosis of long process of incus with lenticular process. Handle of malleus was necrosed in 16 cases. 7 cases that had necrosis of stapes suprastructure also had associated necrosis of malleus and incus. In a series by Gordon Smyth where 900 cases were studied showed 90% with a defective incus and malleus handle.<sup>6</sup> In 44% tympanoplasty was done, in 33% cortical mastoidectomy was done and in 23% canal wall down mastoidectomy was done. In patients with tubotympanic type of disease (safe chronic suppurative otitis media), tympanoplasty (without mastoidectomy) was done. Whereas, cortical mastoidectomy was done in patients with granulation tissue in middle ear, aditus and with early retraction pocket of pars tensa (grade I and II). In patients with cholesteatoma or retraction pocket of pars tensa extending beyond lateral semicircular canal, canal wall down mastoidectomy was done.

Depending upon the remnant ossicular components, in most of our 19 cases (64%) body of incus was used for reconstruction of necrosed ossicle after reshaping. In 7 cases (23%) tragal cartilage was used and in 4 (13%) cases head of malleus was used. This correlated with the malleus-stapes assembly modification of Armstrong<sup>12</sup> and Austin<sup>4</sup> where incus is sculpted and fit into the interval between the stapes head and the malleus handle. Also seen in a study by Bauer et al (2000), the efficiency of the body of incus and that of the cortical bone are seen to be equally good.<sup>13</sup>

In our series improvement of hearing following surgery was 64%. Of which, 9 (45%) patients showed an improvement in air-bone gap of 20 dB, 4 (20%) patients with an improvement of 30 dB and 7 (35%) patients with an improvement of 10 dB. As compared to a study by Bauer et al where 68% of all ears undergone ossicular autograft reconstruction showed air-bone gaps improvement of 20 dB, and 10 dB improvement of 28%.<sup>13</sup> The causes for post-operative hearing loss in our study were residual perforation, retraction of pars tensa, mastoid cavities which retrospectively were presumed to be conducting loss.

Our series showed a failure of 36% as compared to a study by Yung who reported that among disease, extrusion and surgeon-related problems of ossiculoplasty, failures accounted for 56%.<sup>14,15</sup>

Good result in ossiculoplasty depends on case selection and technical ability. One of the most challenging aspects of training ear surgeons in a residency program is the instruction of when and when not to operate in a given situation based on the patient's hearing level, history, and presentation. Variable hearing results in literature after ossiculoplasty is because of lack of understanding and uniform reporting of those middle ear factor that influence the results.

## CONCLUSION

This study was conducted to provide an ossicular replacement prosthesis using an autograft between the tympanic membrane and oval window of a patient's ear, which will be inexpensive, have a low complication rate, and an acceptable hearing result. Ossicular reconstruction with significant improvement of conductive hearing loss remains a surgical challenge. The benefit of reconstructing the ossicular chain is well documented in both canal wall up and canal wall down tympanomastoidectomies. Autograft ossicles are ideal for this procedure, provided that they are disease free. We should thus strive to correct tympanic membrane deficiencies and reconstruct the ossicular chain, in order to improve the quality of life of our patients.

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# Study of Radiation Induced Xerostomia in Head and Neck Cancer in Conformal Versus Conventional Radiotherapy

Fatema<sup>1</sup>, Joseph Benjamin Gandi<sup>2</sup>, Bala Sankar Ramavath<sup>2</sup>, John Winkle Medida<sup>1</sup>, Macha Kiran Kumar<sup>3</sup>

## ABSTRACT

**Introduction:** Head and neck cancers are most common cancers in India. Radiotherapy is common modality of treatment. Xerostomia is most common late side effect of Radiotherapy. The aim is to compare it in conformal and conventional radiotherapy.

**Materials and methods:** Head and neck cancer patients presented to department of Radiotherapy in MNJ Institute of Oncology and RCC during period of 2013-2015 were recruited in present study. 22 patients were allotted in conventional arm and 20 patients in IMRT arm. Xerostomia after Radiation therapy was assessed subjectively by using xerostomia related questionnaire and objectively by comparing the salivary gland function using quantitative salivary gland scintigraphy (QSGS).

**Results:** Analysis of QOL related questionnaire showed mean score of 8.5 in conventional arm and mean score of 4.8 in IMRT arm with p value=0.003. Analysis of EF% showed baseline EF% of 48.47 and follow up EF% of 3.86 in conventional arm whereas baseline EF% of 47.49 and follow up EF% of 15.36 in IMRT arm with p value of 0.001.

**Conclusion:** Xerostomia can be reduced with Conformal Radiotherapy like IMRT which improves the quality of life of patients after irradiation to Head and Neck region.

**Keywords:** Xerostomia, Conformal Radiotherapy, Salivary Scintigraphy.

## INTRODUCTION

Cancer of the head and neck is one of the most common cancers in India affecting both males and females. In India, head and neck cancers constitute 25% to 30% in males and 15% in females.<sup>1</sup> Surgery and radiotherapy with or without chemotherapy are most frequently used therapeutic modalities in head and neck cancers. Surgery or radiotherapy has shown good comparable results in early stage cancers (T1, T2). For advanced stage disease (stage III / IV) with large primary tumors, the primary curative modalities are surgery, radiotherapy and chemotherapy. The conventional RT to head and neck cancers typically involves irradiation of major salivary glands and large area of normal mucosa. It leads to mucositis, dysphagia and xerostomia. Xerostomia is most prevalent late side effect of head and neck malignancy. Also xerostomia is cited by patient as major cause of decreased quality of life.<sup>2</sup>

The main objective of this study was to compare xerostomia subjectively by using xerostomia related questionnaire and to compare salivary gland functioning by using quantitative salivary gland scintigraphy (QSGS) in head and neck cancer patients receiving conventional RT / IMRT.

## MATERIAL AND METHODS

**Source of data:** Patients presenting to the Department of Radiation oncology in MNJ Institute of Oncology and Regional Cancer Centre during 2013 to 2015.

**Sample Size:** 22 patients in conventional arm and 20 patients in IMRT arm based on inclusion/exclusion criteria.

**Patient's inclusion criteria:** Histologically confirmed SCC of the Head and Neck region, which are to be treated by Radiotherapy primarily or postoperatively with age between 15 to 70 years, with ECOG performance status 0-2.

**Patient's exclusion criteria:** Patients with previous head and neck irradiation, preexisting salivary gland disease, tumor involving parotid gland, concurrent illness that would compromise completion of treatment or follow up, patient taking any substitutes like pilocarpine and patients who have a disseminated disease.

**Xerostomia related Questionnaire:** We devised a 14 point questionnaire form. Each participant had to answer, first time during a baseline scintigraphy scanning, and later during the follow up scan. Each patient was scored based upon his or her responses, to a maximum possible score of 14.

- 1) Do you have a normal salivary secretion?  
 YES    0     No    1
- 2) Has there been a change lately in saliva amount?  
 YES    1     No    0
- 3) Is your mouth dry when you are not eating?  
 YES    1     No    0
- 4) Do you have problem with your gums?  
 YES    1     No    0
- 5) Do you have problem while speaking?  
 YES    1     No    0
- 6) Do you drink water during the day because of dry mouth?  
 YES    1     No    0
- 7) Do you have trouble sleeping in the night due to dry mouth?  
 YES    1     No    0
- 8) Do you drink water during the night because of dry mouth?  
 YES    1     No    0
- 9) Do you have any problem while swallowing solid food?  
 YES    1     No    0
- 10) Do you have a problem with the transport of grounded food through your mouth?  
 YES    1     No    0

<sup>1</sup>Senior Resident, <sup>2</sup>Assistant Professor, <sup>3</sup>Junior Resident, Department of Radiation Oncology, MNJ Institute of Oncology and Regional Cancer Centre, Hyderabad, India

**Corresponding author:** Dr. John Winkle Medida, Room No 8, MNJ Institute of Oncology and Regional Cancer Centre, Redhills, Hyderabad – 500004, India

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- 11) Do you have problem during swallowing solid food?  
 YES 1     No 0
- 12) Do you have problem during swallowing grounded food?  
 YES 1     No 0
- 13) Do you experience dry mouth during meals?  
 YES 1     No 0
- 14) Do you need to drink water to swallow your food?  
 YES 1     No 0

### Salivary Scintigraphy Scan

Every patient had to undergo a baseline salivary scintigraphy scan before the initiation of radiation therapy. They were also required to come for a follow up scan after three months from the date of completion of the last fraction of radiation. The maximum delay time allowed for follow up visit was 2 months from the due date.

**Tracer used:** Technetium pertechnetate ( $^{99m}\text{Tc}$ - $\text{TcO}_4^-$ ).

**Dose administered:** 5 mCi, Intravenously.

**Sialagogue used:** Concentrated lime juice, approximately 1ml, administered orally over tongue at the end of 15 min from the beginning of the scan.

**Acquisition technique:** Image acquisition was performed using a millennium MG Dual Head gamma camera, equipped with low energy collimators. Dynamic imaging was performed at a capture rate of 1 min per frame for 30 min, after an intravenous injection of 5mCi of  $^{99m}\text{Tc}$ - $\text{TcO}_4^-$ .15 min post injection of the tracer, 1 ml of lemon juice administered orally as a sialagogue to induce excretion of saliva. The patient was told to distribute lemon juice around his mouth and then swallow it. The pre and post syringe images were acquired for quantification purposes.

**Quantitative analysis:** Four oval regions of interest (ROIs) were drawn over both parotids as well as submandibular glands. One banana shaped ROI was also drawn around right clavicle region. Percentage excretion fraction (EF%) was determined using time activity curves.

The quantification of salivary gland excretion is done by calculating fraction of maximal excretion to maximal uptake of each salivary gland and is called as salivary excretion fraction. Reduction in salivary gland function after (chemo) radiotherapy was described by the relative SEF or SEF ratio. SEF ratios on follow-up at 3 months were correlated with mean parotid doses.

### STATISTICAL ANALYSIS

The analysis of the data was done by chi-square test using Statistical software SPSS 20.0 and OPEN EPI.

### RESULT

The mean age in conventional arm was  $43.31 \pm 21$  years. The mean age in IMRT arm was  $44.7 \pm 26.72$  years. The number of male and females in the conventional arm was nineteen(86%) and three (14%)respectively. The number of male and female in the IMRT arm was fifteen (75%) and five (25%) respectively. The distribution of patients in conventional arm according to stage: two were stage II, eleven were stage III and nine were stage IV and in the IMRT arm, two patients were stage II, eleven patients were stage III and eight patient were stage IV.

As only 16 patients in conventional arm and 14 patients of IMRT arm were available for follow up, the results of xerostomia

related questionnaire and results of salivary ejection fraction measured by Quantitative salivary scintigraphy were analysed only in these patients. Also the mean doses to parotid received in were compared in these patients.

### Mean Dose of Parotid Glands

Mean dose to ipsilateral parotid was  $57.39 \pm 4.81$  Gy ( $\pm 1\text{sd}$ ) and mean dose to contra lateral parotid was  $50.77\text{GY} \pm 10.06$  Gy ( $\pm 1\text{sd}$ ) in conventional arm patients. Mean dose to ipsilateral parotid was  $33.28 \pm 10.99$  Gy ( $\pm 1\text{sd}$ ) and mean dose to contralateral parotid was  $23.92 \pm 3.12$  Gy ( $\pm 1\text{sd}$ ) in IMRT patients (figure-1)

### Xerostomia related QOL questionnaire

Analysis of the mean scores obtained in questionnaire for the two arms was done, for a total possible score of 14 points. The conventional arm had a mean score of  $8.5 \pm 2.47$  ( $\pm 2\text{sd}$ ) whereas the IMRT arm had a mean score of  $4.8 \pm 3.8$  with  $p$  value=0.003 which is significant (table-1).

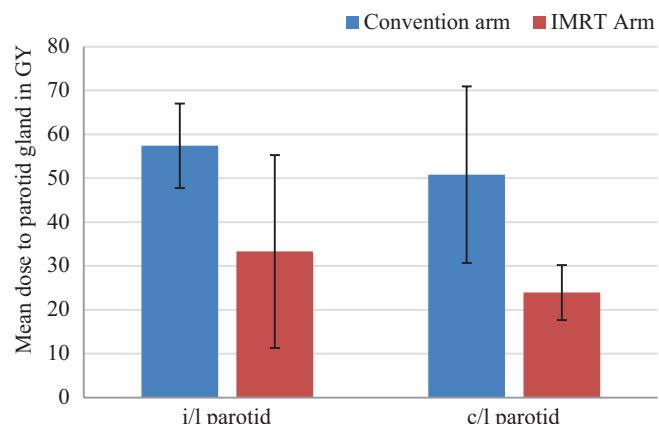
Final analysis was done for the percent excretion fraction (EF%) in the salivary scintigraphy scans between baseline and first follow up after completion of radiotherapy, for patients in both conventional and IMRT arms (figure-2)

Patients in the conventional arm had a baseline EF% of  $48.47 \pm 11.51$  versus a follow up EF% of  $3.86 \pm 6.98$ . In the IMRT arm baseline EF% was  $47.49 \pm 17.03$  whereas follow up EF% was  $15.36 \pm 12.91$  with  $p$  value of 0.001 which is clinically significant (figure-3)

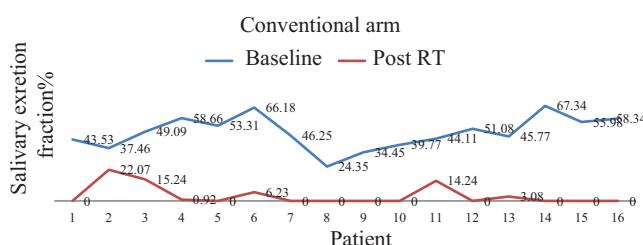
### DISCUSSION

Head and neck cancers are implicated as a major contributor to the burden of cancer of India.<sup>1</sup> Radiotherapy plays a significant role in management of head and neck cancer as the primary treatment modality. One of the most frequent and debilitating long-term side effects of radiotherapy (RT) for head and neck cancer is xerostomia.<sup>2</sup>

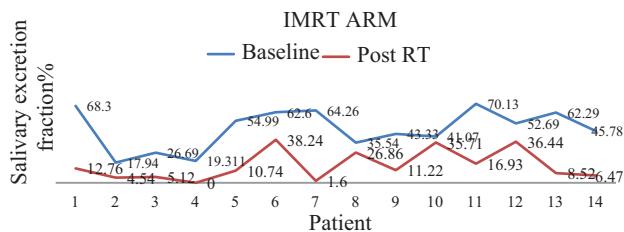
The radiation induced adverse events manifest as either acute reactions (i,e occurring within 90 days of RT) or late/delayed reactions (i.e occurring months to years after RT).The acute reaction includes mucositis, difficulty in swallowing and xerostomia. The delayed effects include xerostomia, nocturnal dry mouth, difficulty in swallowing, speech, dental caries, periodontitis and osteoradionecrosis. This would compromise on the outcome of the patient with respect to the long term physiological functioning and quality of life<sup>3</sup>



**Figure-1:** Mean dose to ipsilateral and contralateral parotid gland in both arm  $\pm 2\text{SD}$



**Figure-2:** Baseline and Post radiotherapy time activity curve in a salivary gland scintigraphy in a patient receiving conventional radiation



**Figure-3:** Baseline and post radiotherapy time activity curve in a salivary gland scintigraphy in a patient receiving IMRT.

Patient number	Conventional arm	IMRT arm
Patient 1	7	3
Patient 2	7	2
Patient 3	8	3
Patient 4	9	7
Patient 5	10	9
Patient 6	6	4
Patient 7	10	5
Patient 8	10	4
Patient 9	8	7
Patient 10	9	5
Patient 11	10	6
Patient 12	8	5
Patient 13	8	3
Patient 14	8	5
Patient 15	9	-
Patient 16	9	-

**Table-1:** Total xerostomia related QOL score in conventional and IMRT arms in each patient.

Clinically, xerostomia has been reported with as little as two or three doses of 2 Gy, although many changes occurring with less than 60 Gy are reversible. However, doses greater than 30 Gy can cause permanent xerostomia.<sup>4</sup> Damage to the salivary glands results in reduced salivary flow, changes in the electrolyte and immunoglobulin composition of saliva, reduction of salivary pH, and repopulation of cariogenic micro flora. When the major salivary glands are included in the radiation field, salivary function often decreases by 50% to 60% in the first week, with basal salivary flow reaching a measurable minimum 2 to 3 weeks. The extent of glandular change is directly related to the dose of radiation to the salivary glands, with the most severe and irreversible salivary dysfunction resulting from damage to (or) loss of salivary acinar cells.<sup>4</sup>

Xerostomia symptoms are usually permanent, which illustrates the importance of prevention. Recent advances in conformal radiation therapy like IMRT, enable us to spare the parotid glands while providing adequate dosimetric coverage of tumour

targets, and have provided a new avenue to prevent xerostomia.

#### Mean Dose of Bilateral Parotid Glands

Intensity-modulated radiotherapy (IMRT) optimizes the delivery of irradiation to irregularly shaped volumes and has the ability to produce concavities in radiation treatment volumes. It can deliver different doses to different target volumes simultaneously sparing the parotid glands and the spinal cord. In this study mean dose to ipsilateral parotid was 57.39 Gy and mean dose to contralateral parotid was 50.77GY in conventional arm patients. Mean dose to ipsilateral parotid was 33.28 GY and mean dose to contralateral parotid was 23.92 in IMRT patients. Xia et al (2000) compared the treatment plans involving IMRT for nasopharyngeal carcinoma. In their series, the coverage to the GTV as well as the CTV was superior with the inverse planned IMRT plans. In addition, when using proper dose constraints to the normal structures, inverse planned IMRT plans achieved the least dose delivered to organs at risk. There was substantial reduction of the mean parotid dose to as low as 21.4 Gy.<sup>5</sup>

The results of present study were also consistent with the above trial. The mean dose to the parotid glands was less than 26Gy in IMRT arm indicating the superiority of IMRT in head and neck cancer patients receiving Radiation treatment.

Eisbruch et al reported that a mean dose of 26 Gy or above to the parotid gland shows significant decrease or immeasurable salivary flow upon stimulation. The radiation-induced xerostomia is an irreversible complication of the parotid glands which has received radiation with a mean dose of 26 Gy or above.<sup>6</sup>

Xerostomia can be defined and graded both subjectively according to patient's symptoms (severity of dryness and/or response on stimulation) as well as objectively using quantified saliva production or excretion (salivary flow and/or scintigraphy). So in our study we have assessed xerostomia in patients subjectively using questionnaire method and objectively by using <sup>99m</sup>Tcpertechnetate salivary scintigraphy. The parotid glands produce maximum saliva during meals whereas submandibular glands are said to be responsible for lubrication in rest. In our study first eight questions in xerostomia questionnaire are related to xerostomia in rest and the latter six questions are related to xerostomia during meals. The aim was to spare at least one of the parotid gland and reducing the mean dose to less than 26Gy in the IMRT group.

Van Rii et al published a study which concluded that Parotid gland sparing IMRT for head and neck cancer patients improves xerostomia related quality of life compared to conventional radiation both in rest and during meals.<sup>7</sup> This study used questionnaire on xerostomia (based on the EORTC HandN 35 Questionnaire, Eisbruchs Questionnaire on xerostomia and an additional trial specific questionnaire).<sup>8-9</sup> Patients treated with IMRT experienced less chewing and swallowing difficulties. They also reported less problems with eating and speaking.

Edmond H. Pow et al in a study compared directly the effect of intensity-modulated radiotherapy (IMRT) vs. conventional radio- therapy (CRT) on salivary flow and quality of life (QoL) in patients with early-stage nasopharyngeal carcinoma.<sup>10</sup> Stimulated whole (SWS) and parotid (SPS) saliva flow were measured and Medical Outcomes Short Form 36 (SF-36), European Organization for Research and Treatment of Cancer (EORTC) core questionnaire, and EORTC head-and-neck

module (QLQ-HandN35) were completed at baseline and 2, 6, and 12 months after radiotherapy. They concluded that in the IMRT group, there was consistent improvement over time with xerostomia-related symptoms significantly less common than in the Conventional RT group at 12 months post radiotherapy.<sup>10</sup> Alexander LIN, M.D., et al did a prospective longitudinal study of head-and-neck cancer patients receiving multi segmental static IMRT.<sup>11</sup>

A validated xerostomia questionnaire and head and neck cancer questionnaire were given to patients. The questionnaires and measurements of salivary output from the major glands were completed before RT started (pre-RT) and at 3, 6, and 12 months after RT. They concluded that after parotid-sparing IMRT, a statistically significant correlation was noted between patient-reported xerostomia and each of the domains of QOL: Eating, Communication, Pain, and Emotion. Both xerostomia and QOL scores improved significantly over time during the first year after therapy.<sup>11</sup>

This study results showed xerostomia related QOL questionnaire scores were better in IMRT patients than conventional RT patients. In the current study the total mean score of xerostomia related QoL was 8.5 in conventional arm vs 4.5 in IMRT arm.

The radiation induced injury of the salivary gland functioning with irradiation has already been reported in literature by measuring salivary flow rates or quantitative salivary scintigraphy. Dynamic quantitative pertechnetatescintigraphy has emerged as a simple, reproducible and minimally invasive test for quantification of post radiotherapy salivary function of individual major salivary glands. It provides quantitative estimates of parenchymal and excretory function of individual major salivary glands. It can be a suitable alternative to salivary flow rate measurements for quantification of post radiotherapy salivary dysfunction.<sup>12</sup>

The salivary glands possess an iodide-trapping mechanism and  $^{99m}\text{Tc}$ -pertechnetate ( $^{99m}\text{Tc}$ ), like radioiodine, is concentrated in the intralobular ductule cells by means of this trapping-mechanism with subsequent ductal epithelium secretion and discharge into the excretory ducts. This agent is particularly useful for scintigraphic analysis of the function of the salivary glands after irradiation. Salivary excretion of  $^{99m}\text{Tc}$ -pertechnetate can be induced by local stimulation (e.g., by ingestion of citric acid) or by parasympathetic stimulation (e.g., by subcutaneous administration of carbachol).<sup>13</sup>

By salivary scintigraphy, the major salivary glands can be examined noninvasively, simultaneously, and continuously over a period of time. This technique has gained widespread acceptance in evaluating a variety of salivary glandular disorder and its usefulness to evaluate salivary function after radiotherapy has been demonstrated in patients with head and neck malignancies.<sup>13</sup> In this study, we compared the salivary glandular scintigraphy results using  $^{99m}\text{Tc}$ -pertechnetate in a group of patients who had received conventional radiotherapy with group of patients receiving Intensity Modulated Radiotherapy.

A comparison of the EF% values for each patient, at baseline and post radiotherapy was done in both the arms. In the conventional arm about 62.5% (10 out of 16 patients) showed zero EF% post radiotherapy. In the IMRT arm, only one patient showed zero EF%. This shows that there is better salivary excretion function

when there is sparing of the parotid gland in the IMRT arm. For the change in relative saliva excretion rate before and after treatment, the fall in excretion fraction from baseline to post radiotherapy at 3months was analysed. The fall in salivary excretion fraction from baseline to post radiotherapy at 3 months was 45% in conventional arm whereas in IMRT arm is around 32%. It means the excretion percentage was better in the IMRT arm compared to the conventional arm.

Maria Golen et al. conducted a study where Pre- and post-treatment SEFs were measured in 31 patients treated by IMRT and in 9 patients treated by conventional RT. Salivary excretion fraction (SEF) was lower by 52% at six weeks and 35.5% at 6months in conventional arm vs. 34% at six weeks and 29.3% at six months in the IMRT arm.<sup>14</sup>

A similar study done by Tejpal Gupta et al at Tata memorial cancer institute where salivary excretion fraction percent was performed before and after receiving radiation.<sup>15</sup> It showed in IMRT patients the median SEF ratios (IQR) of the parotid glands were 25.7% at 3months, 38.2% at 12 months, 59.0% and 65.3% at 24-months indicating substantial recovery of salivary function over time, mostly within the first two years of follow up.<sup>15</sup> But in our study scintigraphy was performed only at first follow up at 3 months.

## CONCLUSION

Due its conformity, IMRT reduces the mean dose to bilateral parotid glands and related xerostomia. The subjective assessment of xerostomia through Quality of life questionnaire clearly showed better scores in IMRT arm than conventional arm. The objective assessment by quantitative salivary scintigraphy also clearly showed better salivary gland functioning in IMRT arm than conventional arm implying the usefulness of IMRT in head and neck cancer patients for sparing parotids and less xerostomia symptoms and better quality of life.

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# Prevalence of Extramural Uncinate Process and its Correlation with Sex: A Computed Tomographic Study

Sharma Shalini<sup>1</sup>, Tiwari Gopal<sup>2</sup>

## ABSTRACT

**Introduction:** Extramural uncinate process i.e pneumatization of uncinate process is the extension of the Agger nasi cell within the anterior and superior portion of the uncinate process. It is supposed to be related to osteomeatal obstruction, narrowing of the infundibulum and producing impaired sinus ventilation. The present study was conducted to observe the prevalence of pneumatization of uncinate process and its relationship with gender.

**Material and methods:** Computed tomographic (CT) images of sinonasal region (100 subjects; 62 males and 38 females) were obtained from the Department of Radiodiagnosis, King George's medical University, Lucknow, from the period Aug 2013 to July 2014. The CT scans were analyzed to determine the prevalence of pneumatization of uncinate process and its relationship with gender.

**Results:** Out of total 100 subjects studied, uncinate process pneumatization was found in 4% of study population which included proportionately higher number of male subjects (4.84%) than female subjects (2.63%). This difference was statistically insignificant ( $p=0.585$ ). Unilateral UP pneumatization was found in higher proportion of females (2.63%) as compared to males (1.61%) but this difference was not found to be statistically significant ( $p=0.724$ ). Bilateral Uncinate process pneumatization was found only in males (3.23%) and not in females insignificantly ( $p=0.263$ ).

**Conclusion:** In the present study prevalence of extramural uncinate process was observed to be high suggesting further work in this field to determine its correlation with pathological conditions of sino nasal region.

**Keywords:** Extramural, Uncinate process, pneumatization, computed tomographic images.

## INTRODUCTION

The lateral wall of the nasal cavity consists of an Osteomeatal complex (OMC) that includes maxillary sinus ostium, ethmoidal infundibulum, the Uncinate process (UP) and bulla ethmoidalis. Uncinate process is a thin semilunar piece of bone projecting downwards and backwards from the ethmoidal labyrinth.<sup>1-4</sup> Any anatomical variation or mucosal hypertrophy may cause stenosis of OMC causing obstruction and stagnation of secretions leading to chronic rhinosinusitis. One such variation is pneumatization of uncinate process that can cause narrowing and ventilatory impairment of osteomeatal complex resulting into pathological consequences for which uncinectomy becomes mandatory.<sup>2</sup>

The ethmoid bone is having two labyrinths filled with three air cell groups (anterior, middle, and posterior) that exhibits highly variable arrangement.<sup>5-8</sup> The extensions of these cells within the ethmoid complex are intramural, and extensions to the middle turbinate, superior turbinate, the uncinate process, agger nasi, sphenoid bone and orbital plate of the maxilla are extramural giving rise to anatomical variations like concha

bullosa, pneumatization of superior turbinate, pneumatization of the uncinate process, Agger nasi cells, Onodi cells, and Haller's cells respectively.<sup>9-12</sup> The extension of the Agger nasi cell within the anterior and superior portion of the uncinate process results in Pneumatization of uncinate process.<sup>13-15</sup> Aim of the present study was to analyze the overall prevalence of extramural uncinate process from coronal and axial CT scans and its correlation with sex.

## MATERIAL AND METHODS

Sinonasal computed tomographic images of 100 subjects (62 males and 38 females) were obtained from the Department of Radiodiagnosis, King George's Medical University (KGMU), Lucknow, from the period August 2013 to July 2014 and were analyzed for the presence of extramural uncinate process. Ethical clearance from the college ethical board and the informed consent from the patients was obtained before the start of the study.

All patients' males or females, 15 to 60 years of age, undergoing computed tomography of sinonasal region, in the Department of Radiodiagnosis, KGMU were included in the study. Any person with obscured or altered sinonasal anatomy due to inflammatory disease, previous surgery, facial trauma and paranasal sinus neoplasms. The observed variations were analyzed and noted.

### Method

Coronal sections were performed in a plane perpendicular to axial plane with the patient in prone position with extended neck. Axial sections were acquired in a plane parallel to the hard palate with the patient in supine position. The slice thickness was kept 5 mm, table feed 7 mm and pitch 1.4. Images were reconstructed at 4 mm intervals with an image overlap of 1 mm. We considered Pneumatization of the uncinate process as the extension of the agger nasi cell within the anterosuperior portion of the uncinate process. In coronal CT scan of the posterior sections the uncinate process can be visualized as a thin bone with a posterior free edge that is attached to the inferior turbinate inferiorly.

## STATISTICAL ANALYSIS

The comparison of extramural uncinate process and its association concerning the gender was conducted using the

<sup>1</sup>Assistant Professor, Department of Anatomy, <sup>2</sup>Assistant Professor, Department of Orthopaedics, RMCH, Bareilly, U.P, India

**Corresponding author:** Dr. Shalini Sharma, 62, Faculty Residence, Rohilkhand Medical College and Hospital, Pilibhit Bypass Road, Bareilly, U.P, India

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Chi square statistical test with Statistical Program for Social Science (SPSS) version 16.0. A p-value < 0.05 was considered statistically significant.

## RESULTS

Majority of female and male subjects i.e 97.37% and 95.16% respectively did not show any uncinate process pneumatization (Extramural Uncinate process cells). Uncinate process pneumatization was found in 4% of study population which included proportionately higher number of male subjects (4.84%) than female subjects (2.63%). This difference was statistically insignificant ( $p=0.585$ ). Both bilateral as well as unilateral of extramural uncinate process cells were seen during the course of study. Unilateral UP pneumatization (Figure-2a) was found in higher proportion of females (2.63%) as compared to males (1.61%) but this difference was not found to be statistically significant ( $p=0.724$ ). Bilateral Uncinate process pneumatization (Figure-2b) was found only in males (3.23%) and not in females and this difference was not found to be statistically significant ( $p=0.263$ ) (Table-1, Figure-1).

## DISCUSSION

The uncinate process is functionally essential for the proper ventilation and drainage of the nasal cavity and the sinuses rather than being just a vestigial remnant.<sup>3</sup> The reported prevalence of Pneumatization of uncinate process ranges from 7-10.9% in the literature.<sup>3,10,13,15-17</sup> The extension of the Agger nasi cell within the anterior and superior portion of the uncinate process results in Pneumatization of uncinate process.<sup>3</sup> In present study, Pneumatization of uncinate process was observed in 4 patients (4%) which is similar to that as was reported in Italian<sup>11</sup> population. Gupta<sup>2</sup> et al, reported a prevalence of 4.34% in Indian population. The prevalence was found to be low in Caucasian<sup>3</sup> and UK Population<sup>4</sup> (Table-2). Bolger<sup>3</sup> et al, report its prevalence as 2.5% in sinus patients and Kennedy and Zinreich<sup>16</sup> as 0.4% in non-sinus patients.

In consensus with the findings of Kayalioglu<sup>7</sup> et al, in the present study, it was also noted that, there was no statistically significant association of Pneumatization of uncinate process with gender.

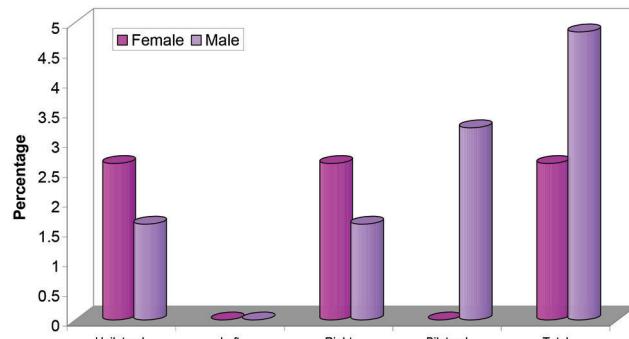
## CONCLUSION

In the present study prevalence of extramural uncinate process

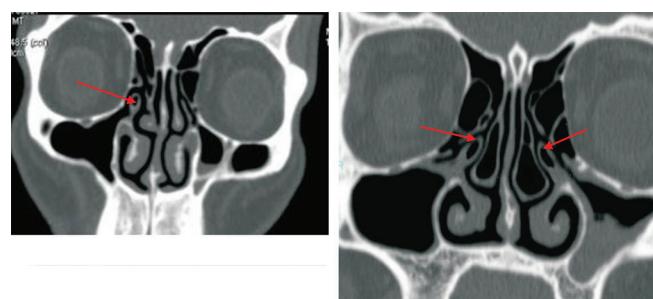
was observed to be high suggesting further work in this field to determine its correlation with pathological conditions of sino nasal region. Moreover, preoperative evaluation of variations of uncinate process and its pneumatization helps to avoid intraoperative damage to surrounding structures that alters normal ventilation.

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**Figure-1:** Bar diagram showing Genderwise comparison of prevalence of Uncinate process pneumatization.



**Figure-2a:** Coronal CT image showing unilateral extramural uncinate process (UP); **Figure-2b:** Coronal CT image showing bilateral extramural uncinate process

Extramural Uncinate process cells (UP pneumatization)	Females (n=38)		Males (n=62)		Statistical Significance	
	No.	%	No.	%	$\chi^2$	'p'
ABSENT	37	97.37	59	95.16		
PRESENT						
Unilateral	1	2.63	1	1.61	0.125	0.724
Bilateral	0	0.00	2	3.23	1.251	0.263
Total	1	2.63	3	4.84	0.299	0.585

**Table-1:** Genderwise comparison of Prevalence of extramural Uncinate process cells (UP pneumatization)

Author(year)	Population	N	Type of study	UP Pneumatization %
Bolger <sup>3</sup> et al. (1991)	Caucasian	202	CT	2.5
Badia <sup>4</sup> et al. (2005)	UK Population	200	CT	2
Mazza D <sup>11</sup> et al. (2007)	Italian	100	CT	5
Adeel <sup>1</sup> et al. (2012)	Pakistani	87	CT	5.2
K.Gupta <sup>2</sup> et al. (2012)	Indian	69	CT	4.34
Present Study (2014)	Indian	100	CT	4

**Table-2:** Prevalence of uncinate process (UP) pneumatization in different population.

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# A Study of Computer Vision Syndrome at the Workplace - Prevalence and Causative Factors

Soumya Harapanahalli Venkatesh<sup>1</sup>, Anita T Girish<sup>1</sup>, Shashikala<sup>2</sup>, Praveen Kulkarni<sup>3</sup>, Snigdha Mannava<sup>4</sup>, Rajendra Rajarathnam<sup>5</sup>

## ABSTRACT

**Introduction:** Computers are an essential part of our everyday life. More and more people are experiencing ocular and extra-ocular symptoms related to computer use – eyestrain, headache, blurred vision, dry eyes, neck/back ache – collectively known as Computer Vision Syndrome which is a widely spreading and largely unknown occupational hazard. Study aimed to determine the prevalence of symptoms, knowledge and practice of computer use in software professionals and to evaluate the association of various ergonomic factors with the occurrence of Computer Vision Syndrome.

**Material and methods:** Cross sectional study was conducted among the software professionals of a multinational company. Informed consent was obtained from the study subjects after inclusion criteria were met. Data was collected using a self-administered pre tested questionnaire. Data was analysed using SPSS version 22 program.

**Results:** The prevalence of vision related problems were reported by 83.5% of subjects in our study. Association of duration of computer use and visual symptoms was noted. Only 38.8% of them were aware of Computer Vision Syndrome. Symptoms were more in people who did not use anti-glare glasses.

**Conclusions:** Visual problems constitute an important part of computer vision syndrome. This warrants vigilance in identifying and effectively treating this condition. The study has also thrown light on various ergonomic factors contributing to its occurrence. Effective management requires a multidirectional approach combining health education, modification of ergonomics and appropriate ocular therapy.

**Keywords:** Asthenopia, Computer vision syndrome, Ergonomics, Health education, Software professionals

the most frequently reported health-related problems, occurring in over 70% of computer workers.<sup>4</sup> It is estimated that nearly 60 million people suffer from CVS globally, and that a million new cases occur each year.<sup>4</sup> Since personal computers are one of the commonest office tools used extensively, CVS will continue to cause significant and growing contribution to diminished productivity at work while also reducing the quality of life of a computer worker.

Many studies have been conducted in an attempt to address questions concerning safety and health for visual display terminal (VDT) users.

Reddy SC et al in 2013 studied the knowledge and practices of computer usage in university students in Malaysia.<sup>5</sup> Srivastava SR and Bobhate PS in 2012 analysed computer related health problems among software professionals in Mumbai, India.<sup>4</sup> Akinbinu and Mashalla assessed the knowledge of computer vision syndrome among computer users in Nigeria.<sup>1</sup>

This study aimed at determining the prevalence of CVS symptoms in software professionals, to assess the knowledge and practices of computer use in relation to CVS. The study also looked into the association between various ergonomic factors and occurrence of CVS.

## MATERIAL AND METHODS

### Study design and setting

A cross sectional study was carried out among the software professionals of a multinational software company at Mysuru, Karnataka in July 2014. Prior permission was obtained from the concerned authorities. Approval was obtained from the institutional ethics committee for conducting the study. Prior informed consent was obtained from the participants of the study.

### Methods of measurement

A research questionnaire was prepared after reviewing the articles available on computer vision syndrome. The questionnaire included demography details, knowledge about CVS, spectacle use, symptomatology, work practices, ergonomics

<sup>1</sup>Assistant Professor, <sup>4</sup>Intern, <sup>5</sup>Professor, Department of Ophthalmology,  
<sup>3</sup>Assistant Professor, Department of Community Medicine, JSS Medical College and Hospital, JSS University, <sup>2</sup>Faculty, Department of Community Medicine, Mysore Medical College and Research Institute, Mysore, Karnataka, India

**Corresponding author:** Soumya Harapanahalli Venkatesh, 1498/6A, 'Geeta', Ram Iyyer Road, Krishnamurthyapuram, Mysore- 570004, Karnataka, India

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and preventive measures taken. A pilot study was conducted and the questionnaire was edited for easy understanding by the subjects. Simple random sampling technique was used for subject selection.

Study included subjects who used computers since past 6 months and working on them for at least 3 hours/day in this study. Those who did not consent for the study were excluded.

## STATISTICAL ANALYSIS

Data entry and statistical analysis were done using SPSS version 22 program with the help of descriptive statistics like mean and percentages. Chi square test was used for comparison and calculating the p value.

## RESULTS

291 participants were included in this study. Out of them 182 (62.5%) were males and 109 (37.5%) were females. Table-1 shows the presence of symptoms of CVS according to gender. Females had more disturbing symptoms than males. The mean age of the study subjects was 26.6 (6.3) years with the majority of population between 25-29. Among all study participants, the eldest person was 49 years. Male to female ratio was 1.6:1. 243 (83.5%) out of 291 subjects had one or more complaints suggestive of CVS. 79.5% (116) subjects complained of symptoms suggestive of CVS were in the 25-29 year age group. The most disturbing symptom was eye strain (53.9%). 37.8% of the study participants had been prescribed spectacles for distant vision, near vision or both. 28.4% of the subjects who did not use the prescribed spectacles regularly complained of CVS symptoms. 81.4% of subjects who had CVS symptoms did not use anti-glare coated glasses during computer use ( $P=0.05$ ). Only 27.5 % ( $P=0.01$ ) consulted an ophthalmologist for their symptoms. The most disturbing visual complaint was eyestrain

	CVS ( N= 243)	No CVS(N=48)	Total
Males	145(79.6%)	37(20.3%)	182
Females	98(89.9%)	11(10%)	109

Table-1: Gender and computer vision syndrome

Sl no	Symptoms	No of subjects	Percentage
1	Eye strain	157	53.9%
2	Headache	112	38.5%
3	Neck/shoulder/wrist ache	90	30.9%
4	Backache	83	28.5%
5	Dry/irritated eyes	66	22.7%

Table-2: Distribution of visual complaints among software professionals

(53.9%) followed by headache. Non ocular symptoms included neckache and backache (Table-2).

51.2% of the participants practiced one or more of the following measures during computer use: Taking regular breaks, looking at far-off objects in between work and use of eye drops.

## DISCUSSION

This study aimed at estimating the prevalence of CVS symptoms and studying the association of various ergonomic factors in relation to CVS among software professionals in a multinational company at Mysuru, Karnataka.

The prevalence of Computer Vision Syndrome in our study was 83.5% (243/291). The observation was on par with the results obtained by Lograj M et al, Talwar et al and Iwakiri et al who reported 80.3%, 76% and 72.1% respectively.<sup>7,8</sup>

Majority of the subjects (79.5%/116) were in the 25-29 year age group in our study. Talwar et al in their study found 58.5% of subjects being in the age group of 20-29 years.<sup>8</sup>

We found that females had more CVS symptoms than males which was similar to shantakumari et al who also reported higher symptoms in females.<sup>6</sup>

The difference in the prevalence rate of computer-related problems in various studies depend upon factors like knowledge and awareness levels, workstation set up, degree of immobilization and levels of constrained postures, and practices of workers regarding computer ergonomics.<sup>4</sup> Present study had statistical significance with few of the ergonomic factors with the occurrence of symptoms of computer vision syndrome (Table-3).

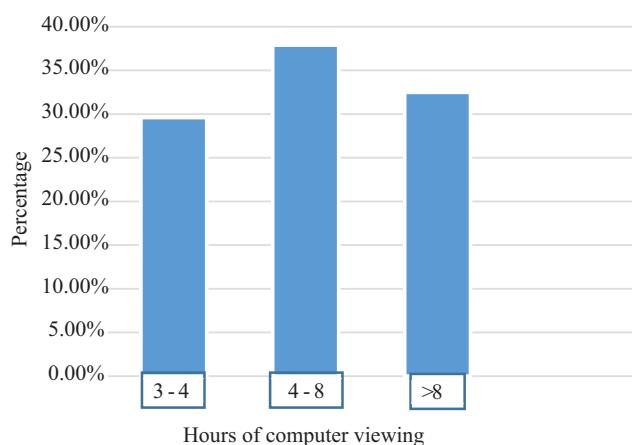
38.8% of study population were aware of CVS. Thus the knowledge of study subjects were assessed. Majority of the symptoms were in the 4-8 hour group. Association between hours of computer viewing and presence of CVS symptoms ( $P=0.08$ ) was observed (Figure-1).

The most disturbing symptom in our study was eye strain (53.9%) followed by headache (38.5%) similar to Shantakumari et al who also reported eye soreness (53.3%) as the common symptom.<sup>6</sup> Akinbinu and Mashalla also found eyestrain (30.9%) and headache (30.9%) as most disturbing complaint.<sup>1</sup>

Visual problems were found to be directly related to average computer hours per day. Our study found that majority of symptoms were in people who used computers 4-8 hours /day (36.8%) followed by subjects who used more than 8 hours/day (31.9%). The reduced number of symptoms in subjects using computers for more than 8 hours/day could be explained by some form of alternate mechanisms to prolonged exposure that happens resulting in reduced sensitivity and less response of the employee.<sup>1</sup> Lograj et al in their study also did not find

Factor	Response	CVS present n=243	CVS absent n=48	P value
Brightness of the room	Medium	194(82.2%)	42(87.5%)	0.391
Position of AC	Overhead	142(58.4%)	33(68.8%)	0.243
Adjustable chair height	Yes	188(77.4%)	38(79.2%)	0.784
Armrests at the level of desk	Yes	133(54.7%)	77(35.4%)	0.134
Position of hard copy	Below the screen	127(52.3%)	27(56.2%)	0.613
Viewing distance	25-30 inches	114(46.9%)	20(41.7%)	0.796
Anti-glare filter	Yes	74(30.4%)	21(43.7%)	0.07
Level of top of display screen	Equal to eye level	134(55.1%)	30(62.5%)	0.261

Table-3: Association of various ergonomic factors with the occurrence of CVS



**Figure-1:** Distribution of subjects based on hours of computer viewing.

statistically significant difference for the symptoms of CVS between those who used computers for more than 6 hours and less than 4 hours.<sup>4</sup>

37.8% of the study participants had been prescribed spectacles for distant vision, near vision or both. Only 28.4% of the subjects who did not use the prescribed spectacles complained of CVS symptoms. The rest of the subjects used spectacles and also had CVS symptoms. This is similar to Reddy SC et al and Logaraj et al (72.2%) who found statistically significant difference.<sup>5,7</sup>

73.1% of subjects who had CVS symptoms did not use antiglare screen during computer use ( $P=0.05$ ) in our study. This is similar to Talwar et al who found 85.2% having symptoms did not use antiglare filters.<sup>8</sup>

The viewing distance from the display screen was less than 25 inches for 34.7% of the participants. This is in concordance with Stella C et al where 26.2% subjects had a viewing distance less than 25 inches.<sup>9</sup>

178 (80.5%) out of 243 who had CVS symptoms did not use the prescribed medication regularly. ( $P=0.02$ ). Thus the practice of the subjects in preventing CVS were assessed.

However, our study did not find significant association between some of the ergonomic factors and CVS. The limitations of our study were small sample size, questionnaire based recording of symptoms which were assumed to be entirely due to computer use.

## CONCLUSION

Computers are an essential part of modern life. The exponential increase in their use have ushered in a new era of occupational hazard collectively known as computer vision syndrome. A variety of ergonomic factors like level of top of display screen, viewing distance from the screen, position of AC, brightness of the room, use of anti-glare filters, regular breaks, etc. play an important role in the development of this syndrome. Emphasis on proper computer ergonomics can go a long way in reducing the burden of visual problems. Despite its wide prevalence, CVS remains an underestimated and poorly defined issue at the workplace. Primary prevention lies in creating awareness and providing health education to the general public, health professionals, the government and private industries. Effective management of CVS requires a multidirectional approach combining health education, modification of ergonomics and

appropriate ocular therapy.

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# Evaluation of Various Treatment Modalities of Femoral Head Fractures

Irshad Ali Usmani<sup>1</sup>, R. S. Topwal<sup>2</sup>

## ABSTRACT

**Introduction:** The injuries involving the femoral head fractures are relatively uncommon but for the prevention of post-sequel complications like osteoarthritis, the treatment of such kind of fractures is of utmost importance. Less than 20 % of the cases of posterior hip dislocations have been observed to be associated with fractures of femoral head. Several cases have been published in the literature ever since the first description of a femoral head fracture, no firm conclusions have been reached regarding optimal treatment. Hence; we compared the various treatment modalities available for the treatment of femoral head fractures.

**Material and methods:** The present study included 26 patients of femoral head fractures who reported in the department of Orthopedics and Traumatology of the institution from June 2002 to July 2012. The patients were classified in accordance with Pipkin's proposal. Surgical treatment was performed in all cases. Analysis of the post-surgical results was done by performing separate assessment for clinical and radiological features separately. For the follow up purposes, cases that underwent total primary hip arthroplasty.

**Results:** 75% were males and 25% were females out of total 26 patients. The mean age of the patients was 34.5 years and ranged from 18 to 60 years. 47 % of the total cases were of type I while type 2 contained 24 % of the individuals according to Pipkin classification. Type 3 and 4 contained 14 % and 15 % individuals respectively. 12 out of the 26 patients showed excellent result when evaluated both clinically and radiographically according to Thompson and Epstein criteria.

**Conclusion:** Surgical treatment should be followed while treating femoral head fractures. Different personalities are presented by femoral head fractures and therefore the treating clinician must have the proper understanding of the pattern of the fracture on the basis of which, they should do the treatment planning.

**Keywords:** Femoral, Fracture, Treatment

## INTRODUCTION

Although the injuries involving the femoral head fractures are relatively uncommon; for the prevention of post-sequel complications like osteoarthritis, the treatment of such kind of fractures is of utmost importance. Less than 20 % of the cases of posterior hip dislocations have been observed to be associated with fractures of femoral head.<sup>1-3</sup> Inspite of publication of numerous case reports, ever since the first description of a femoral head fracture, no single point conclusion has been drawn in context to single line of treatment. Historically, poor functional outcomes have been found to be associated with these fracture patterns.<sup>4,5</sup> Hence; we compared the various treatment modalities available for the treatment of femoral head fractures.

## MATERIAL AND METHODS

In the department of Orthopedics and Traumatology of the institution, the present study was conducted and included all

the patients reporting from June 2002 to July 2012. In this study, cases of pressure fracture of the femoral head were not evaluated. A total of 26 patients were included for the present study. In relation to the side affected, 18 hips were on the right side and 8 on the left side. The etiology of the 26 fractures consisted of car accidental cause in 22 cases, train accident in 2 cases and falling from a height in 2 cases. Diagnosis of femoral head fractures was done by doing radiological assessment of all patients. Pipkin's classification protocol was used to classify patients in the present study.<sup>6</sup> Surgical treatment was performed in all cases. Treatment of 10 cases of type I fractures were managed by femoral head resection while internal fixation was used for treatment of type II fractures. Antero-lateral, lateral and posterior routes were used for assessing the lesions. Total hip arthroplasty was done in the other remaining cases since more than 2 months were already over ever since the time of trauma. Thompson and Epstein<sup>7</sup> criteria were used for analysis of the post-surgical results and were done by performing separate assessment for clinical and radiological features separately. Total hip arthroscopy was done in type three fracture patients. Follow-up of the cases was done upto 6 years. For the follow up purposes, cases that underwent total primary hip arthroplasty.

## RESULTS

Out of total 26 patients, 75% were males and 25% were females. The mean age of the patients was 34.5 years and ranged from 18 to 60 years. Table-1 shows the distribution of patient according to Pipkin classification. 47 % of the total cases were of type I while type 2 contained 24 % of the individuals. Type 3 and 4 contained 14 % and 15 % individuals respectively. Table-2 shows the distribution of patient according to the results. 12 out of the 26 patients showed excellent result when evaluated both clinically and radiographically according to Thompson and Epstein criteria.

## DISCUSSION

Hip position at the time of impact determines if the hip dislocates with or without fracturing the head and/or acetabulum. Dashboard is the most frequent cause of hip fracture<sup>8</sup>, in which the generally unrestrained driver or passenger hits his knee on the dashboard during a collision with the force of the impact being transmitted along the axis of the femur.<sup>9</sup> The association

<sup>1</sup>Professor and Head, <sup>2</sup>Assistant Professor, Department of Orthopaedics, Career Institute of Medical Science and Hospital, Iim Road, Lucknow, UP, India

**Corresponding author:** Irshad Ali Usmani, Professor and Head, Department of Orthopaedics, Caerer Medical College and Hospital, Lucknow, India

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Classification	Definition	Percentage of cases
Type 1	Fragment caudal to fovea	47
Type 2	Fragment cephalic to fovea	24
Type 3	Association of type 1 and type 2 with femoral neck fractures	14
Type 4	Association of type 1 or type 2 with acetabular fracture	15

**Table-1:** Distribution of patients according to Pipkin classification

Patient	Pipkin classification	Clinical/Radiographic results
1	1	Good/Good
2	1	Excellent/ Excellent
3	2	Regular/ Regular
4	3	PTA
5	3	PTA
6	1	Good/Good
7	1	Excellent/ Excellent
8	4	Poor/Poor
9	2	Excellent/ Excellent
10	1	Excellent/ Excellent
11	4	PTA
12	2	Excellent/ Excellent
13	1	Excellent/ Excellent
14	1	Good/Good
15	1	Excellent/ Excellent
16	2	Regular/ Regular
17	3	PTA
18	3	PTA
19	1	Good/Good
20	1	Excellent/ Excellent
21	4	Poor/Poor
22	2	Excellent/ Excellent
23	1	Excellent/ Excellent
24	4	PTA
25	2	Excellent/ Excellent
26	1	Excellent/ Excellent
PTA: Primary total arthroplasty		

**Table-2:** Patient distribution according to results

of femoral head fractures with hip dislocations has been reported to range from 4–17%.<sup>10-20</sup> Although still uncommon, the increase in high-speed traffic accidents and the improved resuscitation of the patients have resulted in a growing number of these fractures. Treatment protocols for femoral head fractures are difficult to establish because of their limited incidence and the different outcome classifications used in the literature. A review of the literature by Brumback et al<sup>21</sup> 15 years ago resulted in a total of 144 reported Pipkin cases. However, because of the lack of illustrations, radiographs, descriptions and follow-up, only 78 (54%) of these could be used in their analysis of outcomes. More recently, a similar difficulties encountered in the German review of literature.<sup>22</sup> In most of the published cases, posterior dislocation of hip joint is common in which femoral head fracture was occurred. Only a single case report is published in the literature which quotes fracture without hip dislocation<sup>23</sup> Along with some cases of dislocation of anterior hip portion.<sup>24-27</sup> The largest sample of the latter was reported by DeLee et al, consisting of 13 patients.<sup>28</sup> According to other authors, in cases of doubt, computed tomography should be

performed for deciding both diagnosis and treatment planning. Lack of uniform criteria for classifying the femoral head fractures, small number of sample size in the reported studies creates lots of difficulties while making comparison of different results of various studies.<sup>23,30</sup> In making the final analysis on the treatment, according to, Hougaard and Thomsen, cases which were painless and with absence of abnormal hip movements were categorized under good results.<sup>31</sup> Thompson and Epstein used the criteria which analyzed the clinical and radiographic factors separately. Keeping in view the results seen in our study, non-surgical mode of treatment should be followed while doing reduction in cases of hip dislocation. Greenwald and Haynes<sup>32</sup> demonstrated different approaches for treating type I and type II lesion of the fracture of femur. Results of treatment of a huge series of cases were reviewed by Kloen et al who highlighted the posterior hip dislocation cases. From the results, they concluded that better visualization and ability to internally fix these fractures could potentially improve the outcome. They also introduced a modified, anterolateral approach to femoral head fractures based on a digastrics trochanteric osteotomy.<sup>33</sup>

## CONCLUSION

From the above the results, it can be concluded that surgical treatment should be followed while treating femoral head fractures. Different personalities are presented by femoral head fractures and therefore the treating clinician must have the proper understanding of the pattern of the fracture on the basis of which, they should do the treatment planning.

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# Nasolabial Cyst- A Case Report of Rare Non-Odontogenic Cyst

A.G.S. Bawa<sup>1</sup>, Manpreet Kaur<sup>2</sup>

## ABSTRACT

**Introduction:** Nasolabial cyst is a rare nonodontogenic, soft-tissue lesion, embryonic in origin occurring in the nasolabial region and comprising approximately 0.6% of all jaw cysts. Most of time it is an asymptomatic deformity of face and rarely can result in nasal obstruction.

**Case Report:** In this paper, we describe a case of nasolabial cyst in a 45 year old female patient and discusses relevant considerations. For the removal of cyst, incision was given at the upper gingivolabial sulcus below the pyriform apertures followed by dissection.

**Conclusion:** There is one reported case of malignant degeneration of the cyst in the literature. So its surgical removal is important.

**Keywords:** Klestadt's cyst; Non-odontogenic cyst

## INTRODUCTION

Nasolabial cyst is a rare nonodontogenic, soft-tissue, developmental cyst occurring in the nasolabial region comprising approximately 0.6% of all jaw cysts.<sup>1</sup> Zuckerkandl first described this cyst in 1882, McBride reported the first case in 1892 and Brown-Kelly described it in greater detail in 1953.<sup>2</sup> There is still much debate about the origin of nasolabial cysts. It is considered to be originated due to the persistence of epithelial remnants from the nasolacrimal duct or from epithelial cells that retained within the mesenchyme after fusion of the nasal processes and the maxillary prominence during fetal life.<sup>3</sup> This cyst can occur in any age group, however they are very uncommon in patients younger than 10 years and are commonly observed in the 30 to 50 years age group.<sup>4</sup> Moreover, there is a strong female gender bias for nasolabial cysts, with female to male incidence ratio 3:1.<sup>5</sup> Here we present a case of nasolabial cyst in a 45 year old female patient.

## CASE REPORT

A 45 year old female patient came to Out Patient Department of ENT, GGSMC and H, Faridkot with complaints of a slowly enlarging asymptomatic swelling over right nasolabial area which elevated the ala and right sided nasal blockage which has progressively increased over time since one and half year. Patient was conscious, cooperative, well oriented to time, place and person. Vital signs were within normal range, pulse was 78/min, blood pressure was 120/90 mmHg, temperature was 98°F and respiratory rate was 24/min. Pallor, icterus, cyanosis, lymphadenopathy, oedema were not present. On palpation, there was a nontender, firm swelling which obliterated the right nasolabial fold, elevating the ala and the floor of the nose with nasal obstruction (figure-1). Computed tomography (CT) showed a soft-tissue density mass lesion in the region of right nasal cavity, preantral region of right maxilla with mild smooth scalloping in anteromedial aspect of right maxillary antrum (figure-2). Routine investigations were within normal limits. The cyst was excised by intraoral enucleation technique with a

sublabial approach. The upper gingivolabial sulcus was incised just below the pyriform apertures followed by dissection. A well-circumscribed cyst swelling superficial to bony floor of nose was removed, some portion of floor of nose that had adhered to the cyst was removed under general anaesthesia. Histopathology was consistent with diagnosis of Klestadt cyst.

## DISCUSSION

A nasolabial cyst presents as a smooth, mobile, soft-tissue mass between the upper lip and nasal aperture, producing protrusion of the upper lip, elevation of the nasal ala and inferior turbinate, and effacement of the nasolabial fold.<sup>6</sup> In the present case, firm swelling which obliterated the right nasolabial fold, elevating the ala and the floor of the nose with nasal obstruction. Nasolabial cysts are sometimes asymptomatic unless they become infected or are associated with facial deformity. It is manifested by swelling and nasal obstruction base implantation of nasal wing. Pain is an unusual sign signifying infection.<sup>6</sup> In the present case lesion was slowly enlarging asymptomatic swelling over right nasolabial area which elevated the ala and right sided nasal blockage which has progressively increased over time since one and half year.

The lesion is submucosal and extraosseous, it expands via the gingivobuccal sulcus and expands all the soft-tissues outwards.<sup>7</sup> Despite the fact that they are soft tissue cysts and are situated extra-osseously, they can at times cause bone destruction.<sup>8</sup> Although developmental in origin, clinical manifestations do not appear until adulthood. The nasolabial cyst is also called as Klestadt's cyst, nasoalveolar cyst, mucoid cyst of the nose and nasal vestibular cyst.<sup>7</sup>

Nasolabial cyst usually presents as unilateral with bilateral incidence in about 10% of patients and is more commonly located on left side of the jaw. The present case reports lesion on the right side of the jaw.<sup>9</sup>

Radiographs can reveal this soft tissue lesion only after significant maxillary bone erosion. However magnetic resonance imaging (MRI) and computed tomography (CT), detects the cystic characteristics of these lesions with greater detail and reliability, bone involvement and their location in relation to the nasal alae and the maxillary bone, which assists the diagnosis.<sup>10</sup> In the present case, Computed tomography (CT) demonstrated a soft-tissue density mass in the region of right nasal cavity, preantral region of right maxilla with mild smooth scalloping margins in the anteromedial aspect of right maxillary antrum. Computerized tomography provides a high contrast

<sup>1</sup>Associate Professor, <sup>2</sup>Post Graduate Student, Department of ENT, GGS Medical College and Hospital Faridkot Punjab, India

**Corresponding author:** A.G.S. Bawa, Associate Professor, Department of ENT, GGS Medical College and Hospital, Faridkot, Punjab, India

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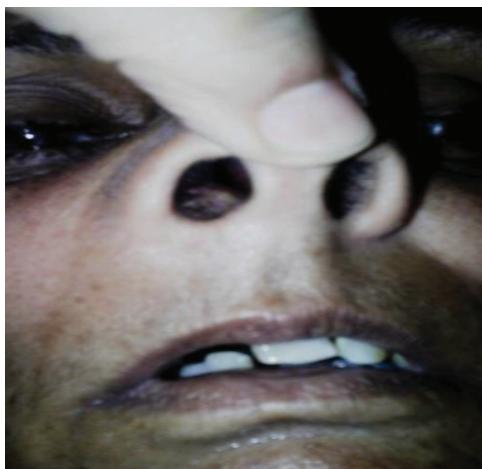


Figure-1: Clinical picture



Figure-2: CT scan

resolution along with good bone and soft tissue definition. CT is preferable to MRI because of its lower cost for the diagnosis of suspected case of nasolabial cyst.<sup>11</sup>

The differential diagnosis of nasolabial cysts consists of various lesions presenting similar location that includes cystic lesions which consists mucous retention cyst, dermoid, epidermoid cyst and oral heterotopic gastrointestinal cyst; various jaw bone lesions with cortical perforation such as nasopalatine duct cyst, radicular cyst, dentigerous cyst and glandular odontogenic cyst.<sup>4</sup> The histopathology of this lesion was first described by Brown-Kelly in 1898. The cyst comprises of respiratory epithelium (stratified ciliated cylindrical or pseudostratified ciliated cylindrical epithelium with goblet cells), however squamous metaplasia may occur in infected cysts. Fluid present within cysts is produced by goblet cells.<sup>10</sup> The final diagnosis in the present case was confirmed by the histopathological examination.

The common method of treatment is surgical excision using intraoral sub-labial technique, even though care must be considered to avert perforation or collapse of the cyst. The surgical outcome of this method is usually successful; though, complications associated with this procedure include gingival numbness, facial swelling, decreased sensation of the teeth, and wound infection. An alternative method of treatment is transnasal approach that allows endoscopic marsupialization of the cystic cavity.<sup>12,13</sup>

## CONCLUSION

The clinico-radiographic and histological characteristics of the present case were suggestive of nasolabial cyst. The intraoral enucleation technique with a sublabial approach was used to excise the cyst. Incision was given at the upper gingivobuccal sulcus below the pyriform apertures followed by dissection. There is one reported case of malignant degeneration of the cyst in the literature. So its surgical removal is important.

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# A Study of Clinical and Laboratory Profile of Dengue Fever in a Tertiary Care Hospital, Nizamabad, Telangana State, India

Md. Yousuf Khan<sup>1</sup>, C. Venkateshwarlu<sup>2</sup>, N. Sandeep<sup>3</sup>, A Hari Krishna<sup>4</sup>

## ABSTRACT

**Introduction** Dengue is a mosquito-borne viral disease that has rapidly spread in all regions. The global incidence of dengue has grown dramatically in recent decades. About half of the world's population is now at risk. So the present study was done to analyse varied clinical and laboratory profile of confirmed Dengue IgM antibody positive adult patients admitted at Government General Hospital, Nizamabad.

**Materials and Methods:** Prospective observational study was undertaken among 150 adult IgM Dengue Antibody positive cases admitted. All Patients were evaluated clinically and subjected for relevant laboratory investigations and were followed up daily till they were discharged.

**Results:** In our study, male to female ratio was 1.67:1. Most common symptom followed by headache 115 (76.77%). Bleeding manifestations occurred in 29 (19.33%) patients, of whom malena 13 (44.82%) was the most frequent. Skin rash mainly maculopapular and diffuse flushing were noted in 44 (29.33%). The tourniquet test was positive in 28 (18.66%) patients. Isolated hepatomegaly and splenomegaly was found in 19 (12.66%) and 23 (15.33%) respectively. Ascites and plural effusion was found in 22 (14.66%) and 17 (11.33%) patients respectively. There were 21 (14.00%) cases of dengue with DHF / DSS. 25 (16.66%) had complications of which most common was hepatic dysfunction 17 (11.33%) followed by hypotension 11 (7.33%) and renal failure 7 (4.66%). Raised haematocrit (>45%) was found in 35 (23.33%) and leukopenia (<4000/cmm) was found in 58 (38.66%) patients. Thrombocytopenia was observed in all the patients with varying severity, severe (<20000/cmm) was observed. Raised Serum bilirubin (>2mg%) was observed in 17 (11.33%).

**Conclusion:** Younger age group commonly presented with classical dengue fever promptly responded to conservative therapy as a result of an early confirmation of diagnosis and early institution of therapy.

**Keywords:** Flavivirus, Dengue fever, Dengue Haemorrhagic Fever, Clinical Profile.

## INTRODUCTION

Dengue fever is caused by Infection with one of the four serotypes of Dengue virus (DENV) which is an arthropod born single stranded RNA virus of genus Flavivirus.<sup>1</sup> It is comprised of four closely related but antigenically distinct serotypes, DENV1, DENV2, DENV3, and DENV4. Infection with one dengue serotype confers lifelong homotypic immunity to that serotype and a very brief period of partial heterotypic immunity to other serotypes, but a person can eventually be infected by all four serotypes.<sup>2</sup> All 4 serotypes have been isolated in India, DENV1, DENV2 serotypes are widespread.<sup>3</sup> Dengue is transmitted by mosquitoes of the genus Aedes, principally Aedes aegypti. The seasonal transmission of dengue is common in monsoon and post monsoon period.

Initially dengue infection may be asymptomatic (50-90%)<sup>4</sup>,

may result in a nonspecific febrile illness or may produce the symptom complex of classic dengue fever(DF). Classic dengue fever is marked by a rapid onset of high fever, headache, retro-orbital pain, diffuse body pain (both muscle and bone), weakness, vomiting, sore throat, altered taste sensation and a centrifugal maculopapular rash. The illness caused by DENV infection manifest either as classical dengue fever or severe dengue(Dengue Haemorrhagic fever/Dengue shock syndrome) which includes severe plasma leakage with severe haemorrhage and severe organ impairment.

Globally 2.5 - 3 Billon individuals lives in approximately 112 countries that experience dengue transmission. Annually, approximately 50-100 million individuals are infected. Currently close to 70% of global population exposed to dengue are in Asia Pacific region.<sup>5</sup> In India the incidence has increased due to deficient water management, unplanned urbanization and migration of population to urban areas. Although initially reported from urban areas, dengue is now being reported from urban and rural areas alike.

In India dengue virus was isolated for the first time in 1945, first evidence of occurrence of dengue fever was reported in 1956 from Vellore district of Tamil Nadu and the first dengue haemorrhagic fever outbreak occurred in Calcutta(WB) in 1963. Outbreaks are now reported quite frequently from different parts of our country. In last decades major outbreaks and deaths are occurred in Northern India (Haryana, Punjab, UP), Southern India (Andhra Pradesh, Tamil Nadu, Karnataka), Western India (Gujarat, Rajasthan) and Eastern India (West Bengal). The case fatality has increased to above 1% in last ten years.<sup>6</sup> Dengue is endemic in 31 states/UTs. During 2013 about 74168 cases were reported with 168 deaths, the highest number of cases were reported from Punjab followed by Tamil Nadu, Gujarat, Kerala and Andhra Pradesh<sup>7</sup>

At present very few studies have been conducted in this part of our country. As also exact clinical and laboratory profile is important for diagnosis and successful management thus crucial for saving life, hence this study was undertaken to analyse varied clinical and laboratory profile of serologically confirmed

<sup>1</sup>Assistant Professor, <sup>2</sup>Associate Professor, <sup>3</sup>Senior Resident, <sup>4</sup>Junior Resident, Department of General Medicine, Government Medical College and Government General Hospital, Nizamabad-503001, Telangana State, India.

**Corresponding author:** Dr.Md. Yousuf Khan, Assistant Professor of General Medicine, Government Medical College, Government General Hospital, Nizamabad-503001, Telangana State, India.

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(Dengue IgM antibody positive) adult patients admitted at Government General Hospital, Nizamabad during the period of August to December 2015.

## MATERIAL AND METHODS

This hospital based prospective study was performed at Govt. General Hospital, Nizamabad (Tertiary Care Hospital) in Telangana State, over a period of 5 months from August - December 2015. 150 Adult IgM Dengue antibody positive cases were enrolled for this study who are admitted in hospital for treatment. Ethical clearance was obtained from institute and also informed consent was taken from patient.

### Inclusion criteria

1. Patients of both sexes of age more than or equal to 12 years, who were willing for admissions and who were positive for Dengue IgM antibody by ELISA.

### Exclusion criteria

1. Patients of less than 12 years of age, tested negative for dengue IgM antibody by ELISA or who were not willing for admission.

2. Patient with concomitant malaria, typhoid, leptospirosis.

The diagnosis of dengue fever, dengue haemorrhagic fever and dengue shock syndrome was based on WHO criteria.

Dengue haemorrhagic fever (DHF) is defined as an acute febrile illness with minor, major bleeding, thrombocytopenia (platelet count <1 lac/cmm), and evidence of plasma leakage documented by haemoconcentration (Haematocrit increased by at least one-fifth or decreased by the same amount after intravenous fluid therapy), plural or other effusions, or hypoalbuminaemia or hypoprotinaemia. Dengue Shock Syndrome(DSS) is defined as DHF with signs of circulatory failure, including narrow pulse pressure (20mm Hg), hypotension, or Frank shock.<sup>8</sup>

All patients were evaluated clinically by taking history and thorough physical examination. Laboratory investigation done were haemoglobin%, TLC, DLC, Platelet count, Haematocrit, Liver function test, Blood urea, serum creatinine, blood sugars, ECG, Chest X-ray and USG Abdomen. Blood counts were monitored periodically as and when required. Other differential diagnosis were excluded by appropriate tests. IgM dengue antibody was estimated using dengue IgM capture ELISA, a solid phase immunoassay based on an immunocapture principle. Data collected was analysed and compared with available studies.

## STATISTICAL ANALYSIS

Statistical analysis was done with the data with the help of the descriptive statistics. SPSS version 21 was used for statistical analysis.

## RESULTS

Total number of the patients were 150, of whom 94(62.66%) were male and 56 (37.33%) were female (Table-1).

150 Adult dengue IgM antibody positive dengue fever patients admitted to medical wards over 5 months period from August - December 2015 were selected for this study. Most of the dengue cases were admitted during the month of September to November indicating clustering of cases during monsoon and post-monsoon period.

Of total 150, 94 (62.66%) were male and 56 (37.33%) were

female, the maximum number of patients belong to the age group 21-40 years, 89 (59.33%) followed by 12-20 years, 33 (22%) (Table-1).

### Clinical Features

The mean duration of the symptoms was 5 days. The average duration of stay of the patient in the hospital was 7-10 days. Fever was documented in all 150 (100%) patients, the most common symptom followed by headache 115 (76.77%), myalgia 108 (72%), abdominal pain 63 (42%), vomiting 35 (23.33%), sore throat 32 (21.33%), Retro-orbital pain 30 (20%) and Pruritus 19 (12.66%) (Table-2). Bleeding manifestations occurred in 29 (19.33%) patients, of whom malena 13 (44.82%) was the most frequent followed by venae Puncture bleed 9 (31.03%), epistaxis 5 (17.24%) and gum bleeding 5 (17.24%). Petechiae 4 (13.79%), Ecchymosis 3 (10.34%), haematuria 3 (10.34%) and hematemesis 2 (6.89%) were less common (Table-2). Bleeding manifestations were more likely with lower platelet counts, 12 patients has more than one bleeding manifestations. Skin rash mainly maculopapular and diffuse flushing were noted in 44 (29.33%), Jaundice was observed in 14 (9.33%) and bradycardia (Heart rate <60/min) was noted in 17 (11.33%) (Table-2). Most of the patients have sinus bradycardia. Tourniquet test

Age (yrs)	Male	Female	Total	%
12-20	21	12	33	22
21-40	56	33	89	59.33
41-60	13	8	21	14
>60	4	3	7	4.66
Total	94(62.66%)	56(37.33%)	150	100

Table-1: Age and sex distribution(n = 150)

Clinical Features	No Of Patients (%)
Fever	150(100%)
Headache	115(76.77%)
Retro-Orbital Pain	30(20%)
Myalgia	108(72%)
Arthralgia	31(20.66%)
Nausea/Vomiting	35(23.33%)
Abdominal Pain	63(42%)
Diarrhoea	15(10%)
Coryza/Sore Throat	32(21.33%)
Breathlessness	15(10%)
Pruritus	19(12.66%)
Insomnia/Lethargy	9(6%)
Bleeding Manifestations:	29(19.33%)
Gum Bleeding	5(17.24%)
Epistaxis	5(17.24%)
Haemoptysis	1(3.44%)
Hematemesis	2(6.89%)
Malena	13(44.82%)
Haematuria	3(10.34%)
Venae Puncture Bleed	9(31.03%)
P/V Bleed	3(10.34%)
Petechiae	4(13.79%)
Ecchymosis	3(10.34%)
Skin Rash	44(29.33%)
Bradycardia	17(11.33%)
Jaundice	14(9.33%)
Positive Tourniquet Test	28(18.66%)

Table-2: Distribution of clinical features of dengue fever cases

was positive in 28 (18.66%) (Table-2), test was positive more commonly among young male patients. Isolated hepatomegaly and splenomegaly was found in 19 (12.66%) and 23 (15.33%) respectively while hepatosplenomegaly was found in 12 (8%). Ascites and Plural effusion was found in 22 (14.66%) and 17 (11.33%) patients respectively. While both pleural effusion and ascites were found in 7 (4.66%) patients, 10 (6.66%) patient had gall bladder oedema (Table-3).

There were 21 (14.00%) cases of dengue with DHF / DSS among 150 (100%) as per WHO case definition. 25 (16.66%) had complications of which most common was hepatic dysfunction 17 (11.33%) followed by hypotension 11 (7.33%) and renal failure 7 (4.66%) (Table-4), 14 patient had more than one complications.

### Laboratory Parameters

Among haematological parameters, raised haematocrit (>45%) was found in 35 (23.33%) and leukopenia (<4000/cmm) was found in 58 (38.66%) patients. Thrombocytopenia was observed in all the patients with varying severity, severe (<20000/cmm) was observed in 23 (15.33%) patients while moderate (20000-50000/cmm) in 62 (41.33) patients (Table-2). Platelet count at presentation was <50000 in about 56.66% of the patients though it kept falling further during hospitalisation. Minimum platelet count noted was 9000/cmm. Among biochemical parameters, raised serum bilirubin (>2mg%) was observed in 17 (11.33%) while raised SGOT (>45 IU/L), raised SGPT (>45 IU/L) were observed in 61 (40.66%) and 42 (28%) respectively, 7 (4.66%) patients had raised serum creatinine (>1.5mg/dl) (Table-5). All patients were managed conservatively with IV fluids, antibiotics and antipyretics. Platelet transfusion was reserved for patients with active bleeding or prophylactically at a count of <10000/cmm.

### DISCUSSION

Dengue is emerging as a major health problem in India, regular outbreaks of dengue infection have been occurring throughout India with more number of deaths.

In our study, male to female ratio was 1.67:1, similar pattern of male preponderance was found in previous studies conducted by Seema Avasthi et al<sup>9</sup>; Karolie et al<sup>10</sup> Malavige et al, Sri Lanka<sup>11</sup> and G Lepakshi et al.<sup>12</sup> Fever was the most common presentation (100%) which is in unison with most of the studies from India<sup>12-17</sup> and South East Asia.<sup>18-20</sup> Headache was found in 76.77% of the patients which is similar to the most of the previous studies<sup>10,12,14,20</sup>; however study conducted by Munde D et al<sup>17</sup> showed lower incidence of 25%. Myalgia was noted in 72% of the patients which is comparable with previous studies conducted<sup>15,24</sup>, however study conducted by Mohamed Murtuza Kauser et al<sup>14</sup> showed lower incidence (32.87%). Abdominal pain was found in 63% of the patients which correlates with the previous studies<sup>10,20</sup>; however Studies conducted by Ragini Singh et al<sup>21</sup> and Munde et al<sup>17</sup> showed slightly lower incidence of 3.6% and 15% respectively. In our study, 23.33% of the patients presented with vomiting comparable to 25% in study conducted by Munde et al<sup>17</sup>; however Rajesh Deshwal et al<sup>13</sup> and Ragini Singh et al<sup>21</sup> reported only 5.4% and 11.4% respectively. Sore-throat was noted in 21.33% of the patients in our study comparable to the studies of Ragini Singh et al<sup>21</sup> (18.6%); however study done by G Lepakshi et al<sup>12</sup> has noticed

Criteria	No of Patients (%)
Hepatomegaly	19(12.66%)
Splenomegaly	23(15.33%)
Ascites	22(14.66%)
Pleural Effusion	17(11.33%)
Gall Bladder Oedema	10(6.66%)
Both Pleural effusion and ascites	07(4.66%)
Hepato splenomegaly	12(18%)

Table-3: Ultrasonography Findings in dengue fever cases

Complication	No of Patients (%)
Renal Failure	7(4.66%)
Hypotension	11(7.33%)
Cholecystitis	0(0.00%)
ARDS	0(0.00%)
Encephalopathy	0(0.00%)
Multi-Organ Failure	01(0.66%)
Pneumonia	03(2.00%)
Hepatic dysfunction (14 Patient had more than one complications)	17(11.33%)

Table-4: Complications of dengue fever cases

Laboratory Parameters	No of Patients(%)
Haematocrit > 45%	35(23.33%)
Leukopenia <4000/cmm	58(38.66%)
Platelet Count <20000/cmm	23(15.33%)
20000-50000/cmm	62(41.33%)
50000-1 lakh/cmm	42(28%)
1-1.5Lakh/cmm	23(15.33%)
Serum Bilirubin >2mg%	17(11.33%)
SGOT(>45IU/L)	61(40.66%)
SGPT(>45 IU/L)	42(28%)
Serum Creatinine >1.5mg/dl	7(4.66%)

Table-5: Laboratory parameters of dengue fever cases (n=150)

in 50% and Rachel Daniel et al<sup>20</sup> has noted in only 5.2% of the patient. Retro-orbital pain was noticed in 20% of the patients in present study comparable to Rajesh Deshwal et al<sup>13</sup> (18.3%) and G Lepakshi et al<sup>15</sup> (14%); however study done by Nandini Chatterjee et al<sup>22</sup> had 90%. Pruritus was noticed in 12.66% similar to the previous studies<sup>13,21</sup>; however Mohamed Murtuza Kauser et al<sup>14</sup> has noticed in 2.73% only.

In present study bleeding manifestations occurred in 29 (19.33%) of whom malena was the most common symptom noticed in 44.82% of the patient, similar to the previous studies<sup>12,22</sup>; however studies done by Mohamed Murtuza Kauser et al<sup>14</sup> and Ashwin Kumar et al<sup>23</sup> has noticed only in 1.36 and 4.7% respectively, however our findings are in contrast to the findings of Horvath R et al<sup>24</sup> from Australia and Sharma et al<sup>25</sup> from India who had noticed in 63% and 69% respectively. Venaepuncture bleed was found in 31.03% comparable with G Lepakshi et al<sup>12</sup> (57.14%). Epistaxis was found in 17.24% similar to study G Lepakshi et al<sup>12</sup> (14.28%) and NP Singh et al<sup>26</sup> (14%); however studies of Mohamed Murtuza Kauser et al<sup>14</sup> and Ashwin Kumar et al<sup>23</sup> has noticed in only 2.73% and 2.6%. In present study gum bleeding was found in 17.24% similar to Malavige et al<sup>11</sup> from SriLanka (17%); however study done by G Lepakshi et al<sup>11</sup> showed higher (33.33%) and study by Mohamed Murtuza

Kauser et al<sup>14</sup> and Ashwin Kumar et al<sup>23</sup> showed lower 1.36% and 5.2% incidence respectively. Petechiae was found in 13.79% comparable to study done by Ashwin Kumar et al<sup>23</sup> (18%). Ecchymosis was found in 10.34%; however study done by Ashwin Kumar et al<sup>23</sup> showed 6.2%. Haematuria was noticed in 10.34%. Hematemesis was found in 6.87%; however study done by G Lepakshi et al<sup>12</sup> showed higher incidence (38.09%) and studies of Mohamed Murtuza Kauser et al<sup>14</sup> and Ashwin Kumar et al<sup>23</sup> showed lower incidence of 2.05% and 3.00% respectively. Skin rash was found in 29.33% similar to previous studies<sup>13,25,28</sup>; however studies done by Rajesh Deshwal et al<sup>13</sup> showed 66% and Basavaraj Raju et al<sup>16</sup> showed 69.5% however Ragini Singh et al<sup>21</sup> showed 15% and Rachel Daniel et al<sup>20</sup> showed 13.2% only.

In our study jaundice was observed in 9.33%; however Ragini Singh et al<sup>21</sup> noticed in 17.1%. Bradycardia was found in 11.33%; however Rachel Daniel et al<sup>20</sup> found in 16.8%. Tourniquet test was positive in 18.66% similar to study done by Rajesh Deshwal et al<sup>13</sup> (16.5%) and Vanamali D R et al<sup>27</sup> (20%); however slightly higher in Nandini Chatterjee et al<sup>22</sup> (31%) and Rachel Daniel et al<sup>20</sup> (33.7%).

In present study hepatomegaly was found in 12.66% comparable to the previous studies<sup>13,23,25</sup> in India, Thailand<sup>28,29,30</sup> and Australia<sup>25</sup>, while splenomegaly was found in 15.32% comparable to Rajesh Deshwal et al<sup>13</sup> (13.2%) and G Lepakshi et al<sup>12</sup> (18%). Combined hepatosplenomegaly was found in 12.8%.

In present study ascites was found in 14.66% similar to studies by Rajesh Deshwal et al<sup>13</sup> (16.33%), Nandini Chatterjee et al<sup>22</sup> (17.7%) and Rachel Daniel et al<sup>20</sup> (12%); however study conducted by Ragini Singh et al<sup>21</sup>, G Lepakshi et al<sup>12</sup>, Sanjay Kumar Mandal et al<sup>15</sup> noticed in 38.6%, 22% and 8.1% respectively. Pleural effusion was found in 11.33% similar to Mohamed Murtuza Kauser et al<sup>14</sup> (13.69%) and Rachel Daniel et al<sup>20</sup> (13.2%); however studies done by G Lepakshi et al<sup>12</sup> (18.91%), Sanjay Kumar Mandal et al<sup>15</sup> (18.9%), Rajesh Deshwal et al<sup>13</sup> (20%) showed slightly higher incidence. Both ascites and Pleural effusion was noticed in 4.66%.

DHF/DSS found in 14% similar to Vanamali D R et al<sup>27</sup> (12.6%) and Sharma et al<sup>25</sup> (13.5%). The most common complication noticed was hepatic dysfunction found in 17(11, 33%)

Raised haematocrit(>45%) was found in 23.33% comparable to previous studies.<sup>12,13,15,20</sup> Leukopenia (<4000/cmm) was noticed in 38.66% comparable to previous studies<sup>16,23,25</sup>; however studies done by Munde et al<sup>17</sup> and Ritu Karolis et al<sup>10</sup> noticed in 50% and 89% respectively. Platelet Count <50000/cmm noticed in 56.66% similar to previous studies<sup>13,20</sup>, however Munde et al<sup>17</sup> found in 75% and Karolie et al<sup>10</sup> found in 89%.

Raised bilirubin (>2mg/dl) was seen in 11.3%, Raised SGOT(>45 IU/L) was found in 40.66% comparable with previous study Vanamali D R et al<sup>27</sup>; however Rajesh Deshwal et al<sup>13</sup>, Nandini Chatterjee et al<sup>22</sup>, Ragini Singh et al<sup>18</sup> found in 88.54%, 72% and 50% respectively, similarly Ritu Karoli et al<sup>10</sup> and Rachel Daniel et al<sup>20</sup> found in 92% and 83.9% respectively.

Raised SGPT(>45IU/L) was found in 28% similar to the previous studies Vanamali D R et al<sup>27</sup> (23%). Raised serum creatinine(>1.5mg/dl) was found in 4.66% similar to Mohamed Murtuza Kauser et al<sup>14</sup> (1.36%).

No deaths were present in our study which indicates prompt

diagnosis and early management, creating significant changes in prognosis.

## CONCLUSION

The current outbreak of dengue fever was predominantly affecting the male younger age group people mostly a febrile illness with headache and myalgia, GIT Symptoms and mild to moderate bleeding tendencies. Proper confirmation of diagnosis, early institution of therapy lead to prompt response to conservative treatment with no fatality rate.

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# Study on Prevalence of Anemia among Pregnant Women attending Antenatal Clinic at Rural Health Training Centre (RHTC) and Chalmeda Anand Rao Institute of Medical Sciences Teaching Hospital, Karimnagar, Telangana, India

Rajamouli J<sup>1</sup>, Ravinder A<sup>2</sup>, SCK Reddy<sup>1</sup>, Sujatha Pambi<sup>3</sup>

## ABSTRACT

**Introduction:** Anemia is the nutritional deficiency disorder and 56% of all women living in developing countries are anaemic (World Health Organization). It is the second most cause In India and 20% of total maternal deaths are due to anemia. Aims and Objectives: 1. To study the prevalence of anaemia in rural pregnant women. 2. To study the factors associated with anemia.

**Material and Methods:** The study was conducted on pregnant women, attending the Maternity Clinic of Rural Health training Centre and teaching hospital of Chalmeda Anand Rao Institute of Medical Sciences Karimnagar Telangana, India. **Study period** is one year from 1<sup>st</sup> October- 2014 to 30th September 2015. Anemia was classified as per the World Health Organization criteria. The Participants were 269, interviewed by using a pre- structured and pretested questionnaire. Inclusion criteria: The study subjects age <20 years to 30 and > 30 years. We have also observed the anemia in 1<sup>st</sup>, 2<sup>nd</sup> & 3<sup>rd</sup> trimester. Exclusion criteria: Recently blood transfused, chronic renal disease and ante partum hemorrhage were excluded. The diagnosis of anemia was undertaken by peripheral blood smear examination and standard hemoglobin estimation by shale's method.

**Results:** Among 269 subjects, the prevalence of anemia is 58.36% including mild, moderate & severe anemia. Highly significant factors association was found with the mother's age, education, socio-economic status, parity and dietary habits. Other factors like family structure, size and attainment of menarche were not significantly associated with anemia.

**Conclusion:** High prevalence of anemia (58.36%) indicates strict implementation of National Nutrition Anemia prophylaxis programme.

**Key Words:** Pregnancy, Anemia, Rural.

## INTRODUCTION

Anemia during pregnancy is a major public health problem throughout the world, particularly the developing countries. Anemia refers to a condition in which the hemoglobin (Hb) content of the blood is lower than normal for a person's age, gender and environment, resulting in the oxygen carrying capacity of the blood being reduced.<sup>1,2</sup> During the pregnancy plasma volume expands (maximum around 32 weeks) resulting in haemoglobin dilution. For this reason, haemoglobin level below 10gm/dl at any time during pregnancy is considered anaemia. Hb level at below 9gm/dl requires detailed investigation and appropriate treatment.

The main causes of anemia in developing countries include: inadequate intake and poor absorption of iron, malaria, hookworm infestation, diarrhoea, HIV/AIDS, genetic disorders(e.g., sickle cell anaemia and thalassemia), blood loss during labor and closely

spaced pregnancies.<sup>1,2</sup> The pregnant women suffering from Iron deficiency anemia are with associated risk, born babies with low birth weight, preterm delivery, increased peri-natal and neonatal mortality.<sup>3-5</sup> In another analysis, iron deficiency anemia (IDA) was an underlying risk factor for maternal and perinatal mortality and morbidity.<sup>6</sup>

The ministry of Health, Government of India has recommended intake of 100mg of elemental iron with 500 mcg folic acid tablets in second half of the pregnancy for a period of at least 100 days. In the World Health Organization (WHO) / World Bank rankings, IDA is the third leading cause of disability-adjusted life years lost for females aged 15–44years.<sup>1,7</sup> In 1993, the World Health Organization instituted its Safe Motherhood Initiative with a goal of reducing the number of maternal deaths by half before the year 2000.<sup>8</sup> In India, anemia is the second most common cause and accounting for 20% of total maternal deaths.<sup>9</sup>

The prevalence of anemia ranges from 33% to 89% among pregnant women and is more than women from 60% among adolescent girls with wide variations in different regions of the country.<sup>10</sup> The study shows that Pregnant women in rural Maharashtra, one of the developed states of India registered a prevalence of anemia 56.4%.<sup>11</sup>

1970 National Nutritional Anemia Prophylaxis Programme (NNAPP) was initiated in India, with the aim to reduce the prevalence of anemia to 25 percent.<sup>12</sup> Since 1992, the daily dosage of elemental iron for prophylaxis and therapy has been increased to 100 mg and 200 mg, respectively under Child Survival and Safe Motherhood (CSSM) Programme.

The present cross sectional study was designed to estimate the haemoglobin levels in pregnant women attending at Rural Health Training Centre (RHTC) Annaram and teaching hospital CAIMS Karimnagar revealed 58.33%. In developed countries Prevalence of anemia in pregnancy 2-45%. Global prevalence

<sup>1</sup>Associate Professor, <sup>2</sup>Assistant Professor/Statistician, <sup>3</sup>Assistant Professor, Department of Community Medicine, CAIMS, Karimnagar, Telangana, India

**Corresponding author:** Dr. Rajamouli J, MD (Community Medicine), Associate Professor, Department of Community Medicine, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar-505001, Telangana, India.

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of anemia among pregnant women is 55.9% (WHO) and higher in developing countries (5-90%). In India prevalence of anemia has been reported to be in the range of 33%-89%.

#### Aims and objectives

- To study the prevalence of anemia among pregnant women in RHTC Annaram & CAIMS teaching Hospital Karimnagar.
- To study the various factors influencing among the anaemic groups.

#### MATERIAL AND METHODS

The Cross sectional study was conducted on the pregnant women attending in the Anti-natal Clinic in Rural Health Training Centre Annaram, and Obstetric clinic at teaching hospital CAIMS, Karimnagar. Total sample of study subject was 269 pregnant women, interviewed by using 29 Pre designed and pre tested questionnaire, including prime gravida, second gravida and > second gravida. We have used purposive sampling technique to select the sample.

**Inclusion criteria:** The study subjects age of less than 20 years to 30 and > 30 years. We had also observed the anaemia in 1<sup>st</sup>, 2<sup>nd</sup> & 3<sup>rd</sup> trimester.

**Exclusion criteria:** In our study group recently blood transfused, who had chronic medical diseases, diagnosed haemo-globinopathies, and bleeding disorders or ante partum

haemorrhage were excluded. The diagnosis of anaemia was estimated by using the standard peripheral blood smear examination and shale's acid haematin method of Haemoglobin estimation.

**Study period:** 1 year i.e.: from 1<sup>st</sup> October- 2014 to 30th September 2015. Anaemia was classified as per the World Health Organization (WHO) grading criteria is taken to be 11 g/dL. WHO further divides anaemia in pregnancy in to mild anaemia (haemoglobin 10-10.9 g/dl), moderate anaemia (haemoglobin 7.0-9.9 g/dl) and severe anemia (haemoglobin <7 g/dL).

#### STATISTICAL ANALYSIS

Data were analyzed using SPSS version 17.0 and chi square test for categorical data were performed. P<0.05 was considered statistically significant.

#### RESULTS

The total study subjects were 269 pregnant women. Among them 157 pregnant women (58.36%) suffered with mild, moderate and severe anemia. Table-1 shows 77.3% of pregnant women were 20-29 years of age group among participants. This result shows that Anti-Natal Cases majority are in the age group below 30 years.

Table-2 shows that high prevalence anaemia (96.8%) among housewife's and agricultural labours as compared with employees. Chi.square test: 7.71 & P< 0.021 (significant). Results indicate that agricultural labours and housewives were not utilizing the health care services which provide prophylaxis doses of iron & folic acid (100 days) for prevention of anaemia. Table-3 showed that among the parity group second gravid majorities (43.3%) suffered with anaemia. This shows that causes of anaemia like close pregnancies, malnutrition, not taking prophylaxis doses of iron & folic acid tablets may be

Age group	Number	Percentage (%)
<20years	59	22
20-24 years	159	59.1
25-29 years	49	18.2
≥30 years	2	0.7

Table-1: Distribution of participants according to age

Groups		Severity Of Anemia						Total	
		Mild		Moderate		Severe			
		N	%	N	%	N	%		
Age years	<20	18	11.4	23	14.6	3	1.9	44 28.0	
	20-24	32	20.4	50	31.8	8	5.0	90 57.4	
	25-29	12	7.6	8	5.0	3	1.9	23 14.6	
	≥30	0	0	0	0	0	0	0 0.0	
Education	Illiterate	32	20.3	35	22.2	6	3.8	73 46.4	
	Primary school	9	5.7	25	15.9	3	1.9	37 23.6	
	Secondary school	12	7.6	15	9.5	3	1.9	30 19.2	
	Graduate/Pg	9	5.7	6	3.8	2	1.2	17 10.8	
Occupation	Housewife, agricultural Working Women	62	39.4	78	49.6	12	7.6	152 96.8	
	Employed women	0	0	3	1.9	2	1.3	5 3.2	

Table-2: Distribution of Anemia in study group according to age, education & occupation

Parity	Normal N(%)	Mild Anemia N(%)	Moderate Anemia N (%)	Severe Anemia N(%)	Total Anemic N (%)
Primi gravida (1)	88(32.7)	24 (8.92)	31 (11.52)	5 (1.85)	60(38.2)
Gravida 2	21 (7.80)	28 (10.40)	33 (12.26)	7 (2.60)	68(43.3)
Gravida >2	3 (1.11)	10 (3.71)	17 (6.31)	2 (0.74)	29(18.5)

Table-3: Anemia distribution among parity

Diet	Normal N(%)	Mild Anemia N(%)	Moderate Anemia N (%)	Severe Anemia N(%)	Total Anemic N (%)
Mixed	50 (18.58)	20(7.43)	24(8.92)	5(1.85)	49(18.21)
Veg	62 (23.04)	61(22.67)	38(14.12)	9(3.34)	108(40.14)

Table-4: Prevalence of anemia among vegetarian's & mixed diet.

reason for high prevalence of anaemia in second gravid. Table-4 showed that vegetarian group suffered with high prevalence of anaemia (40.14%) as compared with mixed diet. Results showed that readily available iron absorbed better in mixed dietary groups.

## DISCUSSION

The prevalence of anaemia in pregnant women of RHTC & CAIMS Hospital was high (58.36%) among the 269 study subjects of Pregnant women. The similar study was done on pregnant women in rural Maharashtra, one of the developed states of India registered a prevalence of 56.4%.<sup>10</sup> Similar reports from WHO shows that up to 56% of all women living in developing countries are anaemic.<sup>17</sup>

In India, National Family Health Survey -2 in 1998 to 99 shows that 54% of women in rural and 46% women in urban are anaemic.<sup>18</sup> The National Nutritional Anaemia Prophylaxis Programme (NNAPP) was initiated in 1970 with the aim to reduce the prevalence of anaemia to 25 percent.<sup>11</sup>

Table-1 reveals that the maximum participant of pregnant women was in the age group of 20 to 29 years (77.3%) at both RHTC & CAIMS Hospital. The similar study was conducted in Aurangabad city, India by Pushpa O Lokare, found that maximum (87.2%) subjects were between ages above 20 to 30 years.<sup>21</sup>

Table-2 shows anemia among age group 20 years to 29 years were in total 72.0% (mild 28.0%, moderate- 36.8% severe 6.9%). Among the education category, majority suffering with anaemia were illiterates (46.4%) as compared with other education levels, less in primary school (23.6%), secondary school (19.2%) and graduates/ PG's (10.8%).

The similar study done in 7 states by K.N.Agarwal, D.K.Agarwal and group of health care & Research Association revealed that the anaemia in illiterates (those who neither read nor write) among pregnant women was highest in M.P (68.0%) followed by 46.3%, 45.3%, 30.7% 28.7%, 8.8% and 1.3% in the states of Orissa, Assam, Haryana, Tamilnadu, H.P and Kerala, respectively.<sup>22</sup> The similar study done by Pushpa and all revealed that proportion of pregnant women suffering from anaemia were 96.4%, 94.8%, 92.1% and 91.5% among illiterates, those educated up to primary, middle school and high school respectively. it was found that the lower the educational level of women, the probability of suffering from anaemia during pregnancy.<sup>21</sup>

Among occupation category, shows that the high prevalence of (96.8%) anemia among housewives and agricultural labours as compared with employees (3.2%) was anemic. The similar study shows that the proportion of pregnant women suffering from anaemia in classes I and II were less (47.61% and 71.42%, respectively) as compared with the lower socioeconomic status (93.51%, 94.49%, and 94.11% in classes III-V, respectively). It was obvious that as the socioeconomic status decreased, the prevalence of anaemia increased. This association between the socioeconomic status of the family and anaemia in pregnancy was found to be statistically significant ( $P < 0.05$ ).<sup>21</sup>

Table-3 shows, higher prevalence of anaemia (43.9%) seen in second gravid and 25.7% 2<sup>nd</sup> trimester pregnant women. The same explanation was given by similar study, with the mean gestational age at booking of 22 weeks in this study; physiologic

haemo dilution in pregnancy may explain the increased prevalence of mild anemia.<sup>17</sup>

Women who receive daily antenatal iron supplementation are less likely to have iron deficiency anaemia at term.<sup>19</sup> Even two injection of iron dextran (250 mg each) given intramuscularly at 4 week intervals along with tetanus toxoid injection have been recommended for better compliance and adequate results.<sup>20</sup>

Table-4 shows that dietary habits have influence on anaemia. The vegetarian group of pregnant women were maximum (40.14%) with anaemia as compared with having mixed dietary habits (18.21%). In similar study by Baig Ansary.N, Badruddin SH it was stated in the literature that tea consumption and low intake of red meat were associated with anaemia.<sup>23</sup>

Meat is a good source of high quality protein, iron, zinc and all the B vitamins except folic acid. Meat consumption reported to be 21kg/ capita/ year for Turkey, 124 kg/capita/year for USA and 100kg/capita in European countries.<sup>24</sup> These data explains the lower anaemia prevalence among those developed countries.

## CONCLUSION

A very high prevalence of anaemia (58.36%) in pregnant women is an indicator of the failure of national and WHO programmes to address this problem. Shift in the programme to mandatory regular supply of IFA tablets to adolescent girls and pregnant women from 24<sup>th</sup> week onwards till 12 weeks of postpartum period. We have to rectify the nutritional deficiencies with Food fortification and timely interventions for reducing the burden of the malaria, worm infestations and other infectious diseases. All practitioners handling obstetrics cases should be motivated for prescribing iron preparations and balanced diet with good compliance.

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# A Study of Benign Histopathological Changes in Cholecystectomy Specimen: Experience at a Referral Hospital

Swagata Dowerah<sup>1</sup>, Rashmi Deori<sup>2</sup>

## ABSTRACT

**Introduction:** Cholecystectomy or surgical removal of the gall bladder is one of the most commonly performed operations in a surgical setup. We carried out a study of the benign morphologic changes observed in cholecystectomy specimen to emphasise the importance of their proper diagnosis, as many of these may be misdiagnosed as malignant by the inexperienced eye.

**Material and methods:** A one year study of all cases of cholecystectomy specimen received in histopathology section was carried out. Three sections were taken from each specimen, stained with H and E and analysed by microscopy for histomorphological changes.

**Results:** Of a total of 103 cases studied, 95 cases were benign (92.2%) and only 8 cases were malignant. 85.4% cases showed chronic cholecystitis, 2.9% showed acute cholecystitis, 3.9% eosinophilic cholecystitis and 0.9% showed xanthogranulomatous cholecystitis. Other cases noted were empyema, mucocoele and polyp. A spectrum of epithelial changes were noted which included hyperplasia, metaplasia, cholesterolosis, dysplasia and adenomyomatosis.

**Conclusion:** The present study was conducted to describe the histomorphological spectrum of gall bladder disease. A histopathologist well conversant with all the alterations and changes of the gall bladder is of utmost importance for proper diagnosis and treatment.

**Keywords:** Benign changes, gall bladder, cholecystectomy

## INTRODUCTION

Cholecystectomy or removal of the gall bladder by surgery is one of the most commonly performed operations in a surgical setup. Its indications include inflammation of the gall bladder, symptomatic gall stones, risk factors for gall bladder malignancy and pancreatitis caused by gallstones. Laparoscopic cholecystectomy is nowadays the procedure of choice. The histopathological diagnosis in most of the cholecystectomy specimens is chronic cholecystitis. However, chronic cholecystitis specimen often show other associated lesions such as cholesterolosis, hypertrophy of muscle layer, parietal fibrosis, polypoid and adenomatous proliferation of mucous glands, and changes such as metaplasia, hyperplasia and dysplasia.<sup>1-3</sup> Knowledge and awareness of these findings is important as many of them may be missed and an erroneous diagnosis of malignancy can be made. Aim of the study was to describe the benign morphologic changes observed in cholecystectomy specimen and to emphasise on the importance of their proper diagnosis.

## MATERIAL AND METHODS

A one year study of all cases of cholecystectomy specimen (103) received in histopathology section of Assam Medical College and Hospital was carried out for the period of January 2015 to December 2015. The study was carried according to the institutional ethical guidelines for such studies. The clinical

findings were noted and gross examination was done according to standard protocol. Three sections were taken, one from the fundus, one from the body and one from the neck. Sections were prepared and stained with H and E and evaluated for histomorphological changes.

## STATISTICAL ANALYSIS

Microsoft office 2007 was used for tabulation and analysis. Descriptive analysis like rates and proportions using percentage were used to infer results.

## RESULTS

Of a total of 103 cases studied, 95 cases were benign (92.2%) and only 8 cases were malignant. 3 cases showed acute cholecystitis with denuded mucosa, congestion, hemorrhage and oedema; the remainder were all showing changes of chronic cholecystitis (Figure-1). There were 4 cases of eosinophilic cholecystitis with marked infiltration of the gall bladder wall by eosinophils; apart from these, a variable number of eosinophils were observed in many of the specimen of chronic cholecystitis. One patient showed xanthogranulomatous cholecystitis with an inflammatory infiltrate in the wall comprising of foamy macrophages and foreign body type of giant cells.

There were 2 cases of empyema gall bladder and 1 case of mucocoele which were diagnosed from gross and microscopic findings. There was a single case of fibrous polyp of gall bladder. Other non neoplastic epithelial alterations in the resected specimen included glandularis proliferans (14 cases, 13.6% of the total cholecystectomy specimen), spongiod hyperplasia (4 cases, 3.8% of total cases studied) (Figure-2), cholesterolosis (5 cases, 4.9%), adenomyomatosis (2 cases, 1.9%), pseudopyloric metaplasia (1 case).

Low grade dysplasia was observed in 7 cases (6.8%) (Figure-3). The malignancies reported included adenocarcinoma (6 cases), undifferentiated carcinoma (1 case) and a single case of neuroendocrine carcinoma.

While the mean age group for malignant lesions was 48 years, that of benign lesions was 39 years. The mean age of patients showing low grade dysplasia was 42.43 years.

## DISCUSSION

Histopathological examination of every resected gall bladder

<sup>1</sup>Assistant Professor, Department of Pathology, Silchar Medical College,

<sup>2</sup>Assistant Professor, Department of Pathology, Assam Medical College India

**Corresponding author:** Dr. Swagata Dowerah, Department of Pathology, Silchar Medical College, India

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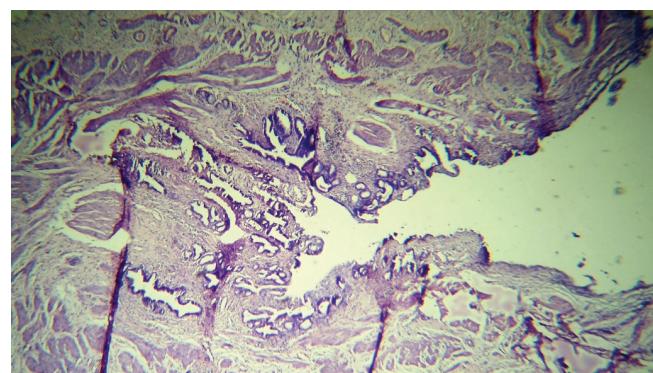
is of utmost importance. While the diagnosis in most cases is chronic cholecystitis, a spectrum of other morphological changes are commonly seen which include acute inflammation, cholesterosis, metaplasia and hyperplasia. Uncommonly, cholecystectomy specimen may reveal an unexpected gallbladder carcinoma. Therefore a detailed knowledge of the architectural variations of the gall bladder is essential so that none of these changes are misdiagnosed as malignant and no case of malignancy is missed.

In our study of 103 cases of cholecystectomy, there were 95 cases showing benign changes, almost exclusively associated with gall stone disease. The male to female ratio was calculated to be 1:4.6. In a study by Selvi et al, gall stone disease was predominantly seen in females (61.5%) as compared to males (38.4%).<sup>2</sup> In another study of cholecystectomies by Shah et al, the overall male to female ratio (M:F) was observed to be 1:2.3 and in cases with gall stones, the ratio was 1:2.7.<sup>3</sup> Thus it appears that gall bladder disease is more common in females. Female sex hormones and sedentary habits of most women in India expose them to factors that possibly promote the formation of gallstones.<sup>4-6</sup>

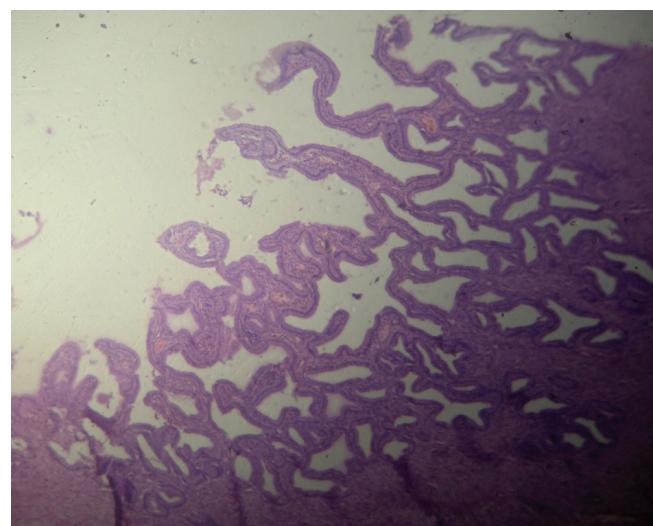
The average age of patients showing benign disease was 39.33 years while for malignant cases, it was 48 years, the average age of patients showing dysplastic changes was 42.43 years. Benign disease occurred at an earlier age group than dysplastic lesions. Likewise, malignancies were seen to occur at a more advanced age. This corroborates with the findings of several other studies. The most common finding in our study was chronic cholecystitis. Chronic cholecystitis is the most commonly encountered disease of the gallbladder; therefore the majority of cholecystectomies are performed for this condition.<sup>7-9</sup> The degree of chronic inflammation may vary and comprise of predominantly lymphocytes with few plasma cells, histiocytes, and occasional eosinophils. Acute cholecystitis on the other hand is mainly a clinical entity caused by abrupt injury of the gall bladder. It is an acute destructive process typically associated with ischemia, congestion, edema, epithelial denudation, vascular leakage, hemorrhage and fibrin deposition. In our study, there were 88 cases (85.4%) of chronic cholecystitis and only 3 cases (2.9%) of acute cholecystitis. Other variants of cholecystitis encountered were eosinophilic cholecystitis (4 cases) and one case of xanthogranulomatous cholecystitis (Table-1). There were 2 cases (1.9%) of empyema gall bladder and one case of

mucocoele. Selvi et al<sup>2</sup> had reported 85.8 % cases with chronic cholecystitis, 2.5% with acute cholecystitis, 2.5% polyp, 1.2% granulomatous cholecystitis, 1.2% empyema, 5.1% eosinophilic cholecystitis and 1.2% carcinoma. The proportion of malignant cases was higher in our study with 8 reported cases (7.7%). Terada et al in their study found incidence of malignancy to be 2.2%<sup>10</sup>, while in another study Ghimire P et al<sup>11</sup> showed it to be 1.28%.

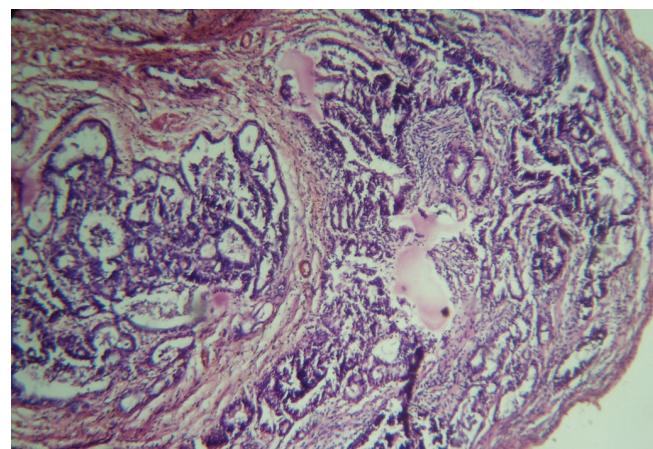
Apart from these, a wide variety of epithelial alterations were recorded which included hyperplasia including spongoid



**Figure-1** Showing gall bladder mucosa with features of chronic cholecystitis



**Figure-2:** Showing so called "spongoid hyperplasia" of gall bladder



**Figure-3:** Showing hyperplasia of the mucosa of gall bladder with mild dysplastic changes

Changes observed	Number of cases	Percentage
Chronic cholecystitis	88	85.4 %
Acute cholecystitis	3	2.9 %
Eosinophilic cholecystitis	4	3.9 %
Xanthogranulomatous cholecystitis	1	0.9 %
Empyema	2	1.9 %
Mucocoele	1	0.9 %
Hyperplasia	14	13.6 %
Cholesterolosis	5	4.9 %
Spongoid hyperplasia	4	3.8 %
Adenomyomatosis	2	1.9 %
Pseudopyloric metaplasia	1	0.9%
Gall bladder polyp	1	0.9 %

**Table-1:** Non malignant changes seen in cholecystectomy specimen

hyperplasia, metaplasia, cholesterolosis, adenomyomatosis and dysplasia (Table-1). Shah et al<sup>3</sup> in their study found chronic cholecystitis to be the most common pathology reported in 80.4% cases. Other benign lesions were, acute cholecystitis in 10.2% and empyema in 4.5% cases. There were 2 cases (0.3%) each of cholesterosis, adenomyoma and hyperplasia and 1 case of metaplasia in their study.

It is important for the pathologist to be familiar with these benign alterations of the gall bladder mucosa as an untrained eye may erroneously label these changes as malignant. Further studies are needed to properly elucidate the cause of these changes and to understand their relevance in the clinical setting.

## CONCLUSION

The present study was conducted to describe the histomorphological spectrum of gall bladder disease. While the most common diagnosis noted was chronic cholecystitis, a wide range of other findings were also observed which included hyperplasias, metaplasia, adenomyomatosis and cholesterolosis. A histopathologist well conversant with all the alterations of the gall bladder is of utmost importance for proper diagnosis and treatment.

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# A Prospective Randomized Controlled Study of Sevoflurane's Effect on the Onset Characteristics and Intubating Conditions of Rocuronium under Routine Clinical Practice

Nazmeen I Sayed<sup>1</sup>, Deepa Shriyan<sup>2</sup>, Dipankar Das Gupta<sup>3</sup>

## ABSTRACT

**Introduction:** The search for mechanism of "immobility" caused by volatile anaesthetics has been the forerunner for studies of their effect on neuromuscular junction. The aim of our study was to evaluate the effect of co-administration of sevoflurane on the intubating conditions and onset characteristics of rocuronium, during routine intravenous induction of anaesthesia.

**Material and methods:** 60 adult patients were randomly divided in sevoflurane and control group of 30 each. After induction patients in sevoflurane group were ventilated with 2% inspired concentration of sevoflurane in a fresh gas flow of 5 l containing 66.66% nitrous oxide and 33.33% oxygen and patients in control group were ventilated without sevoflurane. Intubating conditions of the trachea at 2 mins after 0.6mg/kg of rocuronium were assessed.

**Results:** No significant difference was found in any of the parameters between the two groups. Sevoflurane and control group had clinically acceptable intubating conditions of the trachea in 28 (93.3%) and 25 (83.3%) of patients respectively ( $p = 0.42$ ). The lag time of rocuronium was 34.9 (11.8) and 35.4 (12.8) seconds in the sevoflurane and control group respectively ( $p = 0.88$ ). The onset time for deep muscle relaxation was 144.7 (74.7) and 188.6 (124.9) seconds in the sevoflurane and control group respectively. ( $p = 0.10$ ). Relaxation at 2 min was 92.7 (10.3) % and 89 (13.1) % in sevoflurane and control group respectively. ( $p = 0.23$ ).

**Conclusion:** In healthy adults, ventilating the lungs with 2 percent inspired concentration of sevoflurane during routine intravenous induction has no incremental beneficial effect on intubating conditions of 0.6mg kg<sup>-1</sup> of rocuronium at 2 minutes.

**Keywords:** Train of four, Lag time, Accelerometer, Deep muscle relaxation.

## INTRODUCTION

It is known that inhalational anaesthetics inhibit the withdrawal reflex at the spinal cord level and have effects on the nicotinic acetylcholine receptor at the neuromuscular junction.<sup>1,2</sup> All in all inhalational agents have some muscle relaxation property.

Innumerable article are present emphasizing the potentiating effect on neuromuscular blockers by volatile anaesthetics.<sup>3-6</sup> These studies have exposed the patient to steady state of inhalational agents for periods inappropriate for routine clinical induction. Study designs resembling routine exposure to inhalational agents, have studied onset and recovery time but not the intubating conditions in patients.<sup>7-9</sup> Intubating conditions of rocuronium with high concentration of sevoflurane have been studied in children, however inhalational induction is not the mode of choice in adults.<sup>10</sup>

We wanted to study whether sevoflurane, in concentrations used routinely during intravenous induction, augments the

neuromuscular block of rocuronium enough to have an incremental benefit on intubating conditions. The aim of our study was to evaluate the effect of co-administration of sevoflurane on the intubating conditions of rocuronium, its lag time and onset time for deep relaxation during routine intravenous induction of healthy adults posted for elective surgery. Through this study we endeavour to improve our knowledge of the interaction of the two drugs at induction of anaesthesia.

## MATERIAL AND METHODS

It was a prospective randomized controlled trial, conducted after approval from local review board with valid, written, informed consent from patients. Study was carried out at Jaslok hospital and Research centre, Mumbai, over a period of 3 year from April 2004 to November 2006. A thorough pre-anaesthetic evaluation was carried out in all the patients, with airway examination. 60 patients were enrolled in the study. Patients included in the study were of ASA I-II physical status and age 18 to 65 years with Mallampatti classification I and II. Exclusion criteria were patient refusal, patients with neuromuscular disorders, patient on drugs that affect neuromuscular block and pregnant and lactating mothers. For premedication tablet diazepam 5mg was given a night before and at 6am on the day of the surgery with sips of water. 60 patients were randomly divided in sevoflurane and control group of 30 each with toss of a coin. The accelerometer TOF-Watch<sup>®</sup> SX (Organon) was used for neuromuscular monitoring. It was attached in the pre-anaesthesia room. The chosen hand was cleaned with spirit over the area around the ulnar nerve and the thumb. Two surface electrodes were applied over the ulnar nerve at the wrist and acceleration transducer was applied to ipsilateral thumb. The temperature probe of the accelerometer was attached on the thenar eminence. In the operation theatre routine standard monitors were attached. Palmer temperature was recorded. 18 G intravenous line was secured and a drip of ringer lactate started. Patients were pre-oxygenated with 100 percent oxygen. Induction in both the groups was with intravenous fentanyl 2 microgram per kg and thiopentone sodium 5mg per kg body weight. The upper limb

<sup>1</sup>Assistant Professor, LTMMC and GH Sion, <sup>2</sup>Assistant Professor, BYL Nair Hospital, <sup>3</sup>Director, Department of Anaesthesia Jaslok Hospital and Research Centre, India

**Corresponding author:** Dr. Nazmeen I Sayed, B-1702, Iraissa CHS, Plot no. 1, Sanpada 19, Navi Mumbai, Maharashtra, India.

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with the neuromuscular monitor was strapped on the arm board. Automatic calibration of TOF watch was performed after the loss of eyelash reflex. Patients in sevoflurane group were ventilated with 2% inspired concentration of sevoflurane in a fresh gas flow of 5 l containing 66.66% nitrous oxide and 33.33% oxygen and patients in control group were ventilated with a fresh gas flow of 5 l containing 66.66% nitrous oxide and 33.33% oxygen. After stabilization of end tidal carbon dioxide at 30–35 mm Hg, 0.6 mg/kg of rocuronium bromide was injected through the running drip in both the groups. The adductor pollicis response to supra maximal stimulation of ulnar nerve was monitored. The parameters recorded were lag time, onset time for deep relaxation, relaxation at 2 mins and intubating condition at 2 minutes after injection of rocuronium. Repeated single twitch mode of stimulation at 1 Hz was started to measure the lag time. Lag time was the time from the injection of rocuronium to first change in single twitch height. The train of four stimulus (2 Hz for 2 seconds at 12 second interval) was then used to record the onset time for deep relaxation. Onset time for deep relaxation was the time from the injection of rocuronium to the disappearance of all four twitches of train of four mode of nerve stimulation. A single experienced anaesthesiologist performed intubation 2 minutes after injection of rocuronium who was not involved in monitoring. TOF ratio was noted at intubation. Relaxation at 2 minutes was measured by TOF ratio. Intubation was judged according to the Copenhagen Consensus Conference scale. Any adverse hemodynamic events were noted. Adverse hemodynamic conditions were defined as a post intubation non invasive systolic and diastolic blood pressure or pulse rate change greater than 30 percent of pre-intubation value.

Based on our pilot studies, the difference in mean onset time for 0.6 mg/kg rocuronium with and without sevoflurane was 51 seconds with a standard deviation of 69 seconds in the sevoflurane group. A sample size of 30 in each group was estimated for a probability of 80 percentage ( $\beta$  value=0.2) with 95 percent significance level ( $\alpha$ =0.05) to detect a true difference of 51 seconds between the two group.

## STATISTICAL ANALYSIS

Qualitative data was assessed by Chi-square test. Analysis of quantitative data between the two groups was done using independent sample t-test. Statistical analysis was done using SPSS version 22.

## RESULTS

120 patients were assessed for eligibility. 60 patients were excluded for age criterion (n=14), for ASA physical status III (n= 18) and Mallampatti class III and IV (n=28). 60 patients were enrolled and analyzed.

The baseline characteristics, ASA physical status and Mallampatti classification are shown in Table 1. Excellent Intubating conditions were seen in 9(30%) patients in sevoflurane group and 6 (20%) patients in the control group. Good intubating conditions were seen in 19(63.3%) patients in both the groups.

Poor intubating conditions were seen in 2 (6.7%) patients in sevoflurane group and 5 (16.7%) patients in the control group (Figure 1). The two patients with poor intubating conditions in sevoflurane group had coughing for more than 10 seconds in response to tracheal intubation. Among the five patients with

poor intubating conditions in control group, four had coughing for more than 10 seconds in response to tracheal intubation and one patient had coughing and vigorous body movement at intubation. There was no difference in the clinically acceptable intubating conditions, lag time, relaxation at 2 mins and onset for deep relaxation of rocuronium in sevoflurane and control group as shown in Table 2.

Sevoflurane and control group had clinically acceptable intubating conditions of the trachea in 28 (93.3%) and 25 (83.3%) patients respectively ( $p = 0.42$ ). The lag time of 0.6 mg/kg of rocuronium was 34.9 (11.8) and 35.4 (12.8) seconds in the sevoflurane and control group respectively ( $p=0.88$ ). The onset time for deep muscle relaxation of 0.6 mg/kg of rocuronium was 144.7 (74.7) and 188.6(124.9) seconds in the sevoflurane and control group respectively ( $p = 0.10$ ). Relaxation at 2 min was 92.7 (10.3) % and 89 (13.1) % in sevoflurane and control group respectively ( $p = 0.23$ ). The palmar temperature in both the groups had no statistically significant difference. The palmar temperature in sevoflurane was 28 (0.15) °C and in the control group was 27.9 (0.19) °C ( $p = 0.88$ ). In sevoflurane group two patients had fall in diastolic blood pressure of more than 30% post intubation and one patient had a rise in diastolic blood pressure more than 30% from pre intubation values. In control group two patients had rise in diastolic pressure of more than 30% from pre intubation value.

## DISCUSSION

We had hypothesized that a decrease in onset time of rocuronium or an improvement in intubating conditions after co-administering of sevoflurane along with intravenous anaesthetics may be observed. We chose to use clinically appropriate doses of both the drugs which is two times ED<sup>95</sup> (0.6 mg/kg) of rocuronium and approximate one MAC of sevoflurane (2% inspired concentration). Though the onset time for deep relaxation of rocuronium was lesser in the sevoflurane group and patients in sevoflurane group had more excellent and less poor intubating conditions of the trachea, none of our parameters showed any statistical significant difference. The lack of difference can be explained by analyzing the mechanisms of potentiation NMB of by inhalational agents. The proposed mechanisms are inhibition of spinal motor neuron, inhibition of post synaptic nicotinic acetyl choline receptor or general enhancement of antagonist affinity at receptor site by inhalational agents.<sup>11,2,12-14</sup> The degree of potentiation of neuromuscular block by volatile anaesthetics depends on their aqueous concentrations. Time for half-equilibration of sevoflurane in muscle group is 70–80 minutes.<sup>15</sup> Low potency neuromuscular blockers like rocuronium have more molecules to equilibrate between central compartment and effect site, thus have faster onset of action. During routine intravenous induction with co-administration of sevoflurane the exposure time is not enough for sevoflurane to equilibrate in muscle compartment. Thus incremental benefit of sevoflurane for intubating conditions were not seen. Our study observed similar results.

Some recent studies have concluded earlier acceptable intubating conditions with sevoflurane under similar anaesthetic conditions in adult.<sup>16</sup> The dose used is more than 2 times ED<sup>95</sup>. In this study calibration of TOF watch was after sevoflurane stabilization. The maximum twitch height achieved in the sevoflurane group

may be lesser than that achieved in the non sevoflurane group and thus the time for onset of maximum depression is less than control.

The dose and time for intubation has been kept constant in our study design which makes the two groups comparable. As in our study lack of effect of sevoflurane on lag time and onset time of 0.6mg/kg has been reported by other studies.<sup>8,17</sup>

Acceptable Intubating conditions with low dose of rocuronium have been found with higher concentration of sevoflurane in children.<sup>10</sup> There are no controls in these studies. The potentiation seen may be due to the depth of anaesthesia. Acceptable intubating conditions with low dose of rocuronium and intravenous anaesthetics have also been reported.<sup>18</sup> The authors, from the analysis of results of present and other studies, propose keeping depth of anaesthesia constant when studying the effects of general anaesthetics on neuromuscular blockers. The drawback of our study was an inability to measure end tidal concentration of sevoflurane due to lack of resources and the study was not blinded. The low blood gas solubility of sevoflurane, presence of 66.66 percent nitrous oxide and a fresh gas flow of 5 l was expected to provide early equilibration of sevoflurane in the central nervous system. The time to half-equilibration in the vessel rich central nervous system is about 2 minutes for sevoflurane.<sup>15</sup>

The onset time in our study is the time for deep relaxation when the TOF count is zero. This is a plane of neuromuscular block when supplemental doses of neuromuscular blockers are not required. We wanted to compare the time to achieve this plane of NMB.

The Copenhagen consensus conference standard suggests maintaining core temperature of 36°C and surface temperature of 32°C for good clinical research practice in neuromuscular monitoring.<sup>19-21</sup> No active means of raising temperature of the limb monitored was used to mimic routine practice. Routinely warmers are started after induction and positioning.<sup>22</sup> The absolute value of lag time and onset time in our study should be compared keeping the temperature and mode of stimulation in mind.

## CONCLUSION

Thus it is seen in our study that in healthy adults, ventilating the lungs with 2 percent inspired concentration of sevoflurane during routine intravenous induction has no incremental beneficial effect on intubating conditions of 0.6mg/kg of rocuronium at 2 minutes.

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#### Appendix

##### Copenhagen Consensus Conference scale

	Excellent	Good	Poor
Laryngoscopy	Easy	Fair	Difficult
Vocal cord(position)	Abducted	Intermediate	Closing
Vocal cord(movement)	None	Moving	Closed
Movement at intubation(body)	None	Slight	Vigorous
Movement at intubation(coughing)	None	Diaphragm	>10 seconds
Copenhagen Consensus Conference scale: Excellent (all excellent conditions), Good (all excellent/good conditions), Poor (any one poor condition). Excellent/Good scale are clinically acceptable. Poor scale is clinically not acceptable.			

# Prevalence of Dermatophytosis in Patients in A Tertiary Care Centre

Sudha M<sup>1</sup>, Ramani CP<sup>2</sup>, Heber Anandan<sup>3</sup>

## ABSTRACT

**Introduction:** Dermatophytosis is an infection of the hair, skin, or nails caused by a dermatophyte, which is most commonly of the *Trichophyton* genus and less commonly of the *Microsporum* or *Epidermophyton* genera. Study aimed to find out the prevalence of dermatophytosis in patients attending tertiary care hospital.

**Material and methods:** Observational Cross sectional study was done on 1000 patients attending outpatient department of Government Rajaji Hospital, Madurai to check the prevalence of dermatophytosis.

**Result:** Clinically the prevalence of dermatophytosis was 13%, it was observed more in males. *T. rubrum* was the commonest species of dermatophyte isolated, which presented as *Tinea corporis*.

**Conclusion:** This study focused on the variations in dermatophytosis presentation and the species involved and found that *Trichophyton rubrum* was the most common affecting the present population.

**Keywords:** Dermatophytes, *Tinea rubrum*, *Tinea corporis*, superficial mycoses

## INTRODUCTION

Skin infections due to dermatophytes have become a significant health problem affecting all age groups. The dermatophytes are hyaline septate molds with more than 100 species described. Nearly 40 % of these are associated with human disease. According to Emmon's morphological classification, the dermatophytes are classified into three anamorphic genera -*Trichophyton*, *Microsporum* and *Epidermophyton* based on conidial morphology.<sup>1</sup> The dermatophytes manifest as infections of keratinized tissue like skin, hair, nails etc., of humans and animals. Some species of dermatophytes are endemic in certain parts of the world and have a limited geographic distribution. *T.soudanense*, *T.gourvillii* and *T.yaoundii* are restricted to Central and West Africa. *T.concentricum* is confined to islands in the South pacific. The increasing mobility of the world's population is disrupting several epidemiological patterns. Some dermatophytes like *E.floccosum*, *T.rubrum* and *T.tonsurans* are globally distributed.<sup>2</sup> Though various Indian and International studies on epidemiology of dermatophytosis are available no such study has been carried out in Madurai. So present study was done to find out the prevalence of dermatophytosis in patients attending tertiary care hospital in Madurai, India.

## MATERIAL AND METHODS

Observational cross sectional study done in 1000 cases attending the Dermatology outpatient department of Government Rajaji Hospital, Madurai. Ethical committee approval and informed consent from the patients was obtained before the start of the study. 1000 Patients were screened for fungal infections. 130 suspected dermatophytosis cases were selected and fungal scrapings from these patients were obtained. Processing

of specimens was done on the same day of the collection of specimen. Direct KOH mount was done for all the specimens and culture was done in Sabouraud's dextrose agar, containing chloramphenicol (0.04gms/litre) and cycloheximide (0.5g/litre) was. For observing the microscopic appearance, using teasing needle, mounts from the culture were made in Lactophenol cotton blue [LCB]. Slide culture was done when needed.

## STATISTICAL ANALYSIS

Microsoft office 2007 was used to make tables. Descriptive statistics like mean and percentages were used to infer results.

## RESULTS

A total of 1000 patients attending skin OPD were first screened for the presence of dermatophytosis and 130 cases (13%) were included for the study. It was observed that the highest number of dermatophytosis was seen in the age group of 31-40 years (40.76%) (Table-1). 130 samples were analyzed, sex wise and it was found that 81 were males (62.3%) and 49 were females (37.7%).

The samples were further analyzed depending upon the clinical manifestations and it was found that 74 cases out of 130 had *Tinea corporis* (56.9%), 37 out of 130 had *Tinea cruris* (28.5%), 7 had *Tinea faciei* (5.4%), 5 had *Tinea capitis* (5.4%) and 7 had *Tinea unguium* (5.4%) (Table-2).

In gender wise correlation of clinical presentation, among males 43 had *Tinea corporis*, 27 had *Tinea cruris*, 5 had *Tinea faciei*, 2 had *Tinea capitis* and 4 had *Tinea unguium*. So in males, *Tinea corporis* was the commonest lesion followed by *Tinea cruris*. Among female, 31 had *Tinea corporis*, 10 had *Tinea cruris*, 2 had *Tinea faciei*, 3 had *Tinea capitis* and 3 had *Tinea unguium*. Here also *Tinea corporis* was the commonest lesion followed by *Tinea cruris*.

Out of 130 samples, 112 were positive by KOH mount (86%) and 100 showed culture positivity (77%). On analyzing the 100 dermatophyte species isolates 74 cultures were *T.rubrum* (56.92%), 22 isolates were *T.mentagrophytes* (16.92%), 2 isolates were *T.Violaceum* (1.54%), one *E.floccosum* and one *M.gypseum*. (Table-4)

It was seen that *Tinea corporis* and *Tinea cruris* are predominantly caused by *T.rubrum*. All *Tinea unguium* cases

<sup>1</sup>Assistant Professor, Department of Microbiology, Kanyakumari Government Medical College, <sup>2</sup>Professor, Department of Microbiology, Institute of Microbiology, Madras Medical College, <sup>3</sup>Senior Clinical Scientist, Department of Clinical Research, Dr.Agarwal's Health care Limited, Tamilnadu, India

**Corresponding author:** Heber Anandan, No.10, South By-pass Road, Vannarpettai, Tirunelveli – 627003, Tamilnadu, India

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are caused by *T. rubrum*. *T. violaceum* was involved in *T. capitis* and *E. floccosum* in *T. cruris* only (Table-5).

## DISCUSSION

India is a tropical country and its climate is conducive for dermatophytosis.<sup>3</sup> Finding the prevalence of Dermatophyte infections and their various clinical presentations helps in the early diagnosis and proper treatment of Dermatophytosis. In this study, it was observed that 40.76% cases were affected with Dermatophytosis in the age group 31-40 years. Similar study by Prasad P.V.S. et al<sup>4</sup> also showed that the common age group involved in Dermatophytosis is 21-40 yrs. The present observation correlates with previous publications. It is obvious that the mean age of 30 years is the period where the laborers exert more physically, resulting in increased perspiration which produces a hot, humid, environment in the body, favoring the

growth of Dermatophytes. Excessive perspiration also washes away fungus killing oils in the skin making it more prone to dermatophyte infection. The male: female ratio was 1.8:1. This correlates with other studies by Prasad PVS et al<sup>4</sup> Suman et al<sup>6</sup> and SS Sen et al<sup>7</sup> where the male:female ratio was 1.75:1.1. Peerapur BV et al<sup>8</sup> and Philpot CM<sup>9</sup> have observed that higher incidence in males might be due to greater physical activity and increased sweating. In the present study, the male cases were mostly labourers and coolies working in sunlight most of the time leading to profuse sweating which in turn resulted in increased dermatophyte infection. Of the 130 cases analyzed in this study, *Tinea corporis* was the commonest presentation [58.8%] followed by *Tinea cruris* [12.3%] which corresponds to Kanwar AJ et al study,<sup>10</sup> Prasad PVS et al<sup>4</sup>, Suman et al<sup>6</sup> who have also showed that *Tinea corporis* was present in 52.8% cases and *Tinea cruris* in 15.6% cases. In this study *Tinea capitis* was seen in 3.8% of patients. All *Tinea capitis* cases were in the age group of 0-10yrs. This corresponds to the study by Philpot in which he reported that *Tinea capitis* was a disease of children. It is said that pubertal changes in hormones results in acidic sebaceous gland secretions which is responsible for decrease in incidence of *Tinea capitis* in adults. In this study, the diagnosis of dermatophytosis cases were made by demonstrating dermatophytes under microscope by KOH mount and culturing the specimen on SDA with cycloheximide media and proved that direct KOH mount was found to be a good screening test for dermatophytosis because 86.2% samples were positive in KOH mount while 76.9% were positive in culture. The study by Kannan, C.Janaki et al<sup>11</sup> and Suman singh et al<sup>6</sup> also showed that KOH mount positivity was seen in 80% of cases. But in contrast to this study, the culture positivity was only 45%.

## CONCLUSION

Clinically the prevalence of dermatophytosis was 13%. Males were more affected. The mean age group of dermatophytosis was 30 years. *Tinea capitis* was seen only in the age group of 0-10yrs. The commonest clinical manifestation was *Tinea corporis*. *Trichophyton rubrum* was the commonest species of dermatophyte isolated.

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Age in years	Patients	%
0 - 10	5	3.84
11 – 20	11	8.46
21 - 30	21	16.15
31 – 40	53	40.76
41 - 50	28	21.54
51 - 60	12	9.23

Table-1: Age wise distribution

Diagnosis	Patients	%
<i>Tinea corporis</i>	74	56.9
<i>Tinea cruris</i>	37	28.5
<i>Tinea faciei</i>	7	5.4
<i>Tinea capitis</i>	5	3.8
<i>Tinea unguium</i>	7	5.4
Total	130	100

Table-2: Clinical Presentation

Diagnosis	Male		Female	
	N	%	N	%
<i>Tinea corporis</i>	43	33.07	31	23.8
<i>Tinea cruris</i>	27	20.8	10	7.7
<i>Tinea faciei</i>	5	3.8	2	1.5
<i>Tinea capitis</i>	2	1.5	3	2.3
<i>Tinea unguium</i>	4	3.07	3	2.3

Table-3: Gender and clinical presentations

Species	Patients	%
<i>T. rubrum</i>	74	74
<i>T. mentagrophytes</i>	22	22
<i>T. violaceum</i>	2	2
<i>E. floccosum</i>	1	1
<i>M. gypseum</i>	1	1

Table-4: Dermatophyte Species Isolated

Species	<i>T.corporis</i>	<i>T.cruris</i>	<i>T.capitis</i>	<i>T.facei</i>	<i>T.unguium</i>
<i>T.rubrum</i>	47 (63.5%)	22(59.5%)		1 (14%)	4(57%)
<i>T.mentagrophytes</i>	14(18.9%)	3(8.1%)	1(20%)	4(57%)	-
<i>T.violaceum</i>	-	-	2(40%)	-	-
<i>E.floccosum</i>	-	1(2.7%)	-	-	-
<i>M.gypseum</i>	-	-	-	1(14%)	-

Table-5: Species Involved in Various Dermatophytosis

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# Sexual Dysfunctions and Lower Urinary Tract Symptoms in Females with Rheumatoid Arthritis

Urmila Dhakad<sup>1</sup>, Bhupendra Pal Singh<sup>2</sup>, Siddharth Kumar Das<sup>3</sup>

## ABSTRACT

**Introduction:** Rheumatoid Arthritis (RA) has profound impact on quality of life. This study aimed to evaluate sexual dysfunctions and urinary symptoms in female RA patients and their association with various disease and patient factors.

**Material and Methods:** In this prospective case control study, 73 females with RA were compared to 50 controls using Female Sexual Function Index (FSFI), Core Lower Urinary Tract Symptoms Score (CLSS), Core Lower Urinary Tract Symptoms -Quality of Life Score (CLSS-Q), Hospital Anxiety and Depression Scale (HADS) and a global question for overall relationship with their partners. Clinical Disease Activity Index (CDAI) was also assessed in RA group. Chi-square test/fisher exact test, unpaired t-test and univariate and multivariate binary logistic regression analyses were used to analyze the data.

**Results:** Sexual dysfunction, anxiety, depression, altered overall relationship with partner and bothersome LUTS were significantly ( $P < 0.05$ ) higher in the RA group as compared to controls. RA group had significantly ( $P < 0.05$ ) lower mean full scale - FSFI score and higher mean CLSS score. Sexual dysfunction in RA was associated with higher age, higher CLSS and higher urinary bother score (CLSS-Q) ( $P = 0.039, 0.027$  and  $0.039$  respectively). Bothersome LUTS were associated with higher CDAI, higher CLSS, lower desire and poor arousal ( $P = 0.035, <0.0001, 0.017$  and  $0.001$  respectively).

**Conclusions:** In females with RA, sexual dysfunction and bothersome LUTS are substantial problems. Their assessment may be warranted in RA patients, especially those with higher age and higher disease activity.

**Keywords:** rheumatoid arthritis, sexual dysfunction, lower urinary tract symptoms, quality of life, arthritis.

## INTRODUCTION

RA is a chronic, systemic, inflammatory disease of unknown etiology that can affect almost every domain of life, including sexual and urinary functions. While the physical problems of RA are the main issues of treatment for patients and physicians, the sexual dysfunctions and urinary symptoms associated with RA are often overlooked. They have widespread social implications, causing discomfort, shame and loss of confidence, which negatively affect their quality of life. RA is reported to adversely affect sexual function in female patients<sup>1,2</sup> and impact on urinary symptoms is not well studied. Responsible patient related, disease related and other factors have not been well described in literature. The potential reasons for under diagnosis of sexual dysfunctions and urinary symptoms in RA may be: (i) patients fail to report the complaints because of shame or frustration and/or, (ii) this subject is rarely called into question by treating physicians.<sup>3</sup> The apparent lack of interest of the doctor in relation to these issues could be explained<sup>4</sup> by many factors like constraints in consultation time due to over

burden, uneasiness during discussion (both by the physician and the patient), and uncertainties about physicians role and relative competence on the issues.

The sexual response cycle in women consists of the following phases<sup>5</sup>: desire, excitation, orgasm and resolution. Sexual dysfunction is an inability to complete the sexual act because of the reduction in sexual drive, arousal or orgasm causing marked distress and interpersonal difficulties.

In women with RA, reasons for disturbances in sexual functioning are multifactorial; include aspects related to the disease itself as well as the treatment. Possible factors which can influence the sexual function include pain, stiffness, decreased mobility of joints and muscle strength, fatigue, perception of a negative body image, anxiety and depression. Drugs used in the treatment of RA may also lead to sexual dysfunction. There are reports of sexual dysfunction related to use of methotrexate including decreased libido. Corticosteroids may influence sexual function by change in body image, depression and psychosis. Medications used to treat comorbid conditions such as fibromyalgia can also influence sexual function in RA patients like tricyclic antidepressants and serotonin reuptake inhibitors may affect libido and orgasm.

The aim of this study was to evaluate sexual dysfunctions and urinary symptoms in females with RA as compared to healthy age and sex matched controls. Further, the association of sexual dysfunctions and urinary symptoms to patient and disease related factors (age, disease duration, disease activity and psychological status) was assessed in RA patients.

## MATERIAL AND METHODS

This prospective case control study was conducted between March 2014 and December 2015, at the rheumatology department of a tertiary care teaching institution. A total of 123 female subjects were recruited based on inclusion/exclusion criteria. Institutional ethics committee approval for the study and written informed consent of participants were taken prior to start the study. Of these, 73 were confirmed cases of RA (age range: 21–50 years) who fulfilled the American College of Rheumatology/European League Against Rheumatism (ACR/ EULAR) 2010 criteria<sup>6</sup> for RA and 50 were healthy

<sup>1</sup>Assistant Professor, <sup>3</sup>Professor, Department of Rheumatology,  
<sup>2</sup>Professor, Department of Urology, King George's Medical University, Lucknow, U.P., India. Pin- 226003

**Corresponding author:** Dr Bhupendra Pal Singh, Professor, Department of Urology, King George's Medical University, Lucknow, U.P., India. Pin- 226003

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controls matched for age and sociocultural status. Inclusion criteria included: married and/or sexually active females who volunteered for participation in the study after explanation of the purpose of the study. Exclusion criteria were uncontrolled other major medical illnesses like diabetes, any neurological involvement and psychological disorders and known drug or alcohol dependence. Age, disease duration, any addiction and other comorbidities were recorded. Patients were subjected to full history taking and a thorough clinical examination. All of the patients were receiving medical treatment for RA (either hydroxychloroquine, sulfasalazine, methotrexate, alone or combinations of them). All participants self-filled the following questionnaires: (i) Female Sexual Function Index<sup>7</sup> (FSFI); (ii) Core Lower Urinary Tract Symptoms Score<sup>8</sup> (CLSS); (iii) Hospital Anxiety and Depression Scale<sup>9</sup> (HADS) questionnaires for psychological health; (iv) Clinical Disease Activity Index (CDAI)<sup>10</sup> were assessed in RA patients to assess the disease activity; and (v) A single question questionnaire regarding deterioration of overall relations with partner, that is, 'Do you feel that your overall relationship with your partner has deteriorated because of your health-related reasons? – Yes/No'. The FSFI is a self-administered 19-item questionnaire of six domains for the assessment of female sexual function. FSFI measures: (1) desire (two questions related to frequency and level) (2) arousal (four questions related to frequency, level, confidence and satisfaction), (3) lubrication (four questions related to frequency, difficulty, frequency of maintaining and difficulty in maintaining), (4) orgasm (three questions related to frequency, difficulty and satisfaction), (5) global satisfaction (three questions with amount of closeness with partner, with a sexual relationship, with overall sex life) and, (6) pain (three questions related to frequency during vaginal penetration, frequency following vaginal penetration, level during or following vaginal penetration). The items 1 to 16 had five likert-type answers from "never" (score 1) to "very much" (score 5) and the items 17 to 19 were leveled from "very much" (score 1) to "never" (score 5). Adding the score of individual items that comprise the domain and multiplying the sum by domain factor obtained individual domain score. Factors were 0.6 for desire, 0.3 for arousal and lubrication, and 0.4 for orgasm, pain, and satisfaction. The overall FSFI score was 2-36. Sexual dysfunction was considered if a total score of FSFI was less than 26.55.

The CLSS questionnaire is used to assess lower urinary tract symptoms (LUTS). It is a simple and comprehensive tool for assessment of female LUTS and comprises ten questions related to day time frequency, nocturia, urgency, incontinence, straining, and urethral pain with maximum score of 31 and one question related to quality of life with maximum score of six. Cut off for bothersome urinary symptoms on CLSS is QoL score >3.

The Hospital Anxiety and Depression Scale (HADS), is a self-assessment scale, to detect states of depression and anxiety. It has total of 14 items, with responses being scored on a scale of 0–3 (3 indicates higher symptom frequencies). Scores for each subscale (anxiety and depression) range from 0 to 21, with scores categorized as follows: normal 0–7, mild 8–10, moderate 11–14, and severe 15–21. In present study, we took a score of >10 to define a case of definite anxiety or depression.

Association of sexual dysfunction and lower urinary tract

symptoms with patient's age, comorbidities, duration of RA, disease activity, anxiety and depression were evaluated in RA group.

## STATISTICAL ANALYSIS

The results are presented in mean±SD and percentages. Chi-square test/fisher exact test was used for comparison between the dichotomous/categorical variables. The continuous variables were compared by unpaired t-test. The univariate and multivariate binary logistic regression analysis was used to find the association of the factors between various groups. The P value <0.05 was considered significant. All of the analyses were carried out by using SPSS 16.0 version (SPSS Inc., Chicago, IL, USA).

## RESULTS

Sexual dysfunction (FSFI score <26.55), bothersome urinary symptoms on CLSS (QoL score >3), anxiety (>10 score) and depression (>10 score) were present in significantly ( $P < 0.05$ ) higher number of RA patients (Table-1).

Mean sexual desire, arousal, lubrication, orgasm, satisfaction domain score as well as full FSFI scale scores were significantly ( $P < 0.05$ ) lower in RA patients. Mean HADS anxiety, HADS depression, CLSS and CLSS-Q scores were significantly ( $P < 0.05$ ) higher in RA patients.

On both, univariate and multivariate binary logistic regression analysis, sexual dysfunction was found to be associated with higher age ( $P=0.039$ ), higher CLSS ( $P=0.027$ ) and higher CLSS-QoL ( $P=0.039$ ). Bothersome urinary symptoms were found to be associated with higher CDAI ( $P=0.035$ ), higher CLSS ( $P<0.0001$ ), less desire ( $P=0.017$ ) and less arousal ( $P=0.001$ ). Anxiety was found to be associated with higher age ( $P=0.031$ ), higher CDAI ( $P=0.014$ ), higher CLSS ( $P=0.017$ ) and poor arousal ( $P=0.018$ ). Depression was found to be associated with higher age ( $P=0.003$ ), higher CDAI ( $P=0.004$ ), higher CLSS ( $P=0.031$ ), poor arousal ( $P=0.007$ ), lower orgasm ( $P=0.044$ ) and poor satisfaction ( $P=0.011$ ).

## DISCUSSION

Only a few studies with limited numbers of patients have been done to address the specific issue of sexual dysfunction in RA patients. The percentage of RA patients who experienced sexual problems ranged from 31% to 76% in various studies.<sup>11-13</sup> Our study is also among few studies to address the urinary symptoms in women with RA. This is also the first study to highlight these QoL issues in Indian women with RA. Using FSFI, our study demonstrates that sexual problems are significantly more prevalent in female RA patients as compared to normal subjects, similar to other studies.<sup>1,2,11-15</sup> A higher (80.8%) prevalence of sexual dysfunction in RA patients in our study population is similar to that reported by other latest studies<sup>14</sup> in literature. Of the six domains of FSFI (i.e. desire, arousal, lubrication, orgasm, overall satisfaction and pain), desire, arousal, lubrication, orgasm and overall satisfaction were found to be significantly lower in the RA group as compared to controls in our study, which is similar to that reported by Coskun B et al.<sup>15</sup> Tristano AG<sup>16</sup> reported problems of orgasm, arousal, and satisfaction in women with RA.

The sexual dysfunction is more common in women of higher age and those with lower urinary tract symptoms<sup>17</sup> and our study

Parameter	RA group(n=73)	Control group(n=50)	P value
Age(mean ±SD)	39.4±7.3	38.4±7.4	0.476 <sup>1</sup>
Co-morbidities(no. of cases)	19(26%)	11(22%)	0.766 <sup>2</sup>
Smoking (no. of cases)	0(0%)	1 (2%)	0.406 <sup>2</sup>
Duration of RA in years(mean ±SD)	6.13±4.72	-	-
Altered overall relationship with partner (no. of cases)	21(28.7%)	2(4%)	0.0009*, <sup>2</sup>
RA Disease Activity Score:			
CDAI(mean± SD)	13.39±13.8	-	-
Lower Urinary Tract Symptom (LUTS) scores:			
CLSS(mean ±SD)	5.5±3.9	3.4±2.6	0.0009*, <sup>1</sup>
CLSS-Q(mean ±SD)	2.2±1.3	0.6±0.9	<0.0001*, <sup>1</sup>
Bothersome LUTS (CLSS-Q >3) (no. of cases)	18(24.6%)	0(0%)	<0.0001*, <sup>2</sup>
Urinary problems duration in years (mean ±SD)	1.36±1.28	1.26± 0.89	0.21 <sup>1</sup>
Female Sexual Function Index scores:			
Desire (mean ±SD)	2.16±1.15	2.64±0.82	0.014*, <sup>1</sup>
Arousal(mean ±SD)	2.29±1.37	3.84±1.58	<0.0001*, <sup>1</sup>
Lubrication(mean ±SD)	3.78±1.16	4.74±0.83	<0.0001*, <sup>1</sup>
Orgasm(mean ±SD)	3.32±1.27	4.62±1.64	<0.0001*, <sup>1</sup>
Satisfaction(mean ±SD)	4.32±1.61	5.52±0.97	<0.0001*, <sup>1</sup>
Pain(mean ±SD)	5.02±1.52	5.28±0.96	0.298 <sup>1</sup>
Full scale score(mean ±SD)	20.86±5.66	26.64±6.34	<0.0001*, <sup>1</sup>
Sexual Dysfunction (FSFI<26.55) (no. of cases)	59(80.8%)	20(40%)	<0.0001*, <sup>2</sup>
Sexual problems duration in years(mean ±SD)	2.03±1.6	1.2±0.6	0.236 <sup>1</sup>
Anxiety and Depression Scale scores:			
HADS-A score(mean ±SD)	10.48±4.21	4±3.72	<0.0001*, <sup>1</sup>
HADS-D score(mean ±SD)	10.82±4.31	5.6±4.32	<0.0001*, <sup>1</sup>
HADS-A Definite (no. of cases)	31(42.4%)	3(6%)	<0.0001*, <sup>2</sup>
HADS-D Definite (no. of cases)	41(56.1%)	5(10%)	<0.0001*, <sup>2</sup>

\*Significant at  $P < 0.05$ . <sup>1</sup>Unpaired t-test. <sup>2</sup>Chi-square test/ fisher exact test. RA, Rheumatoid Arthritis; CDAI, Clinical Disease Activity Index; CLSS, Core Lower Urinary Tract Symptoms Score; CLSS-Q, Core Lower Urinary Tract Symptoms -Quality of Life Score; HADS-A, Hospital Anxiety and Depression Scale –Anxiety; HADS-D, Hospital Anxiety and Depression Scale –Depression.

**Table-1:** Rheumatoid Arthritis vs. Control group – demography and outcomes:

noted these associations in RA patients. Lower FSFI score in RA patients of higher age was also reported by Yimlaz H et al.<sup>18</sup> Similar to our findings, Costa TF et al<sup>14</sup> found no association of sexual dysfunction with RA disease activity although Yimlaz H et al<sup>18</sup> reported an association of sexual dysfunction with higher disease activity. Association between depression and sexual dysfunction in RA has been noted by others<sup>15,18-19</sup> as well. There have been some conflicting reports about prevalence and severity of LUTs in RA patients. While some<sup>20</sup> reported no significant differences between the RA and control groups, others<sup>21</sup> report a higher prevalence and severity of LUTs in RA patients, similar to our findings. Our study is probably the first one to evaluate the prevalence of lower urinary tract symptoms using CLSS questionnaire in RA females without secondary Sjogren's Syndrome. For female LUTs assessment, the CLSS questionnaire, has been reported as a better questionnaire<sup>8</sup> than AUASI questionnaire<sup>22</sup> used by many previous studies. We also found that higher urinary bother score was associated with higher disease activity in RA patients in contrast to report by Aras H et al.<sup>21</sup>

Association of anxiety and depression with higher age, higher disease activity, higher urinary symptom score and various domains of sexual dysfunction in our study depict a complex interrelationship among various psychological and quality of life issues in RA patients. The RA patients with higher age and disease activity may need evaluation of sexual as well urinary quality of life. The studies<sup>23,24</sup> have emphasized the role

of multidisciplinary approach and rheumatologist for better quality of life in patients with chronic autoimmune arthritis. In our opinion, rheumatologist as the primary physician of these patients might play a central role by appropriately highlighting and addressing their sexual as well as urinary issues through a multidisciplinary team approach.

Our study has some limitations: the relatively younger population (mean age – 39 years in RA group) in our study is likely to report higher subjective sexual dissatisfaction because of high sexual expectations in this age group. Some objective tests for LUTs like voiding diary, uroflowmetry or urodynamics could have further elaborated about them. Further, our study was based at a tertiary care centre where patients with more severe RA may be overrepresented leading to poorer scores on the FSFI, CLSS and HADS. Hence our results may not be generalizable to all patients with RA in the community. In spite of these limitations, this modest size case control study on Asian RA females indicates that sexual dysfunction and urinary symptoms are substantial problems and areas of concern in RA patients.

## CONCLUSIONS

In female patients with RA, sexual dysfunction is a substantial problem involving sexual desire, arousal, lubrication, orgasm and overall sexual satisfaction. Compared to healthy controls, female RA patients also report a higher prevalence of bothersome LUTS. Sexual dysfunction in female RA patients

was associated with higher age and higher urinary symptoms/bother. Urinary bother in RA females was associated with higher disease activity, less sexual desire and poor sexual arousal. This may warrant a multidisciplinary treatment approach for RA patients inclusive of rheumatologic, rehabilitative and psychiatric interventions for better management, especially in those at risk. Inclusion of sexual function and LUTs assessment in patient evaluation and follow up protocols in RA may lead to better health-related QOL.

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# Apathy and its Differentiation from Depression

Dip Bhadja<sup>1</sup>, Sudarshan C Y<sup>2</sup>, Shamshad Begum<sup>3</sup>, Hemavathi H<sup>1</sup>

## ABSTRACT

**Introduction:** Apathy is difficult to distinguish from depression as they share common clinical signs. Indian research in this area is lacking. In this background present study is planned to assess the extent of apathy and its relationship to major depressive disorder. Hence this study was planned to assess apathy in depressive disorder and correlate the various dimension of apathy and depression along with its severity.

**Material and methods:** This is a hospital based cross sectional study. Consecutive patients attending Psychiatric OPD having Major Depressive Disorder (MDD) as per DSM-IV (Diagnostic and Statistical Manual of Mental Disorders) criteria. Apathy was assessed using Lille's Apathy Rating Scale (LARS) and severity of depression was measured using Montgomery-Asberg Depression Rating Scale (MADRS). Statistical analysis was done using SPSS version 17

**Results:** Depression was in the upper end of moderate range, 65% of patients had moderate depression. Total apathy was correlated with depression irrespective of severity of depression. Positive correlation was observed between all sub-scale of apathy except novelty seeking and depression.

**Conclusion:** Total apathy was correlated with both levels of severity of depression. However various aspects of apathy differentially correlated with severity of depression. Depression is more related to emotional aspects of apathy compared to cognitive aspects of apathy.

**Keywords:** Apathy, Depression, cognitive dimension, emotional dimension and behavioural dimension.

## INTRODUCTION

In English language apathy is described as lack of interest or emotion. This can result in lack of desire or state of inactivity. By 19th century it was referred to states of psychological and physical non reactivity.<sup>1</sup>

Apathy is multi-dimensional concept whose components are still debated. Cognitive, behavioural and emotional dimensions of apathy have been proposed. Cognitive dimension includes response to novelty stimuli, awareness about self, interest in surrounding and social life. Behavioural dimension include taking initiative and voluntary actions, whereas emotional dimension include emotional response to situation and concern to situation or others.<sup>2</sup>

Apart from being a normal experience, apathy can occur in a wide range of neuropsychiatric disorders ranging from depression and negative symptoms of schizophrenia to neuropsychiatric manifestations of neurological diseases such as Huntington's, Parkinson's, and Alzheimer's disease (AD), infections like HIV and endocrine disorders like Hyperthyroidism, Hypothyroidism, Pseudo-hypoparathyroidism can present with apathy.<sup>3,4</sup>

Phenomenologically various researchers have focused on different aspects of apathy. They have differentiated between apathy as a symptom and syndrome. Apathy is seen as a symptom (i.e., of mood disorder, altered level of consciousness,

or cognitive impairment), and as a syndrome of acquired changes in mood (affect), behaviour, and cognition not due to mood disorder, altered level of consciousness or cognitive impairment.<sup>1</sup>

## Apathy in depression

Apathy is so commonly reported along with depression in adults that it is often regarded as model disorder for defining apathy. Apathy is frequently seen in adolescent depression. But however apathy in depression is different from apathy in other disorders. It is difficult to distinguish apathy from depression as they share common clinical signs. Symptomatically, it is important to understand that apathy can occur concomitantly with depression, but is usually different from it. Presence of one symptom doesn't predict the presence of other. Some assessment tools such as MADRS have apathy as a subscale. Therefore, this scale does not evaluate depression only.<sup>5</sup>

The HAMD-21 has an item on "work and activities" that specifically targets apathy. Quite often apathetic patients are misdiagnosed as depressed by practitioners, and consequently prescribed antidepressants wrongly.<sup>6</sup>

Depression has been variably correlated with apathy in the research done so far. In most of the studies apathy was evaluated using apathy evaluation scale but depression was measured using different scales and the diagnosis of the sample differed. This could account for the discrepancies in results of various studies. Most of the studies have focused on depression occurring in neurological disorders.

Hence this study was planned to assess apathy in depressive disorder and correlate the various dimension of apathy and depression along with its severity.

## MATERIAL AND METHODS

This was a hospital based cross sectional study. Consecutive 50 patients attending psychiatry OPDs of hospitals attached to JJM medical college having a diagnosis of major depressive disorder according to DSM IV TR, who met the inclusion criteria (age group of 18 to 60 year, both gender) and did not get excluded (severely ill, uncooperative, drug induced Parkinson's, substance dependence and mental retardation) were recruited to the study by purposive sampling. Sample was collected from December 2013 to November 2014. Prior to starting study, approval for this study was obtained from the institute's ethical committee.

<sup>1</sup>Post Graduate Resident, <sup>2</sup>Professor of Psychiatry, <sup>3</sup>Professor of Clinical Psychology, Department Of Psychiatry, JJM Medical college, Davangere, India

**Corresponding author:** DR. Dip Bhadja, Post Graduate Resident, Department of Psychiatry, OPD 12, JJM Medical College, Davangere, 577004, Karnataka, India

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After obtaining informed consent, socio-demographic data was recorded using the proforma developed for the study.

Apathy was assessed using Lille's Apathy Rating Scale (LARS). It is a 33-item scale to measure apathy. It has nine sub-scales which are clinician administered using a structured interview. It was developed to elicit and quantify apathy in the month prior to the assessment and has been validated in individuals with PD. Items and domains were generated from literature on apathy, concepts of apathy proposed by Marin and Stuss as well as clinical experience with patients having apathy. The nine sub-scales are Everyday productivity (EP), Interests (INT), Taking the initiative (INI), Novelty seeking (NS), Motivation - Voluntary actions (M), Emotional responses (ER), Concern (C), Social life (SL) and Self-awareness (SA). Cognitive dimension includes NS, SL, SA and INT; behavioural dimension includes INI and M; emotional dimension includes ER and C. The first three items of the LARS are scored on a 5-point Likert-like scale (0–4) and the remaining 30 items are scored on a no-versus-yes basis. Scores on the scale range from -36 to +36 with higher and more positive score indicating greater severity of apathy.<sup>2,7-10</sup> The items are presented as positively worded questions to which the subject is expected to answer clearly 'yes' or 'no', in order to reduce subjective interpretations as much as possible. With the exception of the first three questions (which are coded on a five point Likert-type scale), responses are coded by the clinician on a binary (yes/no) scale, with an additional 'NA' (not available) condition for non-classifiable answers or non-applicable items.<sup>11</sup> Categorization into various severities of apathy has been done in studies which have used LARS to measure apathy. -36 to -24- no apathy, -23 to -19- mild apathy, -18 to -13- moderate apathy and -12 to +36- severe apathy.<sup>2</sup>

Severity of depression was assessed by Montgomery-Asberg Depression Rating Scale (MADRS), developed by Montgomery SA, Asberg M et al. It is a 10 item scale. Each item contains responses which have to be rated on a Likert scale ranging from 0 to 6. Severity of depression is rated as follows 0-6 = symptom absent, 7-19 = mild depression, 20-34 = moderate depression

Variable	N=50	
	Mean	Std deviation
Total score on LARS	11.3	10.51
Total score on MADRS	33.62	5.66
Severity of depression	No. of Patients	
Moderate (MADRS 20-34 )	31	
Severe (MADRS 35-60)	19	
MADRS- Montgomery-Asberg Depression Rating Scale, Lille's Apathy Rating Scale (LARS).		

**Table-1:** Total scores of LARS and MADRS in depression and its severity

and 35-60 = severe. depression.<sup>12</sup>

## STATISTICAL ANALYSIS

Analysis was done using SPSS 17 version of software. t test was used for continuous variables and Chi-square test for categorical variables. Pearson's correlation was done for continuous variables. Statistical significance was set at 0.05 level.

## RESULTS

Majority of patients were in age group of 30 to 40 year, females, studied up to SSLC, married and from nuclear family. Sample was equally distributed between urban and rural community. Mean score of Total apathy on LARS was  $11.3 \pm 10.51$  indicating severe apathy. Mean score on MADRS was 33.62 with SD of 5.66 indicating that the sample was having moderate depression. 31 patients had moderate depression and 19 patients had severe depression (Table-1).

Dimensions of emotional apathy, behavioural apathy and some component of cognitive apathy were significantly positively correlated with MADRS scores (Table-2).

Overall apathy was significantly and positively correlated with depression irrespective of severity. All components of emotional dimension were significantly and positively correlated with severe depression. Two out of four components of cognitive dimension like social life and self-awareness were correlated with moderate depression (Table-3).

## DISCUSSION

Mean score of Total apathy on LARS was  $11.3 \pm 10.51$  indicating severe apathy. Scores on various sub-scales in LARS ranged from 0.42 to 1.82, the possible scores ranging from -4 to +4. This indicates high scores on all sub-scales, motivation sub-scale having the highest score. Other researchers have documented prevalence of apathy ranging from 53.3% to 94% in major depression.<sup>13,14</sup>

The prevalence of apathy when self-reported is low, but when reported by informant the prevalence is high. Self-rated apathy is positively correlated with depressive symptoms but no significant relationship is found between informant rated apathy and depression.<sup>6</sup> However the severity of apathy has not been commented upon in these studies.

Mean score on MADRS was 33.62 with SD of 5.66, indicating that the whole sample had moderate depression, 38% of the sample had severe depression. Total score of apathy and all dimensions of the apathy were significantly positively correlated with MADRS scores. Literature in the area of apathy and major depression in adults are lacking but similar findings have been reported in other studies done on patients having depression in neurological disorders.<sup>15</sup> Levy et al reported that

LARS	MADRS	LARS	MADRS	LARS	MADRS
Cognitive dimension		Behavioural dimension		Emotional dimension	
NS	.166	INI	561**	ER	.306*
SL	.495**	M	585**	C	.425**
SA	.519**			EP	.430**
INT	.541**				
MADRS- Montgomery-Asberg Depression Rating Scale, Lille's Apathy Rating Scale (LARS), Interests (INT), Taking the initiative (INI), Novelty seeking (NS), Motivation - Voluntary actions (M), Emotional responses (ER), Concern (C), Social life (SL) and Self-awareness (SA).					

**Table-2:** Correlation between sub-scales of LARS and MADRS

LARS	Moderate depression (N=31)	Severe depression (N=19)
Cognitive dimension		
NS	.048	0.008
SL	0.436, p<0.01	0.332
SA	0.40, p<0.02	0.435
INT	0.262	0.400
Behavioural dimension		
INI	-0.348	0.370
M	0.264	0.358
Emotional dimension		
ER	0.237	0.734, P<0.000
C	0.261	0.461, P<0.04
Total Score	0.359, p<0.04	0.6000,P<0.007
MADRS- Montgomery-Asberg Depression Rating Scale, Lille's Apathy Rating Scale (LARS), Interests (INT), Taking the initiative (INI), Novelty seeking (NS), Motivation - Voluntary actions (M), Emotional responses (ER), Concern (C ), Social life (SL) and Self-awareness (SA).		
<b>Table-3:</b> Correlation between severity of Depression and subscales of LARS (dimensions of apathy)		

apathy was weakly correlated with depression in various brain insults.<sup>16</sup> However contradictory findings also exist in literature. Marin at al found no significant correlation between apathy and depression when MAH-D variables closely related to apathy were excluded from consideration.<sup>17</sup> Kirsch-Darrow et al found low correlation between apathy and dysphoric mood.<sup>18</sup> In the present study novelty seeking was not significantly positively correlated with depression. Robert et al have reported that depressed mood was related to longer viewing duration to both standard and novel stimuli.<sup>19</sup>

In this study, total apathy was positively correlated with depression across both severities (moderate and severe), while different dimensions of apathy were positively correlated with different levels of severity of depression. Component of cognitive dimension like social life and Self-awareness subscales of apathy were significantly and positively correlated with moderate depression and emotional dimension of apathy was significantly and positively correlated with severe depression. Starkstein et al have suggested that there is significant association between apathy and major depression and not minor depression.<sup>11</sup> There is no other comparative literature available about relationship between severity of depression and dimensions of apathy.

## CONCLUSION

Depression in this sample was in the upper end of moderate range. Nearly about 2/3 of patients had moderate depression. Patients having depression had severe apathy and in them all the three dimensions of apathy were impaired. All components of emotional, behavioural apathy and some components of cognitive apathy were correlated with depression. The correlation between total apathy and depression did not differ with respect to severity of depression.

The definition and concepts of apathy have to be refined. The operational definition which has been proposed has to gain wide acceptance. The inclusion of apathy in scales measuring psychopathology has to be discussed and resolved.

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# Immune Escape Variants in Chronic Hepatitis B – A Clinicopathological Correlation with Sequencing of MHR Region of S Gene Characterizing Influence of ‘A’ Determinant

Mukul Bajpai<sup>1</sup>, Rigvardhan<sup>2</sup>, Rahul Sinha<sup>3</sup>, Rakhi Negi<sup>1</sup>

## ABSTRACT

**Introduction:** Hepatitis B surface antigen (HBsAg) and Anti-HBs antibodies can coexist in 10-25% cases. Major reason is buildup of mutations in the Major Hydrophilic Region (MHR) of the S gene especially within the “a” determinant region leading to change in antigenicity and escape from the host immune system. The aim of this study was to analyze influence of ‘a’ determinant of S gene on creation of these immune escape mutants in CHB by sequencing.

**Material and methods:** 100 cases of CHB reporting for treatment or review were enrolled. HBsAg and anti-HBs was performed on samples using enzyme immunoassay along with determination of biochemical profile. Sequencing of MHR region was done on identified Immune escape variants to determine influence of ‘a’ determinant.

**Results:** Eleven percent CHB patients showed coexistence of HBsAg and Anti-HBs. Seven out of eleven patients were positive for HBV-DNA and sequencing of MHR region of S gene showed common accumulation of mutations seen at position 127. Other common sites of mutation were at positions 128 and 118 in ‘a’ determinant we found point mutations at positions 118, 120, 124 and 137 which have not been described.

**Conclusion:** Accumulation of residue changes within the MHR, including the highly conformational and cysteine-rich loops of “a” determinant can be a possible mechanism for coexistence of HBsAg and anti-HBs antibodies in CHB. Such cases increase the problem of transmission of these variants and can cause widespread vaccination failure and are thus public health concern as these individuals may unknowingly transmit the infection.

**Keywords:** hepatitis B, immune escape variants, MHR

## INTRODUCTION

Hepatitis B virus (HBV) infection and its long term sequelae, which include chronic hepatitis B (CHB), cirrhosis and hepatocellular carcinoma are foremost public health problems throughout the world.<sup>1</sup> Approximately one third of all cases of cirrhosis and 50% of cases of hepatocellular carcinoma are attributable to chronic HBV infection. Overall 30% deaths in these patients are linked directly to consequences of HBV infection.<sup>2</sup> Majority of the patients, however, are known to recover from illness and recovery is characterized by loss of hepatitis B surface antigen (HBsAg) and acquisition of Anti-HBs antibodies.

Although, occurrence of Anti-HBs is a favorable outcome in HBV infection, several authors have pointed out that presence of Anti-HBs antibodies (Ab) does not always mean loss of HBsAg and they can coexist in as many as 10-25% of cases.<sup>3,4</sup> Though the simultaneous presence of anti-HBs in HBsAg positive cases is perplexing, this phenomenon is known since 1976, still the exact cause of presence of both HBsAg and

Anti-HBs antibodies in spite of replicative disease in patients is unknown.<sup>5,6</sup> Major reason cited by many authors is selection of HBsAg immune variants and buildup of residual changes in the Major Hydrophilic Region (MHR) of the S gene especially within the “a” determinant region, which is the main target of anti-HBs, could alter the structure of surface antigen, leading to change in antigenicity and escape from recognition by the host immune system.<sup>7</sup> Antibodies against the group specific “a” determinant, which is a complex antigenic structure with multiple immunogenic epitopes, normally neutralize virus and confer cross protective immunity to all HBV subtypes. Historically, the secondary structure of this epitope is a double loop formed via disulfide bridges between cysteine residues between 124 and 137 and residues 139 and 147. Nucleotide substitution that leads to change in amino acid sequence can lead to decreased binding and failure to detect HBsAg in diagnostic assays using monoclonal and polyclonal antibodies.<sup>7,8</sup> The co-existence of HBsAg and anti-HBsAb are feared to be associated with important clinical concerns. Indeed, such HBsAg-mutated HBV strains may not be fully susceptible to vaccine-induced anti-HBs antibody with the potential risk of vaccine failure including contamination of seemingly protected vaccinated individuals.<sup>6,7</sup>

The detection of such non-protective anti-HBs antibody may also lead to misdiagnosis of chronic HBV infection if detection of HBsAg is not carried out concomitantly. Furthermore, due to the frame-shifted overlap flanked by the open reading frames of HBsAg and HBV polymerase genes, mutations within HBsAg gene might cause structural and functional alterations in the HBV reverse transcriptase (RT) with potential influence on viral replicative capacity and efficacy of antiviral drugs.<sup>1</sup>

In view of these potential implications, the frequency, clinical settings and significance of the presence of concurrent HBsAg and anti-HBsAb in serum remain largely unknown to date. Thus the aim of this study was to analyze the clinic-pathological profile of CHB patients with special reference to Immune escape variants (coexistence of both HBsAg and Anti-HBs) and

<sup>1</sup>Assistant Professor, <sup>2</sup>Associate Professor, Department of Pathology and Laboratory Medicine, Command Hospital (Central Command) Lucknow, UP, <sup>3</sup>Associate Professor, Department of Pediatrics, Military Hospital Jodhpur, Rajasthan, India

**Corresponding author:** Dr Mukul Bajpai, Assistant Professor, Department of Pathology and Laboratory Medicine, Command Hospital (Central Command) Lucknow, UP, India 226002

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determine by sequencing influence of 'a' determinant of S gene on creation of these immune escape mutants.

## MATERIAL AND METHODS

**Study population:** The study comprised of 100 HBsAg positive patients attending Gastroenterology OPD of a tertiary care hospital clinically diagnosed as CHB and enrolled for treatment. The study group consisted of predominantly young males. Age group was 20 to 65 years. All subjects in this study were male. Informed consent and clearance from Institutional ethical committee was taken. A performa with detailed history of past medical and surgical illness, risk factors and predisposing factors was filled for all subjects prior to conduct of study along with routine medical examination.

**Screening:** All subjects were screened for HBsAg (Hepacard Biomed Industries, Parwanoo (HP) - one step cassette style HBsAg detection test, India)

**Biochemical profile:** Routine biochemical parameters of liver function including serum bilirubin, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) was performed on Siemen Dimension EXL 200 analyser using Siemen kits. Quality control protocol was strictly adhered to.

**Virological markers** of CHB infection including Anti HBs antibodies (M.B.S-S.R.L. Medical Biological Service, Milano, Italy), HBeAg (Adatis Italia S.P.A, Bologna Italy) and anti HBcAb (M.B.S-S.R.L. Medical Biological Service, Milano, Italy) were performed on clinical samples using enzyme immunoassay. Negative and positive controls were run simultaneously to ascertain validity of the test.

**Sequencing of MHR region of S gene:** DNA was extracted using QIAamp DNA Mini Kit from QIAGEN Diagnostics. Sequencing HBV PCR products was carried out using ABI PRISM 3100 Genetic Analyzer which is a multi-colour fluorescence-based DNA analysis system using technology of capillary electrophoresis with 16 capillaries operating in parallel.

## RESULTS

### Age profile

Forty were in age group 20-30, 39 in 30-40, 16 in 40-50, four in 50-60 and one in 60-70 years age group. Detailed clinical history revealed that 63% patients did not have any particular risk factor, 11% gave history of exposure to commercial sex workers, 8% gave history of minor surgery, 8% had multiple sexual partners, 7% gave history of blood transfusion and 3% attributed their disease to professional hazard as they were Health Care Workers.

Most of the patients were young and healthy and except for CHB they did not have any other co morbidity. 6% had associated hypertension, 4% had Type-2 diabetes mellitus, 3% gave history of pulmonary tuberculosis and one each were known cases of Non-Hodgkins Lymphoma, Alcoholic Liver cirrhosis, Gilbert's syndrome and rheumatic heart disease.

### Serological markers

Eleven (11%) out of the one hundred patients had coexistence of Anti HBs antibodies while thirteen (13%) were positive for anti hepatitis B core antibody (HBcAb) and nineteen (19%) were positivity for hepatitis B e antigen (HBeAg). Anti-HBs titre of

these 11 cases is summarized in Table-1.

### Clinical profile of immune escape variants

All the eleven patients with co-existence of HBsAg and Anti HBs were asymptomatic with none showing signs and symptoms of chronic active hepatitis. There was no associated co-morbidity in these patients. History of risk factors revealed one patient had received blood transfusion, five had history of exposure to commercial sex worker and one patient each smoked tobacco and consumed alcohol.

**Serological and biochemical profile of immune-escape variants**  
Out of these 11 immune escape mutants three were positive for HBeAg and two were positive for Anti HBc antibody. These 11 patients had, however, normal levels of serum AST, ALT and bilirubin levels except one patient who showed mildly increased AST and ALT.

### Sequencing of MHR region of S gene

Seven samples showed HBV-DNA positivity out of 11 samples, Five samples (1, 6, 10, 22 and 39) out of seven showed same mutation of replacement of proline by threonine at amino acid position 127. Four samples (sample no. 1,10,22,39) showed replacement of threonine by valine at amino acid position 118. Four other samples (sample no. 1,10,22,39) showed replacement of alanine by valine. Sample 14 showed a solitary mutation at amino acid position 137 with replacement of cysteine by arginine. Sample number six showed mutation in amino acid position 125 with replacement of threonine by methionine in addition to mutation at amino acid position 127. Sample number 55 out of these seven samples did not show any mutation in MHR region. All mutations detected were therefore in the MHR region (amino acid sequence 118-137). No mutation was identified in the "C" terminal or "N" terminal of S gene. These are summarized in Table-2 and figure-1.

## DISCUSSION

Several authors have described point mutations resulting in amino acid changes in the S protein antigenic loops in vaccines and hepatitis B immune globulin recipients.<sup>7,8</sup> However, HBV escape mutants may also arise naturally in CHB virus carriers due to increased pressure of the host immune system.<sup>9,10</sup>

The clinical significance of the co-existence of HBsAg and protective levels of anti-HBs antibodies is not well known since clinical data are lacking in most studies. Previous studies have pointed that this profile could be associated with chronic active hepatitis.<sup>7,8</sup> In our study, in contrast to Western data, all

S.No	Sample No	Anti HBs titers
1	1	192
2	6	133
3	10	128.5
4	14	251.11
5	22	214.44
6	39	130.15
7	43	234.4
8	55	24.97
9	62	42.379
10	78	55.8
11	88	161.1

**Table-1:** Anti-HBs titres of 11 cases (more than 100 mIU/ml is considered protective)<sup>7</sup>

these eleven patients were asymptomatic with none showing any signs and symptoms suggestive of chronic active hepatitis. These eleven patients had normal levels of serum AST, ALT and bilirubin levels except one patient who showed mildly increased liver enzymes.

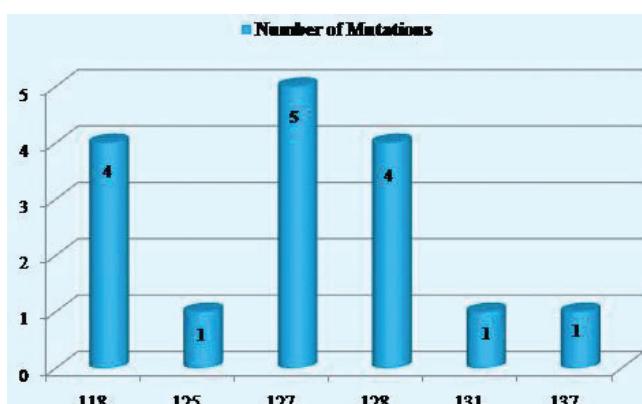
In many Western studies this serological profile usually associated with HBV replication despite the presence of anti-HBsAb at a protective level though in our study in contrast to western data only 3 out of these 11 patients were positive for HBeAg. Median age of patients in this study was lower as compared to Western studies (34 years vs 43-45 years in the West) but this bias in this study could have arisen because the study subjects comprised of young serving soldiers who were comparatively young and 80 out of 100 patients were between 20 and 40 years.<sup>6-8</sup>

Detailed clinical history revealed that 63% patient's did not have history of any particular risk factor. Maximum patients from the group with no associated risk gave history of injections from reusable syringes without proper sterilization for minor illness in their home town. This profile is seen normally in the West in association with orthotopic liver transplant, myeloproliferative

disorders and chemotherapy although in our study none of the eleven patients had any such co morbidity.<sup>3</sup> No noteworthy association of smoking and alcohol was seen associated with this study population.

It must also be emphasized in context of immune suppression which is a main feature associated with this profile and quoted as high as 69% in other studies carried out in South East Asia and Western countries, it was not apparent in any of the 11 immune escape variants detected in this study.<sup>7,11</sup> However, detailed immunological evaluation was not undertaken in this study and, thus, this factor cannot be commented upon with conviction. In comparing HBsAg sequences with the reference sequence, it was striking to notice an accumulation of residue changes in viral strains isolated from those with immune escape variants. Moreover, the distribution of these changes in amino acid sequences was not uniformly distributed along the protein but were accumulated within the MHR, including the highly conformational and cysteine-rich "a" determinant region. This antigenic loop of HBsAg region which is classically described as the main target of the humoral response and any change of its primary sequence will alter its antigenicity and would render any anti- HBs humoral defense against this region less effective.<sup>1</sup> Previous studies have characterized most prevalent residues affected by such changes.<sup>7,11</sup> Thus, positions 145, 144, 129, 126, and 130 were the most likely targets of point mutation but in contrast to Western studies, we found mutations in positions 118, 120, 124, 125, 127, 131 and 137 with maximum mutations in position 127. Although an Indian study carried out by Kumaravelu et al showed presence of mutations at positions 125, 126, 127, 131, 134 and 136 in two immunized children, but point mutation at positions 118, 120, 124 and 137 has not been described.<sup>12</sup> Western and South Eastern studies have also demonstrated changes in HBsAg sub region 4 but no such mutation was found in their study

The description of these residue changes, particularly the G145R change, is remarkable because these substitutions also match up to common mutations described for HBV vaccine



**Figure-1:** Number of mutations present in MHR region; X axis – serial no of AA sequence; Y axis- no of mutations documented

	Standard	Sample 1	Sample 6	Sample 10	Sample 14	sample 22	sample 39	sample 55
118	Threonine	Valine	Threonine	Valine	Threonine	Valine	Valine	Threonine
119	Glycine	Glycine	Glycine	Glycine	Glycine	Glycine	Glycine	Glycine
120	Proline	Proline	Proline	Proline	Proline	Proline	Proline	Proline
121	Cysteine	Cysteine	Cysteine	Cysteine	Cysteine	Cysteine	Cysteine	Cysteine
122	Arginine	Arginine	Arginine	Arginine	Arginine	Arginine	Arginine	Arginine
123	Threonine	Threonine	Threonine	Threonine	Threonine	Threonine	Threonine	Threonine
124	Cysteine	Cysteine	Cysteine	Cysteine	Cysteine	Cysteine	Cysteine	Cysteine
125	Threonine	Threonine	Methionine	Threonine	Threonine	Threonine	Threonine	Threonine
126	Threonine	Threonine	Threonine	Threonine	Threonine	Threonine	Threonine	Threonine
127	Proline	Threonine	Threonine	Threonine	Proline	Threonine	Threonine	Proline
128	Alanine	Valine	Alanine	Valine	Alanine	Valine	Valine	Alanine
129	Glutamine	Glutamine	Glutamine	Glutamine	Glutamine	Glutamine	Glutamine	Glutamine
130	Glycine	Glycine	Glycine	Glycine	Glycine	Glycine	Glycine	Glycine
131	Threonine	Threonine	Threonine	Threonine	Threonine	Threonine	Alanine	Threonine
132	Serine	Serine	Serine	Serine	Serine	Serine	Serine	Serine
133	Methionine	Methionine	Methionine	Methionine	Methionine	Methionine	Methionine	Methionine
134	Tyrosine	Tyrosine	Tyrosine	Tyrosine	Tyrosine	Tyrosine	Tyrosine	Tyrosine
135	Proline	Proline	Proline	Proline	Proline	Proline	Proline	Proline
136	Serine	Serine	Serine	Serine	Serine	Serine	Serine	Serine
137	Cysteine	Cysteine	Cysteine	Cysteine	Arginine	Cysteine	Cysteine	Cysteine

**Table-2:** Mutations in MHR Region from amino acid sequence 118-137.

escape variants or for patients who have been therapeutically administered monoclonal anti-HBs.<sup>7</sup> This hypothesis could not be tested in this study as none of eleven patients showed G145R change and moreover none of these eleven patients gave history of receiving HBV vaccine. It is important that the changes in residues observed in the subjects with presence of both HBsAg and anti-HBs antibodies are not only at the characteristic positions but also throughout loops 2 to 4 of the antigenic loops. However, it is difficult to predict the structural and biochemical effects of these amino acid substitutions.

To summarize, several residue changes within the MHR that are found in patients carrying both HBsAg and anti-HBs antibodies need to be further characterized immunologically, it seems quite compelling that these changes may alter antibody recognition of the S protein. Little is known about the ramifications of such alterations on T-cell epitope recognition.

This coexistence of both HBsAg and anti HBs antibodies in patients can have several deleterious consequences though this profile is not associated with change in HBsAg quantification, differences of HBsAg quantification noticed depended on HBV genotype, and type of antibody (monoclonal or polyclonal) and the targeted epitope used in the assays.<sup>13</sup>

The accumulation of HBV carrying immune escape mutations in CHB patients with fairly high viral loads raises the issue of transmission of such variant virus as they may not be fully neutralized by vaccine-induced antibodies, leading to widespread vaccination failure. In light of our data, chronic carriers possessing both HBsAg and anti-HBs antibodies should be considered potential reservoirs of immune escape variants. Further epidemiological studies are required to scientifically assess the probable threat of such chronic carriers in areas of high endemicity because in this setting, ambiguity about the response of patients to conventional therapies.<sup>14</sup>

There are studies which suggest that these patients may be more prone to advance liver diseases like hepatocellular carcinoma so there can be unknown factors other than immune suppression which may also be responsible for this coexistence of HBsAg and anti HBs antibodies in patients of chronic hepatitis B infection.<sup>15</sup> This profile may not always be associated with chronic active hepatitis as mentioned in Western literature. There is no clinical or biochemical parameter present which can flag these patients, hence high degree of suspicion is necessary to diagnose the condition. Most common accumulation of mutations (5 out of 7 samples) seen in this study was at position 127. Other common sites of mutation were at positions 128 and 118 (4 out of 7 samples).

Finally when screening a patient for the presence of vaccine induced antibodies, it may be useful to propose at least the detection of HBsAg as both markers may be present simultaneously and such an infected person can go undetected

## CONCLUSION

Although our findings are limited by a relatively younger population, accumulation of residue changes within the MHR, including the highly conformational and cysteine-rich “a” determinant can be a possible mechanism for coexistence of HBsAg and anti HBs antibodies in patients of chronic hepatitis B infection. The accumulation of HBV carrying immune escape variants in patients of CHB infection with relatively high viral

loads raises the problem of transmission of such variants as they may not be fully neutralized by vaccine-induced antibodies, leading to wide spread vaccination failure. There is no clinical or biochemical parameter which could be used to flag these patients from other CHB patients hence these patients were indistinguishable clinically. Therefore, when screening a patient for the presence of vaccine induced antibodies, it is useful to propose detection of HBs Ag since both markers may be present simultaneously and a person with hepatitis B infection can thus go undetected.

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# Is the Cost of Laparoscopic Ventral Hernia Repair Justified by Better Wound Results and Early Return to Work

Chaphekar AP<sup>1</sup>, Belgaumwala T<sup>2</sup>

## ABSTRACT

**Introduction:** Ventral hernias are a common condition in a younger working population. These are currently treated by either the open method or by laparoscopic repair. The commonly used open procedure is the onlay mesh which is accompanied by a high rate of wound complications and also requires the placement of a closed suction drain for a variable period of time, during which the patient cannot return to work. The tissue separating mesh used in the laparoscopic procedure involves a several-fold increased cost but does not involve the placement of drains and is accompanied by fewer wound complications. This study was carried out to compare these two methods with respect to wound complications, post-operative pain and specially, early return to work.

**Material and Methods:** Data from laparoscopic repair and open repair for ventral hernias conducted at a large teaching hospital over a 3 year period was collected and analysed. 23 patients underwent laparoscopic repair, 25 patients were subjected to open surgery and 2 patients were converted from laparoscopic to open surgery. The groups were compared for operating time, post-operative pain, analgesic requirement, wound complications, duration of hospital stay, return to normal activities and return to work.

**Results:** The laparoscopic method showed a significant, early return to normal activities and early return to work as compared with the open technique.

**Conclusion:** The laparoscopic method of ventral hernia repair has better outcomes in terms of wound healing and early return to work, potentially justifying, in selected cases the increased costs.

**Keywords:** Ventral Hernia Repair, laparoscopic hernia repair, open ventral hernia, tissue separating mesh.

## INTRODUCTION

The term ventral hernia commonly refers to hernias of the anterior abdominal wall which may be umbilical, paraumbilical, epigastric or following surgery, when they are called incisional hernias. Parastomal, Spigelian, Lumbar and traumatic hernias are also sometimes included in this group, but the present study does not include these latter forms of ventral hernia.<sup>1</sup> The incidence of these hernias has been increasing, occurring in younger patients leading an active working lifestyle and they constitute a large burden on the healthcare system.<sup>2-3</sup>

The advantages of laparoscopic surgery which include decreased postoperative pain, better wound healing and early return to work are well documented for all procedures where the laparoscopic approach can be used.

In the case of ventral hernias, however, there is more to this comparison. The cost of a laparoscopic mesh repair for ventral hernias exceeds that of open repair by several fold. This is due to the cost of the tissue separating mesh and tacking device which need to be used in the repair.

This study was undertaken to see whether there is a sufficient reduction in the time taken to resume normal activities and

normal work, as also a reduction in the incidence of wound complications, which could justify the use of the laparoscopic method in spite of the high cost involved.

## MATERIAL AND METHODS

Data from 50 patients undergoing ventral hernia surgery at BYL Nair Charitable hospital and the associated TN Medical College, a major tertiary care teaching Institution in Mumbai, was collected. In the duration of the study, between May 2011 to May 2013, 25 consecutive patients undergoing laparoscopic repair and 25 consecutive patients undergoing open repair were included in the study based on inclusion exclusion criteria. Ethical clearance from the institutional ethical board and informed consent from the patients were taken before the start of the study.

**Inclusion criteria:** All patients with ventral hernia in the age group 18-70 years who were to be operated on an elective basis were included in the study.

**Exclusion criteria:** All patients below 18 years and above 70 years of age were excluded. Patients who had infection related to the hernia site were excluded from the study. Those patients undergoing open surgery who had been deemed unfit for General Anaesthesia and laparoscopy were also excluded from the study. This exclusion would make the two groups matched as regards respiratory status of the patients.

Patients with size of hernia defect >10cm were excluded as this would preclude laparoscopic repair and a matching patient in the laparoscopy group would not be found. The size of 10cm was based on available evidence in the literature.<sup>4-5</sup>

Patients with intra-abdominal sepsis and peritonitis were excluded.

Patients with ascites, patients with systemic disease like renal failure, liver failure, uncontrolled diabetes mellitus and neuropathies and patients with history of radiotherapy, pregnancy or severe cardio pulmonary disease were excluded. Patients undergoing emergency surgery for Incarcerated or strangulated hernias were excluded.

Patients were worked up as outpatient and admitted one day prior to surgery. All patients were kept nil orally for 6 hours preceding surgery. Urinary catheter was passed before starting surgery in all laparoscopic repair cases and this was optional for open repairs. Urinary catheter was removed at the conclusion of

<sup>1</sup>Associate Professor, <sup>2</sup>Resident, Department of General Surgery, TNMC and BYL Nair Ch. Hospital, Mumbai, India

**Corresponding author:** Chaphekar AP, C-4, dattaguru Society, Deonar Village Road, Deonar, Mumbai - 400088, India

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surgery. For post operative pain charting, Visual Analogue Scale (VAS) pain scoring chart was explained and discussed with the patients pre-operatively.<sup>6</sup>

In case of Umbilical and paraumbilical hernias, a midline incision skirting the umbilical scar was made. In case of Incisional hernias, the scar of previous surgery was excised to the extent required. This was followed by careful dissection to identify the hernial sac. The hernial sac was separated circumferentially from the surrounding fat. The Hernial sac was then opened and in case of incisional hernias, with a finger inserted into the peritoneal cavity, the anterior abdominal wall adjoining the defect was palpated to exclude any more defects. If these were present, the skin incision was appropriately increased in length and further dissection carried out. The redundant hernial sac was then excised. When possible, an anatomical closure of the rectus sheath was performed using non-absorbable polyamide sutures ( 0-Ethilon, Johnson and Johnson, New Brunswick, New Jersey). When anatomical closure was found to involve excessive tension, the hernial sac was closed using absorbable polyglactin sutures(2-0 vicryl, Johnson and Johnson).

The wound edges were then lifted up and a space was created between the subcutaneous tissue and the rectus sheath for placement of the mesh, ensuring at least a 5 cm. overlap of the mesh over the defect. The mesh was then placed as an 'onlay' over the external oblique aponeurosis. It was held in place by sutures of polypropelene. A suction drain was placed. Subcutaneous tissue and skin were closed.

In patients undergoing laparoscopic repair, the procedure was begun by insertion of a 10 mm trocar at palmer's point, using the open technique. This was followed by insertion, under vision of another 10 mm trocar in the flanks at the level of the umbilicus. A third, 5mm trocar was inserted at an appropriate site, as required. After visualization of the anterior abdominal wall, hernial contents were reduced into the peritoneal cavity. Any adhesions between the contents and the sac were divided using sharp dissection. The falciform ligament, as also the fat around the urachus and inferior umbilical arteries was cleared so as to create a uniform surface for placement of the mesh. PROCEED (Johnson and Johnson New Brunswick, New Jersey) mesh of appropriate size was used for the repair. 4 to 6 sutures of non-absorbable polypropelene (Prolene Johnson and Johnson) were taken on the mesh and left long. The mesh was then inserted into the abdomen through one of the 10 mm trocars. Small (1-2mm) incisions were made on the skin and the long prolene sutures were drawn out using a suture passer. The sutures were then loosely tied. The mesh was made flush with the anterior abdominal wall using PROTAC (Medtronic Dublin, Republic of Ireland) tackers, as required. The 10 mm trocar port sites were closed with transfascial sutures.

All patients were administered Injection Diclofenac 50 mg intramuscularly on demand during first 24 hours. Following that the patient was advised to take Tablet Diclofenac 50 mg orally whenever the patient felt significant pain and to record the same in the chart provided. Patients were advised to perform day-to-day activities immediately after recovering from the effects of anaesthesia. VAS pain score chart was filled by each patient as explained at 24 hours, 48 hours and 72 hours after surgery.

The study included a careful record of the following in the operating room:

**Operating Time:** This was the time between incision and closure of skin.

**Intra operative complications:** Trocar injury, Bladder or Bowel injury.

The post-operative record included:

Any Post-operative urinary retention/Ileus beyond 24 hours with vomiting, time taken for oral feeding, time to Ambulation and duration of post-operative stay in the hospital.

Patients were followed up in the outpatient department for presence of Fever, Wound infection, Periumbilical and rectus sheath hematoma, Neuralgia, stitch granulomas and port site hernias.

All patients undergoing open surgery were discharged with the closed suction system. This was removed at follow-up visits, if the drainage was minimal.

Time taken to return to daily activity and Time taken for return to work were noted. In the open repair group, the time taken for drain removal was noted. Follow up examination, to note recurrence of hernia at 1 month, 3 months and 6 months was carried out.

## STATISTICAL ANALYSIS

Statistical testing was conducted with the statistical package for the social science system version SPSS 17.0 (Chicago, IL, USA). Results are expressed as mean  $\pm$  SD, median (min-max) or numbers and percentages. The comparison of normally distributed continuous variables between the groups was performed using Student's t test. VAS scores between the groups were compared using Mann Whitney U test.

## RESULTS

The study included 23 patients with laparoscopic hernia repair and 25 patients undergoing open hernia. The two groups were well matched with respect to the age and sex distribution and size of the defect.

The mean age in the laparoscopy group was 41.6 yrs and in the open surgery group was 44.7 years.

The mean operating time in the laparoscopy group was 89 minutes whereas in the open group was 60 minutes. This was statistically significant ( $P<0.001$ ). However, the increased operative time was attributed to the use of 4 to 6 transfacial sutures being used to fix the mesh.

Pain and analgesic requirement were significantly higher at 24 and 48 hrs. in the post-op. period in the open group as compared to the laparoscopic group ( $P=0.003$  and  $P=0.004$  respectively). However, pain and analgesic requirement was not significantly different at 72 hrs. post-op. and thereafter( $P=0.19$ ).

Median(range) post operative hospital stay for the open group was 4 (3-6) days while it was 3 (2-4) in the laparoscopy group, which was statistically significant ( $P<0.01$ ) (Table-1).

Patients with Open repair took more time to return to normal activities like ambulation, personal dressing and toilet use with mean of  $1.76 \pm 0.6$  days as compared to  $1.39 \pm 0.58$  days in the Laparoscopic repair group which was statistically significant ( $P= 0.036$ , Table-2).

The mean time to drain removal was 10.7 days in the open group.

Patients with Open repair took significantly more time to return to work with mean of  $14 \pm 1.77$  days as compared to  $8.96 \pm 0.88$

Duration of Hospital Stay	Laparoscopic (n=23)(%)	Open (n=25)(%)
2 days	11 (47.82%)	0 (0%)
3 days	9 (39.13 %)	10 (40%)
4 days	3 (13.04 %)	12 (48%)
5 days	0 (0%)	2 (8%)
6 days	0 (0%)	1 (4%)

**Table-1:** Comparison of duration of hospital stay.

	Laparoscopic (n=23)(%)	Open (n=25)(%)	P value
Return to normal Activity (Days)	1.39 ± 0.58	1.76 ± 0.6	0.0359

**Table-2:** Comparison of time taken for return to normal activity

	Laparoscopic	Open	P Value
Return to Work	8.96 ± 0.88	14 ± 1.77	<0.0001

**Table-3:** Comparison of time taken for return to Work.

days in Laparoscopic repair group (Table-3).

There was 1 case of hernia recurrence in the present study in the laparoscopic converted to open group in the follow up till the date of completion of study.

## DISCUSSION

The ventral hernia, whether it is umbilical or following surgery is not covered by healthy skin, but by scar tissue, which might be the umbilical scar or the scar of previous surgery. The approach to the hernial sac involves incising scar tissue and excising as much of it as will allow satisfactory wound closure. The ‘onlay’ technique of hernia repair necessitates dissection of soft tissues, between the external Oblique aponeurosis and the subcutaneous tissues, to create adequate space for the placement of the mesh, with adequate overlap of the hernial defect. This dissection almost always involves injury to or division of the penetrating branches of the intercostal vessels and nerves, which compromises blood supply to the skin and wound edges. The opening up of a large space in the subcutaneous tissues results in fluid collection around the mesh and a closed system of suction drainage needs to be frequently used. Traditional teaching has been that regardless of the location of the mesh, a drain needs to be placed after open mesh repair of ventral hernias, and this is common practice.<sup>7</sup> The suction drain needs to be kept for varying periods of time in the postoperative period. While the drain itself may not be the cause of significant discomfort, it effectively precludes returning to work in most patients. The incidence of wound complications is also significantly higher with discoloration and necrosis of wound edges, being common.<sup>8</sup> The incision may sometimes require the excision of the umbilicus which is found cosmetically unacceptable by many patients.

The Laparoscopic method involves approaching the hernia through a separate port site, that is, through healthy skin. The placement of the mesh is also intraperitoneal, does not involve dissection and creation of spaces and hence involves none of the issues relating to wound healing that are a matter of concern in open surgery as described above.

There is, however a significant difference in the costs of laparoscopic and open repair. The cost of the dual layered mesh is several fold higher than the cost of the mesh used at open

surgery. There is also the cost of fixation devices which are used for fixation of the intraperitoneal mesh.

This study was conducted to find out whether the traditionally claimed advantages of laparoscopic surgery over open procedures, viz. decreased post-operative pain, decreased wound complications and early return to work are observed in sufficient measure in laparoscopic ventral hernia repair.

Our study showed a significant difference, in terms of the length of hospital stay, days taken to return to normal activities and days before return to work. Beldi et al. have found significant decrease in hospitalization time and fewer wound infection rates with laparoscopic repair.<sup>9</sup> They also noted that though the direct cost of surgery was higher with laparoscopy, the overall cost was lower with laparoscopic repair. Bedi et al. have reported similar results.<sup>10</sup>

Our study did not show a significant difference in wound infection rates and rates of seroma formation between the laparoscopic and open groups. However, Sauerland et al. in a review of the literature found consistently that laparoscopy reduced the rate of wound infections.<sup>11</sup>

A randomized controlled trial by Olmi et al. shows shorter hospitalization, early return to work and decreased wound complication rates with the laparoscopic method.<sup>12</sup>

Our study showed an increased operative time in the laparoscopy group. Hasan et al have reported increased operative time and a higher operative complication rate with the laparoscopy group.<sup>13</sup> However, our study did not show an increased rate of operative complications.

Our study was carried out with prospective data and utilizes objective, measurable parameters to compare the two methods of treatment. However, time to resume normal activities and return to work, although clearly measurable tend to vary between patients, depending upon the nature of work, motivation to return to work, physical fitness before and after surgery and considerations like availability of leave from work.

Also, the balance between increased costs and the benefits of laparoscopy would have to be evaluated by each patient individually depending on his/ her particular situation. A cosmetically acceptable umbilicus and early return to work may be perceived as being important by some patients. An urban, working person would be concerned about how a loss of work days during which the patient is required to carry around the suction apparatus will impact his or her job and the financial loss thereof; the presence of a drain would also restrict performance of his/her domestic chores.

**Conclusion:** Ventral hernia repair is an elective procedure. In a young, working, urban patient, the ability to return to domestic chores and to work, after surgery may be critical issues. While the laparoscopic method of repair cannot at present be unequivocally recommended for all patients, In selected patients, the earlier return to normal activity and work could justify the high cost of laparoscopic hernia repair.

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# Recurrent Pain Abdomen Among Children- An Emphasis on Base Line Investigations

Shruti Saraswat<sup>1</sup>, Satish Mohanty<sup>1</sup>

## ABSTRACT

**Introduction:** Recurrent abdominal pain (RAP), a frequent presenting complaint in general practice, first defined by Apley as “episodes of pain occurring at least monthly for three consecutive months with severity that interrupts routine functioning”. Pain is classified as either organic or non-organic, with a plenitude of factors being implicated in genesis. The symptoms tend to be vague and investigations seldom show organic disease. Study was done to determine the causes of RAP in 5-14 years old children visiting the Paediatric OPDs on the basis of baseline tests that includes urine routine examination, stool routine examination and sonography.

**Material and methods:** A total of 112 children with recurrent pain abdomen were enrolled in the prospective observational study. Detailed history was taken following which general and systemic examination was done. Complete blood count, urine and stool routine microscopy and ultrasound abdomen were done. Additional investigations like X-ray chest and abdomen, barium meal study, tuberculin and serological test for tuberculosis were carried out based on their necessity. Patients were categorised into organic and functional (non-organic) groups.

**Results:** Out of 112 children with RAP, 86 were in 5-10 years age group and 26 were in 11-14 years. The site of pain abdomen was categorised as 63 in epigastric region followed by umbilical region and other areas. Among associated symptoms fever and vomiting were present in most of the cases apart from loose stools, constipation, chest pain and burning micturition. Pain in relation to food was observed in 35 children. USG abdomen showed retro peritoneal lymphadenopathy in 4 children and 2 patients were suffering from abdominal tuberculosis. Fifty three children revealed an organic cause from the basic investigations.

**Conclusions:** Baseline investigations can lead to a diagnosis in 47% cases of recurrent abdominal pain in children.

**Keywords:** recurrent abdominal pain, organic or non-organic

## INTRODUCTION

Abdominal pain is one of the common health problems encountered in school aged children. Most parents are ignorant about the complaints presuming the self-limiting and transient nature of such episodes. Very often the etiology is undetectable and are considered as functional.

The term Recurrent Abdominal Pain came into existence as early as 1958. J Apley evaluated abdominal pain among children extensively and concluded nearly 10% of his subjects perceiving recurrent pain abdomen, with a slight female preponderance 12.3% as compared to 9.5% in males.<sup>1</sup> He coined this symptom complex as recurrent abdominal pain (RAP) syndrome and defined it as “episodes of pain occurring at least monthly for three consecutive months with severity that interrupts routine functioning”. RAP is seen among 10-12% of school aged children with female preponderance.<sup>2-5</sup>

Inspite of being one of the most common complaints, this is one

of most difficult symptoms to evaluate at bedside owing to its varying magnitude of etiology. Eliciting a proper localisation from the child and the pretension of abdominal pain when the child is in an uncomfortable or stressful situation or as a result of nausea, or urge to defecate; hinder the pediatrician in reaching a specific diagnosis.

Pain is categorised as either organic or non-organic, depending on whether a specific etiology of the pain is detected. In studies using Apley’s definition of RAP the prevalence ranged from 11% to 45%.<sup>6-9</sup> The present study was undertaken to study the etiological factors related to RAP with an objective to find out organic causes with help of routine investigations.

Study aimed to determine incidence of recurrent abdominal pain in children in the age group of 5-14 years coming to the pediatric OPD of Hi Tech Medical College and Hospital, Bhubaneswar and to study the role of routine urinalysis, stool analysis and ultrasonography of abdomen and pelvis in children presenting with recurrent pain abdomen.

## MATERIAL AND METHODS

This study was conducted in Hi-Tech Medical College And Hospital, Bhubaneswar. This prospective study was done from February 2015 to September 2015 of HMCH after ethical approval from the institutional ethical board and the informed consent from the school authorities/ parents/ children. All children presenting with recurrent pain abdomen in the age group of 5-14 years were included in the study. Subjects with acute pain abdomen, with any previously diagnosed organic cause and girls with any menstrual problems or any suspicion of pregnancy formed the exclusion criteria of the study.

A total of 112 children were evaluated having complaints of recurrent pain abdomen. History of pain abdomen with features like localisation, relieving and aggravating factors, correlation with symptoms, dietary history, family history was taken, followed by thorough general physical examination and systemic clinical examination. Laboratory investigations like complete blood count, urine and stool routine examination and ultrasonography of abdomen and pelvis was done. Special investigations like X-ray chest, tuberculin and serological test for tuberculosis were carried out as and when necessary. Upper gastrointestinal endoscopy and serum amylase were performed,

<sup>1</sup>Paediatrics, Hi Tech Medical College, Utkal University, Bhubaneswar, Odisha, India

**Corresponding author:** Dr. Satish Mohanty, Plot No. VIM-678, Sailashree Vihar, At/PO Chandrashekharpur, Bhubaneswar 751021, Odisha, India

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whenever indicated.

Based on the baseline investigations, the subjects were categorised into organic and non-organic causes of RAP. Children, who were considered to have an organic cause were treated as per the cause and followed for at least 3 months. Organic RAP was labelled when: (a) an organic cause was demonstrated, (b) there was clinical and laboratory response to treatment, and (c) there was sustained remission from abdominal pain for at least three months after treatment. Rest of the patients, labelled as non-organic RAP (NORAP), were assessed by a psychiatrist and accordingly managed for 4-6 months. 32 patients of NORAP who were unable to get relief of pain even after 6 months follow up, were subjected to upper GI endoscopy, EEG and serum amylase estimation.

### STATISTICAL ANALYSIS

Statistical analysis and tables were made with the help of Microsoft office 2007. Descriptive statistics like mean and percentages were used to infer the results.

### RESULTS

A total of 112 subjects were recruited in the study. Out of this 86 were in 5-10 years age group and 26 were in 11-14 years. Male-female ratio was 1.12:1, with slight male preponderance of about 52% than in females. Eighty eight of them had complaints of RAP for 3-6 months and rest 24 children had for more than 6 months duration. 63 children had pain in epigastric region, 32 had around umbilical region, 13 had in lumbar region, and 4 children in iliac region. Associated symptoms such as fever was present in 51 children out of 112, vomiting was present in 32 children, 4 children complained pain abdomen associated with loose motion, constipation in 10, chest pain or heart burn was present in 9 patients and 6 children with burning micturition. As regards to dietary history 77 children had no relation of pain with food intake. The clinico-demographic characters have been summarised in Table-1.

On investigation, UTI was ascertained in 26 cases, urine routine microscopy showed that 15 children had significant pus cells in urine, 6 had epithelial cells, 10 had occult blood and 5 had RBCs in urine examination.

Stool routine microscopy showed worm infestation in 15 children ( 7 had ascaris, 4 had giardia, 2 had hook worm, and 1 each roundworm and strongyloids ). USG abdomen and pelvis showed renal calculi in 1 patient and non-specific retro peritoneal lymphadenitis in 4 children. Upper gastrointestinal endoscopy in 8 patients above the age of seven years revealed esophagitis in 2 and gastritis in 3 with one patient harbouring *H. pylori* infection. Two patients had abdominal tuberculosis confirmed on ultrasonography, tuberculin and ELISA tests and examination of ascitic fluid.

Fifty three children revealed an organic cause for RAP on basis of first line investigation. Remaining were 59 children, in which 18 children were suffering from psychogenic problems related

to family, friend, studies and school. Other 41 children had no obvious cause could be evaluated. psycho-therapy was given in patients with NORAP. Of patients with NORAP, 77% were pain-free within 4-6 months except a few who persisted with pain and in whom endoscopy, EEG and serum amylase levels were normal.

### DISCUSSION

Tackling the problem of pain abdomen is nagging to the children experiencing it as well as for the family and medical professionals owing to its complex origin. A series of investigations may be needed to thoroughly evaluate and establish the diagnosis. In our study most of the children (77%) were between the age group of 5-10 years. In our study majority of patients subjected to RAP were boys in contrast to Apley et al<sup>1</sup> and Galler et al<sup>10</sup> where girls were affected more common than boys. Our findings may have been due to the extra cautiousness with which the male gender is taken care of in comparison to female children. In a society where girl children are still considered as a liability, few parents prefer not to spend much on their daughters. Gadiyar et al<sup>11</sup> found almost equal incidence of pain in abdomen in males and females.

The present study showed worm infestation in 13.3% of children with RAP. Celia et al<sup>12</sup> reported parasitic infections among school children in an African country as follows: Ascaris, trichurus trichura, hookworm and strongyloides stercoralis in 88.5%, 84.5%, 33.1% and 3% respectively. Saxena et al<sup>13</sup> showed oxyuriasis in 34% of patients with vague abdominal pain whereas Gadiyar et al<sup>11</sup> reported 24% of the children were having helminthic infections. Most studies in India have recognized giardiasis, as the leading cause for intestinal parasitic infections causing RAP<sup>14,15</sup>.

About 47% revealed an organic cause for RAP from basis first line investigation. Eighteen (16%) children were suffering from psychogenic problems related to family, friend, studies and school. Rest 37% no cause could be ascertained. Table-2 gives a comparative etiological analysis for RAP done in various parts of the world.<sup>11,17-19</sup>

Gadiyar et al reported organic causes in 62%, psychogenic in 25% and rest 13% were considered idiopathic. Relationship of stress with RAP have been well established.<sup>14,5</sup> Very often there is a family history of similar problems, which may include first-degree relatives too. Campo et al.<sup>16</sup> found that anxiety and depressive disorders were more prevalent in pediatric patients with recurrent abdominal pain.

Psychogenic illness manifests as functional pain abdomen but it is not the only entity that signifies functional abdominal pain. It must be bore in mind that diagnosis of functional pain abdomen is a diagnosis of exclusion. The site of abnormality could be the gut, spinal afferents, central autonomic relay system or brain.

In our study most of the patients perceived pain in the epigastric region followed by the umbilical region. This is contrary to various literatures where the commonest presentation is

	Present study	Reddy et al <sup>17</sup>	Manchanda et al <sup>18</sup>	Gupta et al <sup>19</sup>	Gadiyar et al <sup>11</sup>
Organic	47%	74%	45%	85%	62%
Functional	16%	13%	-	15%	25%
Inconclusive	37%	13%	-	-	13%

Table-2: Comparison with Previous studies

		n=112	Percentage
Age	5-10 years	86	77%
	11-14 years	26	23%
Gender	Male	58	52%
	Female	54	48%
Duration	3-6 months	88	79%
	>6 months	24	21%
Site	Epigastric	63	56%
	Umbilical	32	28%
	Lumbar	13	12%
	Iliac	4	4%
Associated symptoms	Fever	51	46%
	Vomiting	32	28%
	Loose motion	4	4%
	Constipation	10	9%
	Chest pain	9	8%
	Burning micturition	6	5%
Effect of food intake	Aggravates	16	14%
	Relieves	19	17%
	No impact	77	69%

**Table-1:** Demography and Clinical Profile of Subjects

perumbilical pain, which may be associated with nausea and vomiting.<sup>1,4</sup> The growing preference for junk food and the craving for street food leading to gastritis may have been responsible for us getting a high incidence of epigastric localization. Very often when the child reaches the OPD, the pain has already subsided and it is not possible for the child to give the site accurately. In our study 1 patient showed H.pylori infection. Donohue et al.<sup>20</sup> reported no relation between positive serology and a history of recurrent abdominal pain in a large sample of urban school children. It might have been an incidental finding in our case, as there is no strong evidence that H pylori infection perse causes pain.

Several studies point towards a contributory role of lactose malabsorption in the symptoms of RAP<sup>21</sup>, but none of our cases had supportive evidence for such a condition.

Several large-scale studies have been carried out to ascertain the benefit of fiber supplements and lactose restricting diets in relieving episodes of RAP, but they have been inconclusive.<sup>22</sup> Though a few studies like the one done by Feldman, et al.<sup>23</sup> reported a significant benefit of fiber supplementation. Short durations of cognitive- behavioral family treatment (CBT) have resulted in significant improvement of symptoms and fewer school absenteeism in children with RAP.<sup>24,25</sup> However there are a few studies, which question the benefit of CBT.<sup>26</sup>

### Limitations

The present study had limitations like small sample size. Follow up of patients was not done for prolonged period into adulthood, which would help us to know the end result of non-organic subjects. Certain studies show a higher existence of RAP in lower stratas of the society but socioeconomic stratification could not be done in our study.

### CONCLUSION

The importance of baseline investigations must be stressed as they can help in making the diagnosis of 47% of children with RAP having an organic cause. Most cases of RAP localise to epigastric region and perumbilical region, with the commonest

age group of presentation being 5-10 years with male preponderance. In the remaining 53% were non-organic cases. 16% were diagnosed as psychogenic cause for pain abdomen. The rest of the cases may require additional investigations.

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# Clinico-Audiological Comparison between Classical Type-III Tympanoplasty and Ossiculoplasty using Autograft Ossicles in Patients with Austin Type A Defect

Bivas Adhikari<sup>1</sup>, Amit Kumar Ghosh<sup>2</sup>, Sudipta Pal<sup>3</sup>, Faizanul Haque<sup>4</sup>

## ABSTRACT

**Introduction:** Ossicular chain necrosis, a frequent complication of COM can be of various types. Austin type-A defect where only the incus is damaged can be treated by either type-3 tympanoplasty or with ossiculoplasty using sculpted autologous incus as interposition graft. This study was done to compare the hearing outcomes in patients underwent these two procedures in a teaching hospital in India and to analyse and compare the hearing outcomes and graft uptake rates between the above mentioned procedures in Austin type-A ossicular defect.

**Material and Methods:** The Non-randomized prospective clinical study was conducted in the Department of ENT in a teaching hospital, from February 2013 to August 2014. 40 patients were selected based on inclusion and exclusion criteria. They underwent either tympanoplasty using sculpted autologous incus interposition between malleus and stapes or classical type-3 tympanoplasty. Post-operative evaluation and documentation done upto at least 6 months and results were analysed in terms of graft take-up rates and hearing improvement. Hearing results were measured by PTA-air bone gap (PTA-ABG) and graft take-up rate calculated at the end of 6 month.

**Results:** Amongst the 40 patients, 20 underwent tympanoplasty with autologous sculpted incus strut placement were termed as Group-A; other 20 underwent type-3 tympanoplasty were termed Group-B. Mean post-operative AB Gap reduction in Group-A was 31% in comparison to Group B where reduction was 14.4%. Graft uptake rate was almost same in both Groups.

**Conclusion:** This study couldn't establish statistically significant difference in the outcome between the two procedures.

**Keywords:** Chronic otitis media; Austin type-A defect; Tympanoplasty; Ossiculoplasty; Incus auto-graft;

## INTRODUCTION

Chronic Otitis Media (COM) is a chronic inflammatory disease of the middle ear and mastoid that often results in partial or total loss of the tympanic membrane (TM) and ossicles, leading to conductive hearing loss that can range in severity up to 60dB. COM is a common condition seen in patients attending the otolaryngology clinic and is an important public health problem with substantial economic and social costs, affecting 0.5 – 30% of the community. A conservative estimate of the no. of people in the world suffering from COM is over 20 million<sup>1</sup>. As per WHO, the prevalence of COM in Indian population is approximately 7.8% which is comparatively higher than that found in developed countries like that of USA and UK where the prevalence is <1%.<sup>2,3</sup> According to another study, the prevalence of squamous type of COM is approximately 3.4% in India.<sup>4</sup> Among the various causes of ear diseases, COM is a major global cause of hearing impairment and may have serious long term effects on language, auditory, cognitive development

and educational progress.<sup>4</sup>

With the advancement in understanding of the middle ear mechanics, it is now known that the hearing deterioration in COM is attributed to the destruction of ear drum and/or damage to the ossicular chain. So the therapeutic practices and regimes have also evolved over time. Ossicular involvement in COM patients can present in many ways and the commonest finding is erosion of incus but intact malleus and stapes (Austin type-A ossicular defect).<sup>5-7</sup> Over time the otologists have used a wide array of materials and surgical techniques to give the patient maximum benefit, however, till date there is no universal protocol or guidelines to manage these cases.<sup>8</sup>

In this study we selected 40 patients of COM with Austin type-A ossicular defect and subjected them to two surgical procedures-- classical type-3 tympanoplasty or tympanoplasty with placement of incus strut and assessed post-operatively for drum closure and hearing improvement. With both procedures, improved hearing results have been demonstrated earlier in various studies. In this study we intend to document, analyse and compare the result of both the procedures in this particular presentation of COM.

## MATERIAL AND METHODS

A total of 40 patients in the age group between 12 and 65 years, attending ENT OPD of our hospital between February 2013 and August 2014, were included in this study. Study sample was based on the inclusion exclusion criteria followed in the study. The inclusion criteria for the patients were those with chronic otitis media with conductive hearing loss having Austin type-A ossicular discontinuity, ie, patients with intact malleus and stapes superstructure and eroded long process of incus. Patients with sensorineural or mixed hearing loss, gross cholesteatoma, intra-cranial complications were excluded from our study. The patients underwent detailed ENT examination followed by audiological and radiological assessment of temporal bone and after per-operative confirmation of Austin type-A defect (intact malleus and stapes with eroded long process of incus) they were included in the study. These patients randomly underwent two surgical procedures—(a) tympanoplasty with placement of

<sup>1</sup>Associate Professor, <sup>2</sup>Senior Resident, <sup>3</sup>Assistant Professor, <sup>4</sup>Post Graduate Trainee, Department of ENT, Calcutta National Medical College, India

**Corresponding author:** Dr. Amit Kumar Ghosh, 148/C, Linton Street, Kolkata-700014, 2nd floor,

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sculpted autologous incus in between malleus and stapes and ( b) classical type-3 tympanoplasty after removal of the eroded incus. Those who underwent tympanoplasty with placement of sculpted autologous incus in between malleus and stapes were included in Group-A and those who underwent classical type-3 tympanoplasty were included in Group-B. Both the groups were followed post-operatively and assessed clinically and audiologicaly up to the end of 6 months.

Ethical clearance was obtained from the institution's ethical committee for research on human subjects. Written informed consent was obtained from all the cases.

### Surgical Procedures

All procedures were done under general anaesthesia by the same team of surgeons. Post-aural approach through Wilde's incision was done in all the patients. Limited atticotomy was done to expose the ossicular chain which was later reconstructed with tragal cartilage. In cases included in Group-A, the eroded incus was taken out, reshaped and sculpted with the help of 0.5mm diamond burr. The remaining long process was drilled into cylindrical shape with a flat base where a socket for the head of stapes was made. A groove was also made in short process to accommodate the malleus handle. The sculpted incus was then interposed in between malleus and stapes head and the contact sites were covered with small strip of temporalis fascia. To reconstruct the tympanic membrane, sliced tragal cartilage and temporalis fascia graft was used. In patients of Group-B, the eroded incus was disarticulated from the malleus and removed. The head of stapes was covered by sliced tragal cartilage along with temporalis fascia graft placed lateral to the cartilage.

### Outcome Measures

Post-operative PTA was done at end of 6 months follow up using 4 frequencies— 500 Hz, 1 KHz, 2 KHz and 4KHz. Post-operative air conduction threshold (AC), bone conduction threshold (BC) and air-bone gap (ABG) were calculated. Anatomical closure of the perforation and integrity of the neo tympanum was assessed microscopically.

### STATISTICAL ANALYSIS

All data were subjected to standard statistical analysis using

Age distribution (years)	Group A (n=20)		Group B (n=20)	
	Male	Female	Male	Female
15-25	4	1	11	4
26-35	4	3	0	2
36-45	4	4	0	1
46-55	0	0	1	0
56-65	0	0	0	1
Total	12	8	12	8

Table-1: Age and Sex distribution

Group	Pre-op AC (mean) (dB)	Post-op AC (mean) at 6 <sup>th</sup> month (dB)	Statistical test
A(n=20)	47.7	38.05	t test=8.666,p=0.0001
B(n=20)	51.05	44.05	t test=3.908,p=0.0009

Table-2: Pre and post-operative average AC threshold in either

Group	Pre-op AB Gap(dB) (Mean)	Post-op AB Gap(dB) at 6 <sup>th</sup> month(Mean)	Statistical test
A(n=20)	42.6dB	29.6 dB	t test=9.185,p=<0.0001
B(n=20)	42.4dB	36.3 dB	t test=3.954,p=0.0009

Table-3: Pre and post-operative mean AB Gaps in either group

Microsoft excel, 2010 software. Unpaired t-test was used to determine the statistical significance between the two groups and paired t-test was used to analyse the pre-operative and post-operative hearing result in the same group.

### RESULTS

A total of 40 patients were included in the study among which 20 patients underwent tympanoplasty with placement of sculpted autologous incus (Group-A) and other 20 patients underwent classical type-3 tympanoplasty.

#### Age and Sex Distribution

The age of patients in this study varied between 15-65 years. The mean age in Group A was 31.15 years and in Group B was 29.35 years. In both groups majority of patients were males (Group A- 60%, Group B- 60%). The ratio between total male and total female was 3:2. Maximum age in group-A and group-B were 45 years and 63 years respectively, whereas the minimum age in both the groups was 15 years. (Table-1)

#### Graft Take-Up Rate

The graft take-up rate in Group-A at 6th post-operative month was 90% (18 out of 20) where as it was 85% (17 out of 20) in Group-B. Number of graft failure in Group-A was 2(10%) and it was 3 (12.5%) in Group-B. However the anatomical closure rate in the two procedures did not have any statistically significant difference as per the present study.

#### Assessment of Hearing Improvement

On comparing the improvement in mean AC threshold during the post-operative period in Group A, it was found that there was a 24.27% change, from 50.25 dB in the pre-operative period to 38.05 dB at the end of 6 months.(t test=8.666, p=o.0001). Similarly in Group B there was an improvement of around was 13.71 %, from pre-operative 51.05 dB to 44.05 dB in 6 months post-operative (t test=3.908, p=0.0009), hence a significantly better improvement in air conduction threshold could be achieved in both the groups. (Table-2)

The mean post-operative AB Gap in Group-A was 29.6 dB (SD 13.4 ) showing 31% improvement over pre-operative mean AB Gap of 42.6 dB and this was statistically significant (paired t-test: t=9.185,p=<0.0001). Whereas in Group-B this improvement was 14.4%; mean pre-op AB Gap 42.4 dB, mean post-op AB Gap 36.3 dB (SD 12.1), (paired t-test: t=3.954, p=0.0009); (Table-3) and this was also statistically significant. However the difference in hearing improvement between the two groups was statistically insignificant. ( unpaired t-test: test t value=1.644; critical t value=2.024 at p=0.05,ie, test t value< critical t value at p=0.05) So, from this study, it was established that there is no significant difference between the two procedures as far as hearing improvement and perforation closure is concerned.

## DISCUSSION

The term tympanoplasty was coined in 1953 by Wullstein to describe surgical techniques for reconstruction of middle ear hearing mechanism that had been impaired or destroyed by chronic middle ear disease.<sup>5</sup> Tympanoplasty implies clearance of the disease from the middle ear and attic with reconstruction of the hearing mechanism. It may include ossiculoplasty as a part of reconstruction of hearing mechanism. The long process of incus is most commonly eroded because of its peculiar anatomical position and the course of its blood supply.<sup>5,6</sup> And maybe that's why Austin type-A is the commonest ossicular defect found in COM.<sup>7</sup> Various surgical techniques and materials have been used for ossicular chain reconstruction since the second half of nineteenth century, but still there is no standardized technique and ideal material accepted worldwide. Three general classes of materials are used today are autograft, homograft and allograft.<sup>6</sup> Allograft prostheses are readily available, which are pre-sculpted, and made of synthetic materials like hydroxyapatite, plastipore, titanium, glass ceramics, etc., and designed to be biocompatible. But in the long term, ossicular necrosis, extrusion, displacement, and unsatisfactory hearing restoration have been encountered with virtually every type and design. Extrusion of the prosthesis has been reported to be as high as 39%.<sup>9</sup>

Autograft include ossicles (incus, malleus), cartilages (septal, tragal), cortical bone etc. Advantages of autografts include a very low extrusion rate, no risk of transmitting disease, biocompatibility, and no necessity for reconstitution.<sup>10</sup> Cost effectiveness compared to PORP or TORP or other alloprosthetic materials, particularly to the financially challenged patients in our study area and the ease of harvesting were the main reasons to go for autograft in our study.

In this study the mean age in Group A was 31.35yr and 26.95yr in Group B. In Group A the age range was 15-45 years and in Group B it was 15-63 years. However no particular relationship could be established between the age of the patients and success rate of both the procedures as was seen from the studies of Iliana Fukuchi et al.<sup>11</sup>

Quantitatively the drum closure was better in tympanoplasty with incus strut placement at 6th post-operative month than in

classical type-3 tympanoplasty (stapes columella). There was graft failure in 2 cases with incus transposition group and in 3 cases with classical Type 3 tympanoplasty group. None of the patients develop retraction pocket in the newly formed ear drum.

Post-operatively, the patients in Group-A who underwent incus transposition achieved mean post-operative AB Gap of 29.6 dB, that is, 31% improvement over pre-operative mean AB Gap of 42.6dB which was statistically significant. Whereas in Group-B this improvement was 14.4% (mean pre-op AB Gap is 42.4 dB, mean post-op AB Gap is 36.3 dB) and this was also statistically significant. However, 1 patient in Group-A and 3 patients in Group-B had deterioration of hearing post-operatively with increase in the air-bone gap. This may be due to rejection of graft and reinfection in the same patients. Thirty percent of the patients who underwent incus transposition achieved an air-bone gap within 20dB, 40% within 25dB and 85% within 30dB. Whereas among the patients who underwent classical type-3 tympanoplasty only 20% achieved air-bone gap within 20dB but 75% within 30dB (Figure-1). It was seen that hearing improvement was better in those patients who had lesser air-bone gap pre-operatively. However, regarding hearing improvement, there was no statistically significant difference between the two procedures using standard analysis.

Robert C O'reilly et al. study<sup>12</sup> showed that with the use of autograft incus he had achieved a mean postoperative AB gap of 18.6dB. The study by K. Ojala<sup>13</sup> and Naragund et al.<sup>8</sup> attained a mean AB gap of 25.8dB and 24.5dB respectively. Our study achieved a mean post-operative AB gap of 29.6 dB using auto-graft ossicles in Group A patients.

Shrestha BL et al in their study of classical type-3 tympanoplasty<sup>14</sup> achieved a mean post-operative AB gap of 29.8 dB with a variation from 15 to 61.2dB. Je-Yeob Yeon, Woo-Jin Jung et al<sup>15</sup> showed 37.4% hearing improvement with classical type-3 tympanoplasty at 3 month follow-up with a mean post-operative AB Gap of 25.1 dB which became 29.1 dB at 1 year follow-up. In our study the mean post-operative AB Gap with classical type-3 tympanoplasty was 36.3dB.

Iurato<sup>16</sup> reviewed the literature at length to investigate hearing results from ossicular reconstruction in Austin-Kartush type A

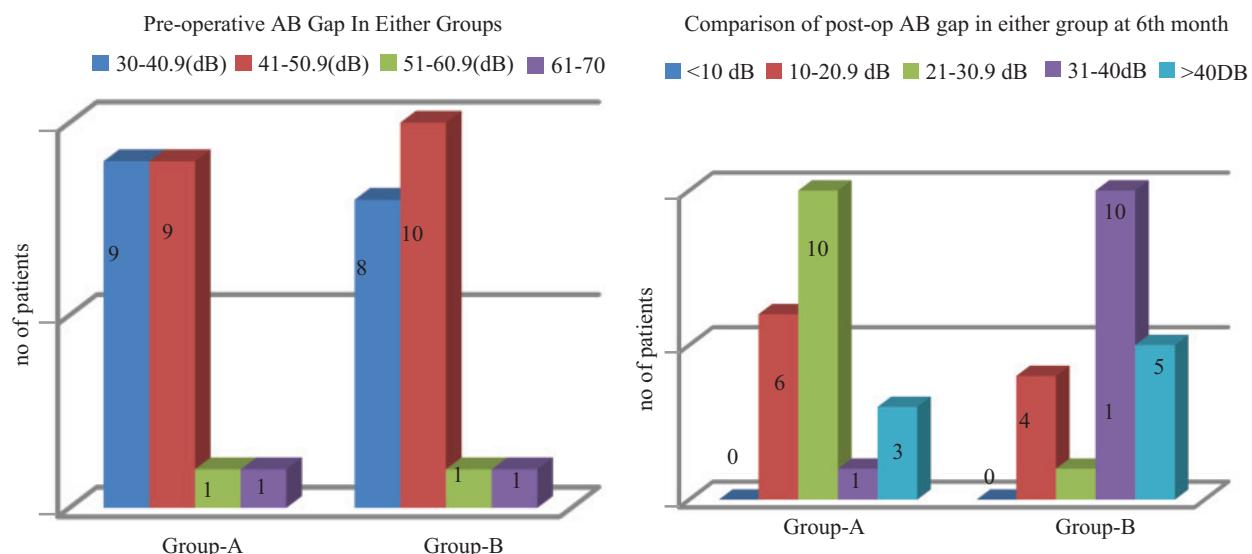


Figure-1: Comparison of AB Gaps pre and post operatively

patients. At 12 months minimum follow-up, 84% patient had air-bone gap within 20dB. Emir<sup>17</sup> reviewed 304 patients who underwent Ossiculoplasty with intact canal wall. Autologous incus interposition resulted in 58% success rate (mean postoperative air-bone gap of less than 20 dB).

Thus it was observed that both the procedure achieved significant improvement over the pre-operative air conduction threshold (AC) and air-bone gap (ABG). However clinical trials, like this study, are less available in the literature which compared both the anatomical and functional outcome of classical type-3 tympanoplasty and tympanoplasty with incus interposition. Although it must be admitted that the follow up is short-term and patient compliance for follow up is a concern in this part of the world.

## CONCLUSION

This study reveals significant hearing improvement with both the procedures in (Austin type-A ossicular defect) chronic otitis media. It was also noted that hearing restoration was better in cases with lesser air-bone gap pre-operatively irrespective of the procedures performed. The lack of statistical difference in the hearing outcome of the two procedures may be due to the limitation of clinical trial with the small sample size and limited statistical power in the comparison of surgical techniques. Besides, the follow up period was also short. So it would be worthwhile to conclude that further clinical trials with a larger sample size and longer follow-up period are needed to standardize a particular procedure or technique to be considered as ideal in the management of particular presentation of COM.

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# HRCT Assessment of Interstitial Lung Diseases

Pankaj Badarkhe-Patil<sup>1</sup>, Dayanand Kawade<sup>2</sup>, Prashant Titare<sup>3</sup>, Varsha Rote- Kaginekar<sup>4</sup>

## ABSTRACT

**Introduction:** Interstitial lung disease (ILD) is a group of diffuse parenchymal lung diseases affecting the pulmonary interstitium. High resolution computed tomography (HRCT) is the most accurate noninvasive, cross section imaging modality for the diagnosis and follow up monitoring of ILD. Study was done to check the basic HRCT patterns associated with Interstitial Lung Disease and correlation of HRCT patterns with clinical data in differential diagnosis of Interstitial Lung Disease.

**Material and methods:** Total 50 patients referred from medicine department of our institute having clinical suspicion of ILD were studied during June 2015 to June 2016. HRCT chest was done in all patients on 6 slice Siemens somatom CT scanner in supine position using standard HRCT protocol. Parenchymal abnormalities were detected and categorized for specific diagnosis of ILD.

**Result:** Majority of the patients (n=25) were between the ages of 60- 80 years (8 males and 17 females). The major complaint was progressive dyspnea (n=48; 96%). The most common interstitial lung disease found in our study was usual interstitial pneumonia (n=18; 36%) followed by nonspecific interstitial pneumonia (n=7; 14%) and acute interstitial pneumonia (n=7; 14%).

**Conclusions:** UIP was the most common interstitial lung disease observed in our study. Westernisation has changed the disease distribution in Indian population for age. In patients with progressive dyspnea ILD should be ruled out as a cause. Clinical and laboratory finding along with HRCT workup is essential for the diagnosis of specific ILD.

**Keywords:** High resolution computed tomography, Interstitial lung disease, Usual interstitial pneumonia.

## INTRODUCTION

Interstitial lung disease (ILD) is a heterogeneous group of diffuse parenchymal lung diseases, characterized by restrictive physiology, impaired gas exchange, pulmonary inflammation and fibrosis.<sup>1,2</sup> In most cases the pathology of ILD lies in the pulmonary interstitium which consists of connective tissue space between the alveolar epithelial cells and the adjacent capillary endothelial cells. Extensive work up is needed for the diagnosis of ILD.<sup>3</sup> Cigarette smoking, aspiration, certain drugs, radiation therapy, cancer, systemic diseases, environmental and occupational factors had been reported in association with the ILD in one third cases.<sup>4</sup> However two-thirds cases of ILD have no reportable association.<sup>5,6</sup>

Chest radiograph (CXR) may be normal during early in the course of the disease and shows few abnormalities hence unable to identify the specific etiology of ILD.<sup>7</sup> Pulmonary function testing (PFT) cannot diagnose a specific ILD or distinguish between active lung inflammations versus fibrosis.<sup>8</sup> HRCT (High resolution computed tomography) is the most accurate noninvasive, high spatial resolution cross sectional imaging modality for evaluation of lung parenchyma. It assesses the presence of disease in lung, type of disease, changes of active

lung disease, biopsy site localization, change in disease activity following treatment, characterization of interstitial lung disease (ILD) in appropriate clinical setting. It is more sensitive than the plain radiograph in identifying ILD (sensitivity greater than 90%) and the image pattern of parenchymal abnormalities on HRCT often suggests a particular set of diagnostic possibilities.<sup>9</sup> Present study aimed to study basic HRCT patterns associated with Interstitial Lung Disease and correlation of HRCT patterns with clinical data in differential diagnosis of Interstitial Lung Disease.

## MATERIAL AND METHODS

The study was hospital based prospective and descriptive which was conducted during June 2015 to June 2016 in our department of radiology. Total 50 patients were studied based on inclusion exclusion criteria, which were referred from medicine department of our institute having clinical suspicion of ILD. Patients of all age and sex were included in the study. Known cases of infective etiology (Tuberculosis, HIV), chronic obstructive pulmonary disease, congestive cardiac failure, lung malignancy, hemodynamically unstable patients were excluded. After inclusion of the patient in the study, detailed proforma was filled. The proforma included the patient's name, age, address, medical record number, complaints, risk factors, past history, laboratory investigation, and chest radiograph findings. Thereafter HRCT chest was done on 6 slice Siemens somatom CT scanner in supine position using standard HRCT protocol. Prone and expiratory scanning was done wherever needed. Parenchymal abnormalities were categorized into four basic patterns of HRCT with their distribution and predominant involvement. Final possible diagnosis was made as per HRCT findings and clinical information.

## STATISTICAL ANALYSIS

Standard statistical analysis was done with the help of Microsoft Excel version 2007. Descriptive statistics like mean (SD) and percentages were used to interpret the results.

## RESULT

Majority of the patients (n=25) were between the ages of 60- 80 years, which include 8 males and 17 females. Fifty percent of population included in this study was in between 60 to 80 years of age, the majority of which were females. (Table-1)

<sup>1</sup>Assistant Professor, <sup>2</sup>PG Resident, <sup>3</sup>Associate Professor, <sup>4</sup>Professor and HOD, Department of Radiodiagnosis, Government Medical College and Hospital, Aurangabad, India

**Corresponding author:** Dr. Pankaj Badarkhe-Patil, Assistant Professor, Department of Radiodiagnosis, Government Medical College and Hospital, Aurangabad, India

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The major complaint was progressive dyspnoea (n=48; 96%), followed by dry cough (n=37, 74%) and joint pain (n=22; 44%) related to connective tissue disorders (Graph-1) Some patients also had varying symptoms like fever, wet cough, tight skin etc. The most common interstitial lung disease found in our study was usual interstitial pneumonia (UIP) / idiopathic pulmonary fibrosis (IPF) (n=18; 36%) followed by nonspecific interstitial pneumonia (NSIP) (n=7; 14%) and acute interstitial pneumonia (AIP) (n=7; 14%) (Graph-2)

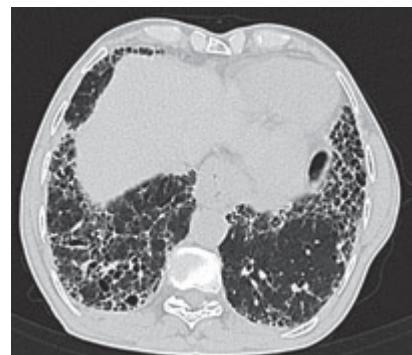
Most commonly found associated risk factor with interstitial lung disease was connective tissue disorder (n=19; 38%) followed by smoking (n=9; 18%), allergy (n=8; 16%) and least was exposure history in three cases which include exposure to chemotherapy, radiotherapy and coal dust particles in coal mine.

The most commonly found pattern associated with interstitial lung disease was reticular opacity (n=37; 64%) followed by increased opacity (n=29; 58%) and decreased opacity (n=29; 58%) on HRCT. Most common specific HRCT findings in our study population were septal thickening (n=37; 64%) followed

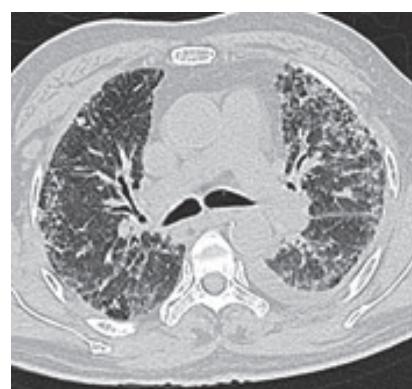
by bronchiectasis (n=26; 52%) and ground glass opacity (n=24; 48%). Diffuse distribution of HRCT findings was seen in 24 cases (48%). Lower lobes were predominantly involved in 37 cases (64%).

## DISCUSSION

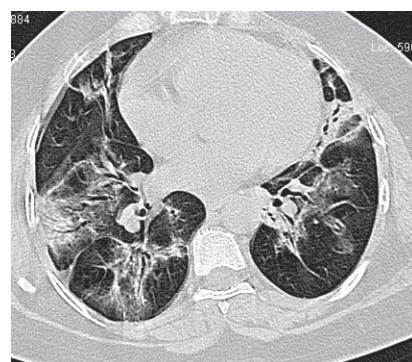
Out of 50 cases, Forty four cases (88%) showed specific patterns associated with interstitial lung disease and six cases (12%)



**Figure-1:** HRCT shows bilateral diffuse extensive fibrosis with septal thickening, honeycombing, traction bronchiectasis predominantly involving bilateral lower lobes in subpleural region and architectural distortion resulting in reduced lung volume. Findings are in favour of usual interstitial pneumonia / idiopathic pulmonary fibrosis.



**Figure-2:** HRCT shows bilateral diffuse interstitial lung disease in the form of interlobular and intralobular septal thickening predominantly in subpleural region with focal areas of tiny honeycombing with left sided pleural effusion. Findings are in favour of idiopathic interstitial pneumonia- nonspecific interstitial pneumonia.

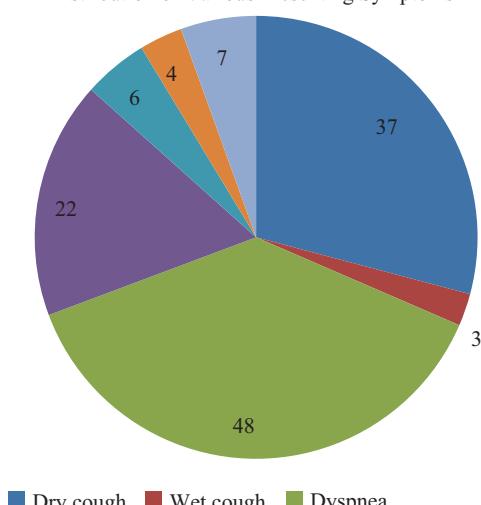


**Figure-3:** HRCT reveals extensive geographic areas of ground glass attenuation with septal thickening and focal areas of consolidation with air bronchograms. Changes are predominantly distributed in bilateral peribronchovascular, subpleural regions and lower lobes. Findings are in favour of cryptogenic organising pneumonia

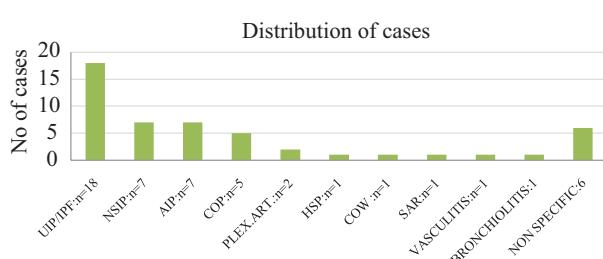
Sr. No.	Age group	No. of patients	Male		Female	
			No	%	No	%
1	Less than 20 year	1	0	0	1	2
2	20- 40 year	4	2	4	2	4
3	40- 60 year	18	6	12	12	24
4	60-80 year	25	8	16	17	34
5	More than 80 year	2	2	4	0	0
	Total	50	18	36	32	64

**Table-1:** Showing age and sex distribution in ILD.

Distribution of Various Presenting Symptoms



**Graph-1:** Distribution of various presenting symptoms in ILD.



**Graph-2:** Distribution of cases in various ILD.

showed nonspecific findings. Out of the six cases, three cases showed no involvement of lung parenchyma.

In our study the most common age group at presentation was 60 to 80 years with 25 patients including 17 females and 8 males. Earlier Indian studies of Maheshwari U et al, Muhammed SK et al showed the age of presentation almost two decades earlier (40-60 year) than western study of Aziz ZA, et al. (60-80 years) with predominance of females.<sup>10-13</sup> The age group of our patients is in variance with previously published Indian studies and matches that of western study. This might suggest a change in the Indian life styles towards more westernisation, small sample size and a more urban bias of the study population.

The most common presenting complaint was progressive dyspnea seen in 48 patients (96%) followed by dry cough (74%) and associated joint pain (44%). These findings were in accordance to those reported by Muhammed SK et al in 2011.<sup>11</sup> Joint symptoms were more commonly found as compared to literature. This might have happened due to more referral bias towards connective tissue disorder from rheumatologist since the inclusion criteria included patients of connective tissue disorder having pulmonary symptoms.

The most common associated risk factor seen in the present study was connective tissue disorder. A total of 19 patients (38%) were serologically positive for connective tissue disorder. In the study conducted by Muhammed SK et al 29 % of study population tested serologically positive for connective tissue disorder.<sup>11</sup> Other associated risk factors recorded in the present study were smoking (18%), allergy (16%). Three patients had history of exposure which included exposure to chemotherapy, radiotherapy in two patients and coal dust particle in coal mine in one patient. Smoking and exposure history as compared to literature was less common. This might have happened due to more females were included in study population, limited sample size and referral bias.

In the present study the most common interstitial lung disease reported on HRCT was usual interstitial pneumonia / idiopathic pulmonary fibrosis (36%) (Table-2). Nonspecific interstitial pneumonia and acute interstitial pneumonia were reported in 7 cases (14%) each. These findings like those reported by Muhammed SK et al, Maheshwari U et al and Sen T Udwadia ZF et al.<sup>10,11,13</sup> As compared to literature, more patients of COP (Cryptogenic organising pneumonia) and AIP (Acute intestinal pneumonia) were noted in our study and which might be due to sampling error. As opposed to this less patient of hypersensitivity pneumonitis (HSP), coal worker pneumoconiosis (CWP) and sarcoidosis were noted and this might be due to a small sample size.

The various patterns found to be associated with interstitial

lung disease in our study population, on HRCT were reticular opacities (n= 37; 64%) followed by increased opacity (n=29; 58%) and decreased opacity (n=29; 58%). These findings were well correlated with the findings of Indian study done by Muhammed SK et al which was very similar to our study, except decreased opacity which were not separately described in that study.<sup>11</sup> Decreased opacity was mainly contributed by traction bronchiectasis and in most conditions it was part of reticular opacity.

Most common pattern seen on HRCT is reticular opacities. These findings correlated with findings of Muhammed SK et al.<sup>11</sup> HRCT was superior to chest radiograph in detection of all basic patterns and their distribution associated with ILD. Chest radiograph is a nonspecific investigation and can be utilized as initial investigation in work up of ILD. However, HRCT of lungs along with clinical data is essential for the diagnosis of ILD as reported by Potente G et al, Grenier P et al, Aziz ZA et al, Raniga S et al and Ghulam Shabbier et al.<sup>14-18</sup>

Septal thickening, honeycombing and traction bronchiectasis were commonest findings observed in almost all cases of UIP seen predominantly in basal and subpleural region corresponding to the findings of the studies done by Maheshwari U et al, Akira M et al, Nishiyama O et al and Misumi S et al.<sup>11,19-21</sup> (Figure-1) In NSIP, HRCT findings predominantly involved the lower lobes and subpleural regions like IPF but the distribution was patchy in contradictory to IPF which showed diffuse distribution of all findings. Honeycombing was also less common than IPF/UIP. These findings are like those reported by TS Kim et al and Elliot TL et al.<sup>22,23</sup> (Figure-2) In AIP, HRCT showed patchy areas of ground glass opacity with discrete areas of alveolar consolidation involving both lungs with predominant involvement of upper lobes (4 cases) and subpleural regions which were consistent with the findings of Primack SL et al and Bonaccorsi A et al.<sup>24,25</sup> High-resolution CT findings consist of ground glass opacities (80%) and/or consolidative areas (80%) distributed along the bronchovascular bundles and along the subpleural lungs. These findings suggestive of COP were as per study done by Ju Won Lee et al.<sup>26</sup> (Figure-3) Diffuse involvement was noted on HRCT in HSP which include tiny centrilobular nodules with groundglass haziness and predominance in upper lobes. These findings were correlated with study done by DA lynch et al.<sup>27</sup> In sarcoidosis, HRCT revealed patchy distribution of septal thickening, peripheral and random nodules. These findings correlated with study done by Nishimura K et al and Mimori Y et al.<sup>28,29</sup> HRCT findings of plexogenic arteriopathy observed were mosaic perfusion without air trapping in 2 cases, suggestive of basic pathology in vessels rather than bronchial pathology.<sup>30</sup> Additional findings were dilated main pulmonary artery,

HRCT Diagnosis	Muhammed SK et.al <sup>11</sup>	Sen T Udwadia ZF et.al <sup>13</sup>	Present study
UIP/IPF	39%	43%	36%
NSIP	24%	18%	14%
Connective Tissue Disease Related ILD	24%	18.6%	30%
COP	4%	2%	10%
AIP	0%	1%	14%
HSP	17%	6%	2%
COW /Silicosis	4%	1%	2%
Sarcoidosis	13%	22%	2%

Table-2: Distribution of interstitial lung diseases and literature comparison

centrilobular nodules and consolidation. HRCT showed patchy areas of ground glass opacity, consolidation, centrilobular nodule, septal thickening and traction bronchiectasis with collapse of apical segment of left lower lobe in a case of pulmonary vasculitis.<sup>31</sup>

Eleven (22%) cases which were serologically positive for rheumatoid arthritis were reported in our study. Out of eleven, one was (9%) male and ten (91%) were females showing a clear female preponderance. Most common pattern found with rheumatoid arthritis was reticular opacity associated with UIP / fibrosing alveolitis (3 cases 27%) in our study. These findings correlated with J K Dawson et al and Kinoshita F et al.<sup>32,33</sup> Out of two cases of systemic lupus erythematosus (SLE), one case showed features of acute interstitial pneumonia and another case showed focal involvement of ground glass opacity in left lower lobe which may represent early changes of inflammation associated with SLE. The findings in the first patient correlate with lung involvement in SLE as reported by Fenlon HM et al and Ooi GC et al.<sup>34,35</sup> The findings in the second patient are nonspecific in nature. Out of four cases of progressive systemic sclerosis, three (75%) cases showed NSIP pattern and remaining one case showed UIP pattern with preserved lung volume. Few of these findings and association with interstitial lung disease correlated with studies done by Chan TY et al and JmSeely et al.<sup>36,37</sup> In our study we found a strong correlation between scleroderma and NSIP pattern.

## CONCLUSION

UIP was the most common interstitial lung disease observed in our study. It is also most common pattern seen in rheumatoid arthritis. Westernisation has changed the disease distribution in Indian population with respect to age. In patients with progressive dyspnoea ILD should be ruled out as this is the most common complaint in ILD patients. HRCT lung is a noninvasive investigation of choice in clinically suspected cases of interstitial lung disease as it is very effective in visualizing the distorted architecture of lung parenchyma. HRCT along with clinical data and relevant laboratory investigations helps in arriving at the closest differential diagnosis in interstitial lung disease.

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# Clinicopathological Significance of E-Cadherin Immunoexpression in Gastric Carcinoma

Nikhil Sisodiya<sup>1</sup>, Rajat Jagani<sup>2</sup>

## ABSTRACT

**Introduction:** Gastric cancer remains the second commonest cancer in morbidity and mortality worldwide. Cadherin is a superfamily of calcium-mediated membrane glycoproteins, which are responsible for the homotypic cell to cell adhesion. These adhesion molecules may play an important role in carcinogenesis and metastasis. A cross sectional study aimed to find out the clinicopathological correlation of E- Cadherin by Immunohistochemistry staining (IHC) as a prognostic marker was carried out.

**Material and Methods:** Present study was a cross sectional study conducted for the period of two months. Data for the study was obtained by using Patient diagnosis, case details and examination of tissue sections. Cases were selected based on the inclusion and exclusion criteria. Permission is taken from IEC before starting the study. Tissue samples of gastric adenocarcinoma were obtained from gastrectomy and biopsy specimens who were analysed using immunohistochemical staining. Statistical analysis is done using SPSS 23 version.

**Results:** Study population was represented by 30 patients with a mean age of 59.34 years (Ranging from 30 Years. to 80 Years.). We have noted aberrant, negative or heterogeneous expression of the E-Cadherin for 14 of the cases (46.67%). Our results showed no existence of a relation between E-Cadherin expression and the tumours localization, being observed negative immunohistochemical or heterogeneous reactions in 43.8% of the gastric antral carcinomas, 43.75% of the gastric body carcinomas and 50% of the cardial carcinomas, 66.7% of the pangastric carcinomas.

**Conclusion:** Abnormal expression of E-Cadherin is associated with the malignant behaviour of gastric carcinoma and is seen more frequently in diffuse type of gastric carcinoma along with advance gastric carcinoma cases. Therefore, it might serve as a marker of differentiation.

**Keywords:** E-Cadherin, Immunohistochemistry, Clinicopathological

## INTRODUCTION

Gastric cancer is the second leading cause of morbidity and mortality worldwide as far as cancer patients are concerned. According to the most recent estimates, gastric cancer accounts for 8% of the total cancer cases and 10% of the deaths for all cancers in the world.<sup>1</sup> Lauren has classified gastric cancer into diffuse and intestinal type that are different in regard to epidemiology, etiology, pathogenesis and behaviour.<sup>2</sup> Cadherin is a superfamily of calcium-mediated membrane glycoproteins. They binds to cytosolic proteins namely  $\alpha$ - catenin,  $\beta$ - catenin, and,  $\gamma$ -catenin which in turn are linked to the actins to form the intracytoskeleton.<sup>3</sup> The cadherins are responsible for the homotypic cell-cell adhesion, Therefore, these play an important role in carcinogenesis and metastasis. E-Cadherin is expressed in all epithelial cell types. Underexpression of the E-Cadherin is

found in gastric, hepatocellular, oesophageal, breast, prostatic, bladder and gynaecological carcinomas and correlates with infiltrative and metastatic ability.<sup>4</sup>

Currently there is no satisfactory tumour marker for diagnosis or monitoring the disease progression. The most frequently used tumour markers in gastric cancer are carcinoembryonic antigen (CEA) and CA19-9, but only a small proportion of patients have higher levels of these markers. With the current advancements in molecular biology, the prognostic and diagnostic indication for cancer has changed in the last few decades. In the present study, E-Cadherin, was chosen as an exemplifying molecular marker for gastric carcinoma. The present cross sectional study aimed to investigate the clinicopathological significance of E- Cadherin by Immunohistochemistry staining (IHC) as a prognostic marker.

## MATERIAL AND METHODS

The study was a cross sectional study conducted during May and June 2015 in a tertiary care hospital. Ethical approval was obtained from Institutional Ethics Committee prior to conducting the study and informed consent was obtained from all the cases. Sample size was 30 cases, which was calculated using the data from previous available literature and convenient sampling scheme. All diagnosed cases of gastric carcinoma and suspected gastric carcinoma cases were included in the study and all cases of lymphoma, squamous cell carcinoma, undifferentiated carcinomas and GIST (Gastro Intestinal Stromal Tumour) were excluded from the study. Tissue samples of gastric adenocarcinoma were obtained from gastrectomy and biopsy specimens which were formalin fixed, paraffin embedded. The normal gastric mucosa adjacent to tumour has been used as an internal positive control. Tumour staging is done in accordance with the unified TNM criteria for gastric cancer.

Standard immunohistochemical staining procedure was used for staining slides. Staining was scored independently by two observers and a high level of concordance was achieved. In case of disagreement, the slides were reviewed and a consensus view is achieved. The E-Cadherin expression in gastric carcinomas was levelled depending on the positive cells proportion found:

- (I) Uniformly positive (+): Over 90% out of the tumoral cells are Immunostained with E- Cadherin at membranous level.

<sup>1</sup>Med Cadet, <sup>2</sup>Sr Adv, Path and Oncopath, Armed Forces Medical College, Pune, Maharashtra, India

**Corresponding author:** Nikhil Sisodiya, Med Cadet, Armed Forces Medical College, Pune, Maharashtra, India

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Clinico-morphological factors		E-Cadherin immunoexpression	
		Normal (n= 16)	Aberrant (n=14)
Lauren's classification	Intestinal type	12 (75%)	05 (36%)
	Diffused type	03 (19%)	07 (50%)
	Mixed type	01 (06%)	02 (14%)
Tumor grade	G <sub>1</sub>	03 (19%)	01 (07%)
	G <sub>2</sub>	07 (44%)	08 (57%)
	G <sub>3</sub>	06 (37%)	05 (36%)
Lymphovascular invasion	Present	09 (56%)	08 (57%)
	Absent	07 (44%)	06 (43%)

Table-1: E-Cadherin immunoexpression in gastric carcinomas

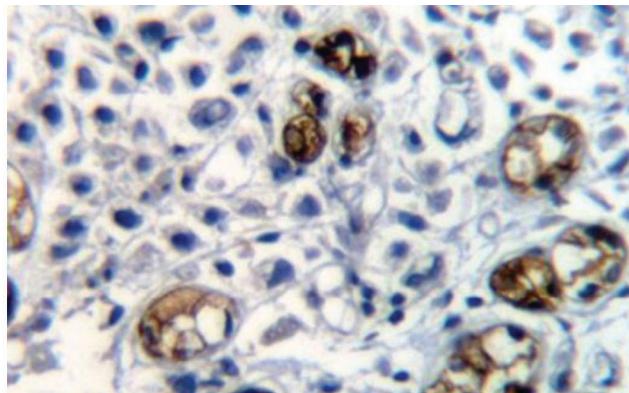
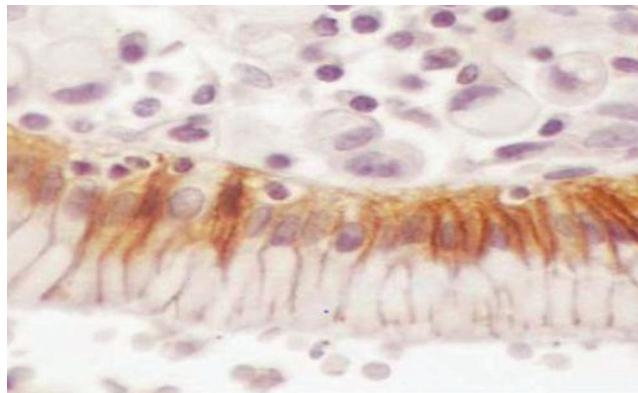


Figure-1: Normal gastric mucosa stained with E-Cadherin; Figure-2: Complete loss of E-Cadherin in diffused variety of gastric carcinoma

Socio-demographic factors		Gastric carcinoma cases (n=30)
Dietary Habits	Veg. diet	12 (40%)
	Non veg diet	18 (60%)
Previous history of any carcinoma	Yes	06 (20%)
	No	24 (80%)
Alcohol Intake	Yes	16 (53%)
	No	14 (47%)
Tobacco Chewing	Yes	08 (27%)
	No	22 (73%)
Family history of gastric carcinoma	Yes	04 (14%)
	No	26 (86%)
Family history of any carcinoma	Yes	17 (56%)
	No	13 (44%)

Table-2: Showing relation of socio-demographic factors with the incidence of gastric carcinoma

- (II) Heterogeneous ( $\pm$ ): Between 05 and 80% of the tumoral cells are immunostained at membranous and cytoplasmic level.  
 (III) Negative (-): Between 0 and 5% of the tumoral cells are immunostained.

## STATISTICAL ANALYSIS

The data collected was analyzed using descriptive statistics for finding out the clinicopathological significance using Statistical Package for the Social Sciences (SPSS) Version 23.0.

## RESULTS

Study population comprised of 30 patients (17 males and 13 females) with a mean age of 59.34 years (Ranging from 30 years to 76 years). In our study we observed that the homogeneous and intense stain for E-Cadherin of the epithelial cells membranes

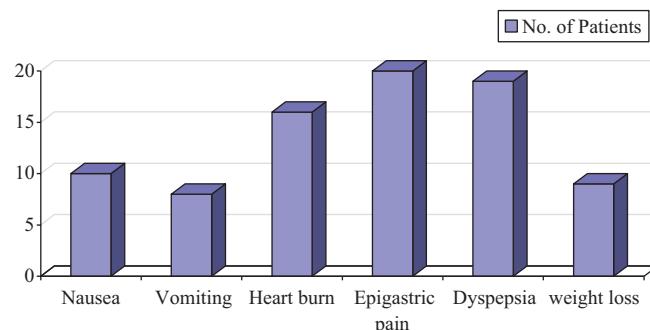


Figure-3: Showing relation of symptoms observed in gastric carcinoma patients

in the normal gastric mucosa, situated in the carcinomas' vicinity, which reflects the normal location of this molecule of intercellular adhesion. The immunostained normal mucosa had served as an internal positive control. We have noted aberrant, negative or heterogeneous expression of the E-Cadherin for 14 of the cases (46.67%). The aberrant E-Cadherin expression was noticed in close proportions in men (47.06%) and women (46.16%). We have also seen 44% carcinomas with aberrant immunohistochemical expression in patients with age  $\leq$ 60 years and 60% carcinomas in patients  $\geq$ 61 years of age. Our results showed no existence of a relation between E-Cadherin expression and the tumours localization, being observed negative immuno-histochemical or heterogeneous reactions in 43.8% of the gastric antral carcinomas, 43.75% of the gastric body carcinomas and 50% of the cardial carcinomas, 66.7% of the pangastric carcinomas. The E-Cadherin aberrant immunoexpression have been observed significantly more frequently in the diffuse type carcinomas in comparison to the intestinal type carcinomas.

Epigastric pain was the most common presenting symptom

followed by dyspepsia and heart burn. The findings of the study are summarized in Tables 1 and 2.

## DISCUSSION

E Cadherin is an important molecule in cell adhesion and loss of E-Cadherin will disrupt proliferation inhibition and lead to more scattered types of tumor like diffuse type which have more malignant behaviour with poorly differentiated cells. We have demonstrated a significant correlation between E-Cadherin expression and tumor histology. In this study E-Cadherin influenced tumor depth of invasion but it was not significantly associated with lymph node metastasis. This reveals that preserved E-Cadherin expression does not necessarily lead to intact cell adhesion mechanisms. It might be a result of malfunctioned E-Cadherin protein despite normal staining in some cases.

In the present study, as in many previously reported studies, abnormal or absent E-Cadherin immunoreactivity was observed in gastric adenocarcinomas, and the proportion of cases displaying abnormal E Cadherin immunoreactivity was greater in diffuse adenocarcinomas. The identification of E-Cadherin in the cytoplasm and not on the membrane is consistent with the notion that loss of membrane E-Cadherin promotes tumor disaggregation and dissemination. Since the normal role of E-Cadherin is to maintain homotypic adhesion in epithelial cells, the abnormal E-Cadherin expression leads to disconnection of cancer cells and thereby facilitating their permeation into the gastric stroma. This is particularly relevant to diffuse adenocarcinoma, which spreads extensively and has a considerably greater likelihood to express little or no E-Cadherin.<sup>5</sup> This preliminary immunohistochemical examination of E-Cadherin raises interesting questions that warrant further study. Analysis of these cases for mutations in the E-Cadherin gene sequence may yield information that better defines the molecular basis of the E-Cadherin alteration responsible for the paranuclear distribution. Although some studies have shown the reduction or absence of E-Cadherin in gastric carcinomas, the results regarding the correlations between the aberrant expression of E-Cadherin, the clinicopathological factors and gastric cancer patients' survival are contradictory.<sup>6</sup> In our study, we have proposed to investigate the E-Cadherin immunohistochemical expression in gastric carcinomas, as well as in the peritumoral mucosa. We noticed that homogeneous and intense immunostaining for E-Cadherin of the epithelial cells' membranes of the gastric mucosa situated near the carcinomas, which reflects the normal localization of this intercellular adhesion molecule. The immuno-marked areas of normal mucosa served as positive internal control. The atrophic chronic gastritis areas and the E Cadherin aberrant immunoreactions have been observed significantly more frequently in the diffuse-type carcinomas in comparison to the intestinal-type carcinomas, thus these data emphasize the strong relation between the Lauren's classification of the gastric carcinomas and the immunohistochemical expression of the E-Cadherin cellular adhesion molecule. The E-Cadherin aberrant immunohistochemical expression was noted more frequently in weakly differentiated carcinomas in comparison to the moderately differentiated and well differentiated carcinomas. The significant correlation between the E-Cadherin

atypical immunoreaction and the tumoral grade is also signaled by other authors.<sup>6-8</sup>

## CONCLUSION

The results obtained in our study suggest the important role of E-Cadherin in the development of differentiated forms of gastric carcinoma, in this case being a histological differentiation marker. However, there is no significant clinicopathological correlation between clinical presentation symptoms and pathological grading.

## ACKNOWLEDGEMENT

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# A Clinical Study on Effect of Dexmedetomidine Added to Spinal Hyperbaric Bupivacaine in Lower Abdominal Surgeries

Anupam Chakrabarti<sup>1</sup>, Monotosh Pramanik<sup>2</sup>, Subhash Ranjan Das<sup>3</sup>

## ABSTRACT

**Introduction:** Spinal anaesthesia is commonly used regional anaesthetic technique all over the world. This study investigates the effect of intrathecal administration of dexmedetomidine added to spinal hyperbaric bupivacaine on the duration of sensory and motor block and postoperative analgesic requirements in lower abdominal surgeries.

**Material and Methods:** Hundred adult patients posted for lower abdominal surgeries were randomized in two groups. Each patient was given 3.5 ml of drug solution intrathecally that consisted of 3 ml 0.5% hyperbaric bupivacaine and 0.5 ml containing 7.5 µg dexmedetomidine in Group D patients or normal saline in Group B patients. Intraoperative Heart rate, arterial blood pressure, sensory level, motor block, pain and level of sedation were assessed and continued up to 24 hours post spinal anesthesia for any complication during the procedure.

**Results:** Time to two segment regression, sensory regression to S1, regression of motor block to modified Bromage 0 and time to first rescue analgesic were significantly prolonged in dexmedetomidine group along with significantly decreased postoperative pain scores.

**Conclusion:** Intrathecal dexmedetomidine in doses of 7.5µg significantly prolong the anesthetic and analgesic effects of spinal hyperbaric bupivacaine.

**Keywords:** spinal anaesthesia, adjuvant, dexmedetomidine, hyperbaric bupivacaine, lower abdominal surgeries

## INTRODUCTION

Lower abdominal surgeries commonly performed under spinal anaesthesia technique because of its rapid onset, less failure rates and cost effectiveness, but it has shorter duration of action and not much effective in view of postoperative analgesia. Many intrathecal adjuvants have been tried in past with the aim of prolonging the duration of block and to solve the purpose of post-operative analgesia. Clonidine an α2-adrenoreceptor as intrathecal adjuvant has been effectively used to increase the duration of spinal anaesthesia using hyperbaric bupivacaine.<sup>1-3</sup> Kanazi et al found that 3 µg dexmedetomidine and 30 µg clonidine are equipotent intrathecally when added to bupivacaine in patients undergoing urologic procedures. Dexmedetomidine is an α methylol derivative with a higher affinity for α2-adrenoreceptor than clonidine which has been started to be used as adjuvant to intrathecal hyperbaric bupivacaine.<sup>4-6</sup> In humans the largest intrathecal dose used was 10 µg.<sup>6</sup> In our institute we conducted a pilot study in which we used different doses of dexmedetomidine and came to a conclusion that 7.5µg will be appropriate for our study population. This prospective randomized double blinded controlled trial was aimed to investigate the effects of adding dexmedetomidine 7.5 µg to hyperbaric bupivacaine in patients scheduled for elective lower abdominal surgeries. The aim of the study was to determine the

time to two segment sensory regression of spinal anaesthesia. Time to sensory block to reach T10, sensory regression to S1, motor regression to modified Bromage scale 0, time to first rescue analgesic, verbal rating pain scores, sedation scores, postoperative analgesic use and occurrence of adverse effects were the objectives.

## MATERIAL AND METHODS

The study was done after receiving the approval of the ethical-cum-screening committee and written informed consent was taken from all patients before initiation of the procedure. Using statistical formula appropriate for the design of the study as advised by statistician, 100 patients between age group 18 to 65 years with ASA physical status I and II undergoing elective lower abdominal surgeries were included as study population. Patients with ASA grading > 2, body mass index ≥30, hypersensitivity to any of the drugs which are to be used in the study, with contraindications for spinal anaesthesia were excluded from the study. All patients were randomly allocated into two equal groups (n=50). All the patients received equal volume of drug (3.5ml) containing 3 ml (15mg) hyperbaric bupivacaine hydrochloride. The study group [Group D (n=50)] received dexmedetomidine 7.5 µg in 0.5 ml 0.9% saline along with hyperbaric bupivacaine. The control group [Group "b"(n=50)] received an identical volume of 0.9% saline added to bupivacaine. On the preceding day of operation, relevant history and informed consent of the patient were taken and visual analogue scale was explained. All the patients were advised for overnight fasting. After arrival in the operating room, patient's identity and informed consent form were checked and all requisite monitors were attached. Preloading was done with Ringer Lactate solution (20ml/kg body weight) 30 minutes before the intrathecal drug administration to all patients. Premedication with pantoprazole and ondansetron were given. ECG, pulse oximetry, and non-invasive blood pressure were monitored and baseline values were recorded at the initiation of the procedure. Lumbar puncture was performed at L3-L4 interspace or L4-L5 interspace if it is difficult through a midline approach using a 25-gauge Quincke needle in sitting posture. All patients then laid on their back in supine position and received oxygen at 2L/

<sup>1</sup>Assistant Professor, <sup>2</sup>Junior Resident, <sup>3</sup>Associate Professor, Department of Anaesthesiology, Agartala Government Medical College and GBP Hospital, Tripura, India

**Corresponding author:** Dr Anupam Chakrabarti, Krishnanagar Nutan Pally, Agartala, Tripura, India

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minute through nasal prong. Surgeons then allowed to position the patients according to their convenience. After 2 minutes, every 2 minutes sensory nerve block was assessed bilaterally by using insensitivity to cold (when cotton swab soaked with alcohol was applied) in the midclavicular line. Motor blockade was assessed by using the modified Bromage scale bilaterally every 2 minutes. The intraoperative vitals that is heart rate (HR), NIBP and oxygen saturation were monitored and recorded at 15 minutes interval intraoperatively and 30 minutes interval postoperatively for next 8 hours. Any side effects in the form of severe hypotension, bradycardia, respiratory depression ( $\text{SpO}_2 < 94\%$ ), nausea, vomiting, dizziness were also recorded. Systolic BP less than 90 mm of Hg was regarded as hypotension and treated with intravenous bolus administration of 500ml of Ringer Lactate over 10 minutes and if needed intravenous 3mg Mephenteramine and its multiplying doses were given accordingly. Bradycardia was defined as heart rate less than 50/minute and was treated with 0.6mg intravenous atropine. Intravenous midazolam at the dose of 0.5mg/kg was allowed if the patient is anxious. Time to reach T10 sensory block level, peak sensory block level, time to reach peak level of sensory block and time to achieve Bromage 3 motor block were recorded before surgery. The regression for sensory level by pin prick and motor block by Bromage scale was checked every 15 minutes in a post anaesthesia care room. Time of 2 sensory segment regressions from peak level, time to regress to S1 level, time to regain Bromage score 0 and time for 1st analgesic request were recorded. The level of sedation was evaluated intraoperatively at 15 minutes interval and postoperatively at 30 minutes interval using Agitation scale. Durations were calculated from the point of intrathecal drug administration. Patients were discharged from the post anaesthesia care room after sensory block regresses to S1 dermatome level and motor block to Bromage 0. No analgesic drug was given in the immediate post-operative period until the patient requested for analgesia and time for first analgesia will be recorded. Intramuscular diclofenac sodium 1mg/kg body weight were used as rescue medication when patient complains of pain ( $\text{VAS} \geq 3$ ). Any incidence of adverse effects in the intraoperative or immediate postoperative period were noted and again patients were followed up at 24 hours in the ward for incidence of nausea, vomiting or any other adverse

reaction. Postoperative nausea and vomiting was treated with 4mg of intravenous ondansetron as and when necessary.

## STATISTICAL ANALYSIS

Data analysis was done using SPSS version 21 (Statistical Packages for the Social Sciences). N and median were used to represent Discrete categorical data whereas continuous data as mean  $\pm$  Standard deviation. Differences in demographic, anaesthetic and post-operative data were tested by independent Student's t-test (continuous data) or by Chi-square test (categorical data). Most of collected data were of normal distribution and student 't' test was applied on them for statistical analysis. A p value less than 0.05 is taken as significant.

## RESULTS

Demographic parameters (age, weight, height, sex ratio), ASA physical status, time to achieve T10 sensory block, time to achieve peak sensory block level, time to achieve Bromage 3 motor block were comparable between two groups with all insignificant p value (table-1).

Time taken by group B patients for 2 sensory segment regressions from the peak level was  $88.38 \pm 6.21$  minutes whereas in group-D patients this time was much higher with  $133.58 \pm 18.8$ . The difference was significant as shown by unpaired student 't' test and the p value was  $<0.0001$  which is extremely statistically significant. So it can be said that dexmedetomidine prolongs the 2 segment regression time when added with hyperbaric bupivacaine as an adjuvant (table-2).

Time taken by group-B patients for regression to S<sub>1</sub> segment level was  $232.64 \pm 13.49$  minutes. In group-D patients this time was higher ( $328 \pm 26.64$  minutes). The parameters were compared with unpaired student 't' test and the two tailed p value was  $<0.0001$ . This difference is certainly statistically significant. So it can be said that dexmedetomidine prolongs the time for regression to S<sub>1</sub> level (table-3).

Group-B patients took  $184.2 \pm 6.65$  minutes to regain Bromage score 0 and group-D patients took  $281 \pm 14.03$  minutes (table-4). Unpaired student 't' test was done and p value was  $<0.0001$  which is considered to highly statistically significant. So group-D patients took significantly longer time than group-B patients to regain Bromage 0 score. This concludes that motor blockade was also prolonged in dexmedetomidine group than in

	<b>Group B</b>	<b>Group D</b>	<b>p value</b>
Age(years)	$42.86 \pm 10.35$	$39.9 \pm 8.41$	0.119
Weight(kgs)	$59.28 \pm 6.67$	$58.52 \pm 5.77$	0.543
Height(cms)	$155.82 \pm 5.92$	$156.98 \pm 5.39$	0.308
Sex(male/female)	25/25	25/25	1
ASA(I/II)	38/12	34/16	0.504
Time to achieve T10 sensory block	$5.8 \pm 2.4$	$6 \pm 1.5$	0.618
Time to achieve peak sensory block level	$13.5 \pm 1.4$	$13.9 \pm 1.5$	0.171
Time to achieve Bromage 3 motor block	$7.84 \pm 2.23$	$7.42 \pm 1.84$	0.306

**Table-1:** Demographic parameters, asa status, time to achieve t10, peak sensory block level, bromage 3 motor block

<b>Time of 2 segment regression from peak level</b>				
<b>Group B</b>		<b>Group C</b>		<b>p Value (Student 't' test)</b>
Mean	Std. dev.	Mean	Std. dev.	
88.38	6.21	133.58	18.8	<0.0001

**Table-2:** Two segment regressions from peak level

<b>Regression of spinal anaesthesia</b>				
<b>Group B</b>		<b>Group D</b>		<b>p Value (Student 't' test)</b>
Mean	Std. dev.	Mean	Std. dev.	
232.64	13.49	328.65	26.64	<0.0001

**Table-3:** Time to regress to S<sub>1</sub> segment

bupivacaine only group.

Similarly, the duration of analgesia was significantly different among the groups. Group D had a significantly longer time to first analgesic requirement than group B. On an average group-B patients required inj. diclofenac sodium after  $157.7 \pm 9.32$  minutes whereas group-D patients requested it much later i.e. after  $253.3 \pm 8.18$  minutes (table-5). When compared with unpaired student 't' test this difference was extremely significant with a very low p value of  $<0.0001$ . So the conclusion is that dexmedetomidine when used as an adjuvant with hyperbaric bupivacaine it increases the time of post-operative analgesia. The incidences of different side effects were low in the perioperative period up to a period of 24 hours and they were comparable between all the groups (table-6). The data was compared with fisher's exact probability test and p values were all very high i.e. statistically Insignificant.

## DISCUSSION

$\alpha_2$ -agonist when administered via intrathecal route produces an analgesic effect in postoperative pain without causing significant sedation. It is considered to be due to the sparing of supraspinal CNS sites which causes profound analgesia without significant sedation. Most of the clinical studies has used clonidine as intrathecal  $\alpha_2$ - adrenoceptor agonists and concluded a synergistic effect with local anaesthetics<sup>7,2,8,9</sup>

Dexmedetomidine is also an  $\alpha_2$ -adrenoreceptor agonist which has about ten times higher affinity for  $\alpha_2$ -adrenoreceptor than clonidine.<sup>10,11</sup> Intrathecal dexmedetomidine produces its analgesic effect by inhibition of C-fibers transmitters release together with hyperpolarization of post-synaptic dorsal horn neurons.<sup>12</sup> The prolongation of motor effect might be caused by direct impairment of excitatory amino acid release from spinal interneurons.<sup>13</sup>

Intrathecal 5  $\mu$ g and 10  $\mu$ g dexmedetomidine were used in previous studies with insignificant effect on blood pressure or heart rate.<sup>14,15</sup>  $\alpha_2$  agonists produce sedative effect by acting on  $\alpha_2$ -adrenergic receptors in locus ceruleus.<sup>12,11</sup> It is unlikely for intrathecal 7.5  $\mu$ g of dexmedetomidine to produce significant increase in sedation score as a previous study which used 10  $\mu$ g of intrathecal dexmedetomidine in patients undergoing transurethral resection of prostate was unable to do the same.<sup>14</sup> In our study we compared the duration of sensory and motor block in the two groups of patients, Group B was given Intrathecal bupivacaine alone and group D was given intrathecal bupivacaine plus dexmedetomidine. Intrathecal 7.5  $\mu$ g of dexmedetomidine provided significant increase in the sensory and motor block of spinal anesthesia in addition to prolonged postoperative analgesia. Highest dose of intrathecal dexmedetomidine used in animal studies was 100  $\mu$ g.<sup>16</sup> Konakci and colleagues<sup>17</sup> reported white matter injury in rats when high dose epidural dexmedetomidine (6  $\mu$ g/kg) was used alone; however, subsequently Brummett and coworkers<sup>18</sup> demonstrated no injury and a protective effect when doses of 26-40  $\mu$ g/kg were used perineurally.

In humans the largest epidural dose used was 2  $\mu$ g/kg<sup>19</sup> and the largest intrathecal dose used was 10  $\mu$ g<sup>14</sup> though neurological adverse events have not been reported. The population involved includes young otherwise healthy patients and the effect in older patients with cardiovascular comorbidities are yet to

Time to regress to bromage 0 motor block				
Group B		Group D		p Value (Student 't' test)
Mean	Std. dev.	Mean	Std. dev.	<0.0001
184.2	6.65	281.4	14.03	

Table-4: Time to regress to bromage 0 motor block

Time to first analgesic requirement				
Group B		Group D		p Value (Student 't' test)
Mean	Std. dev.	Mean	Std. dev.	<0.0001
157.7	9.32	253.3	8.18	

Table-5: Time to first analgesic requirement

Incidence of side effects				
	Group B	Group D	p Value	
Bradycardia	3	5	0.715	
Hypotension	3	8	0.199	
Nausea and vomiting	3	2	1	
Post dural puncture headache	2	3	1	
Arrhythmia	0	0	1	
Sedation	0	0	1	
Respiratory depression	0	0	1	

Table-6: Incidence of side effects

be investigated. In our study, the patients administered 7.5  $\mu$ g intrathecal dexmedetomidine reported prolonged duration of sensory and motor block.

Rampal Singh et al<sup>20</sup> in 2012 compared intrathecal clonidine and dexmedetomidine with intrathecal hyperbaric bupivacaine and concluded the higher efficacy of dexmedetomidine to produce longer duration of sensory and motor blockade. They did not find any increase in side effects. Gupta R et al<sup>21</sup> compared the duration of motor and sensory blockade and haemodynamic stability on adding dexmedetomidine with hyperbaric bupivacaine in patients who underwent lower abdominal surgeries and reported similar findings. Our study has shown similar results.

Thus, dexmedetomidine a newer  $\alpha_2$  agonist seems to be a good adjuvant when added to spinal hyperbaric bupivacaine. Dexmedetomidine with bupivacaine provide prolonged sensory and motor blockade, haemodynamic stability, minimal side effects and excellent intraoperative and postoperative analgesia.

## CONCLUSION

Our conclusion from the study is that dexmedetomidine as intrathecal adjuvant significantly prolongs the sensory and motor blockade of intrathecal hyperbaric bupivacaine without altering the onset of spinal anaesthesia. Patients who receive dexmedetomidine had reduced postoperative pain scores and a longer analgesic duration than those who received spinal bupivacaine alone. Also there is no hemodynamic instability or increased side effects when dexmedetomidine is added to spinal hyperbaric bupivacaine.

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# Our Experience with Percutaneous Tracheostomy at A Tertiary Care Centre

**Shahab Ali Usmani<sup>1</sup>, Suja Sreedharan<sup>2</sup>, Kiran M Bhojwani<sup>2</sup>, Vijendra Shenoy S<sup>3</sup>, Vishnu Prasad<sup>4</sup>, Vinay Raj T<sup>5</sup>**

## ABSTRACT

**Introduction:** Percutaneous tracheostomy (PCT) has become popular all over the world during the past two decades. Our aim was to record the learning curve, safety and complications of percutaneous tracheostomy, when introduced in a teaching hospital and also compare it with the conventional open procedure. We also analyzed the various parameters which can possibly influence the incidence of complications.

**Material and Methods:** 36 patients underwent tracheostomy; 12 in open tracheostomy group, 24 in the percutaneous tracheostomy group which further consisted of 12 patients each in Ciaglia and Griggs methods of tracheostomy.

**Results:** There were 17 (8 major and 9 minor) complications in the percutaneous tracheostomy group and one in the open tracheostomy group. In the percutaneous tracheostomy group, Ciaglia single staged dilatation technique was faster than the Griggs technique. In our study, complications were significantly related to neck girth but not to thyroid notch to suprasternal notch distance, age, sex, place of procedure and technique of procedure.

**Conclusion:** Percutaneous tracheostomy has a steep learning curve in a teaching institution. However, if continually performed, the percutaneous tracheostomy is a safe and rapid alternative to surgical tracheostomy.

**Keywords:** Percutaneous tracheostomy, open tracheostomy, neck parameters, complications

## INTRODUCTION

Tracheostomy has become the most commonly performed procedure in critically ill patients requiring long term mechanical ventilation.<sup>1,2</sup> The standard operative tracheostomy technique presented by Jackson<sup>3</sup> though time tested, has its own disadvantages in ICU settings. More often than not, it requires shifting of critically ill patients to operation theatre and monitoring by an anaesthetist with related extra cost.

The modern era of percutaneous tracheostomy began in 1985, when Ciaglia introduced a percutaneous tracheostomy procedure that used an easy and straight forward Seldinger technique.<sup>4</sup> Percutaneous tracheostomy meets the demand of an alternative to surgical tracheostomy. Apart from ability to perform the procedure bedside in the hands of an experienced surgeon/anaesthetist, percutaneous tracheostomy (PCT) is also fast and easy to perform. In many centers PCT is the procedure of choice in critically ill patients.<sup>5</sup> In this study the aim was to record the learning curve, safety and complications of percutaneous tracheostomy in a teaching hospital at tertiary care centre.

## MATERIAL AND METHODS

This prospective study was conducted in Department of Otolaryngology and Head and Neck surgery, Kasturba Medical College Hospitals, Mangalore and Government Wenlock

Hospital, Mangalore, Karnataka, over a period of 1.5 years between March 2010 and September 2012. Ethical committee clearance was taken from Manipal university ethical committee. Informed consent was taken from patient or 'next of kin'.

The study group consisted of 36 patients (27 men and 9 women), selected by inclusion exclusion criteria and consisted of two groups; the percutaneous tracheostomy group and the open tracheostomy group. The percutaneous dilation tracheostomy group was further subdivided into two groups which had

1. Ciaglia single circumferential dilation.

2. Griggs forceps dilation.

There were 12 patients in each group. We included patients referred for tracheostomy from Intensive care unit (ICU) and patients in whom elective tracheostomy was done before major head and neck surgery. We excluded patients in airway emergencies with unprotected airway, patients who required positive end expiratory pressure greater than 20 cm of water, midline neck mass –thyroid, coagulopathy, very obese patients, short or bull neck, non-palpable cricoid cartilage, gross deviation of trachea, infection at or near site of tracheostomy, previous major neck surgery, previous radiation, unstable cervical spine, malignancy at the site of tracheostomy and in children.

All patients were placed on 100% oxygen and received intravenous sedatives and a short acting paralytic agent. All procedures were performed by faculty members of the department. The neck was extended using a roll under the shoulder and a small rubber head ring is placed under the patients head to stabilise it. The patient's neck was painted and draped in a usual sterile fashion. A subcutaneous injection of 2% lignocaine with 1:100,000 epinephrine was given before the skin incision. The thyroid cartilage was located between the forefinger and thumb and the anatomical landmarks were identified and marked. Possible site of insertion is marked between 1st and 2nd tracheal rings or 2nd and 3rd tracheal rings. Endotracheal tube is deflated, tracheal tube is positioned just below the level of vocal cords and the cuff is reinflated to re-establish the seal. The tube was held in position ensuring the

<sup>1</sup>Senior Resident, Department of ENT and Head and Neck Surgery, King George Medical University, Lucknow, <sup>2</sup>Professor, <sup>3</sup>Associate Professor, <sup>4</sup>Senior Resident, Department of ENT and Head and Neck Surgery, Kasturba Medical College, Mangalore, <sup>5</sup>Assistant Professor, SRMC, Chennai, India

**Corresponding author:** Shahab Ali Usmani, 2/124, Virat Khand, Gomti Nagar, Lucknow, U.P. India 226010, India

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head and neck are in midline and the airway is maintained. A horizontal incision of 1.5-2.0 cm was made at the chosen site. Blunt dissection was performed after this with artery forceps, keeping in midline to identify anatomical landmarks. The 14G needle and cannula with attached 10ml syringe filled with normal saline is inserted in the midline in a caudal direction to avoid likelihood of guide wire being passed into pharynx. Correct placement of the needle was confirmed by aspiration of air into the syringe. In the subsequent steps, a guidewire, cutaneous dilator tracheal dilator and tracheostomy tube was passed using Seldinger technique. In Griggs method, Griggs dilating forceps was used to dilate the trachea, whereas in Ciaglia method, single curved dilator was used to finally dilate the trachea. The tracheostomy tube was finally guided over the guide wire into the trachea.

Open tracheostomy was performed using standard surgical procedure in operation theatre. Intravenous sedation, paralysis and management of endotracheal tube were performed by anesthetist. Patients positioning and infiltration was done in a fashion similar to PCT. A 4 cm incision was given two fingers above suprasternal notch, midline raphe of strap muscles was divided and the thyroid isthmus was retracted upwards. The

trachea was identified, and a horizontal incision was made in interspace between the first, second or third tracheal rings. Under direct visualization the endotracheal tube was withdrawn and tracheostomy tube was placed.

Before the procedure the patient characteristics like indication for tracheostomy, days of intubation, and bleeding parameters of the patient were noted. With the neck extended, the girth of the neck at the level of incision site and distance between thyroid notch to suprasternal notch were noted. Details of procedure like time taken for procedure and complications of procedure were noted. Bleeding during tracheostomy was graded as minimal, moderate and severe.<sup>6</sup> In minimal, there is no bleeding, or bleeding stops by itself on pressure. Moderate bleeding calls for special wound dressing and/or drug. Severe bleeding requires surgical intervention. Hypoxia was defined as an oxygen saturation of less than 90%.<sup>7</sup> The difficulty of procedure was graded using the classification of Fovea and Quintel<sup>6</sup>; no difficulties, some difficulty encountered, and procedure abandoned.

## STATISTICAL ANALYSIS

We used the convenience sampling method and data was

Characteristics	Percutaneous tracheostomy		Surgical Combined	
	Ciaglia	Griggs		
Number of patients	12 (%)	12 (%)	24 (%)	12 (%)
<b>Age</b>				
<50yrs	5 (41.6%)	8 (66.6%)	13 (54.1%)	1 (8.3%)
50-70yrs	5 (41.6%)	1 (8.3%)	6 (25%)	9 (75%)
>70 yrs	2 (16.6%)	3 (25%)	5 (20.8%)	2 (16.6%)
<b>Sex</b>				
Male	9 (75%)	9 (75%)	18 (75%)	9 (75%)
Female	3 (25%)	3 (25%)	6 (25%)	3 (25%)
<b>Days of intubation</b>				
0-5 days	3 (25%)	2 (16.6%)	4 (16.6%)	2 (16.6%)
6-10 days	5 (41.6%)	5 (41.6%)	10 (41.6%)	3 (25%)
11-15days	2 (16.6%)	3 (25%)	5 (20.8%)	0 (0%)
>15 days	2 (16.6%)	2 (16.6%)	4 (16.6%)	0 (0%)
<b>Haemoglobin level</b>				
Normal	11 (91.6%)	9 (75%)	20 (83.3%)	11 (91.6%)
Anaemia	1 (8.3%)	3 (25%)	4 (16.6%)	1 (8.3%)
<b>Platelets</b>				
<50 lakhs	0 (0%)	0 (0%)	0 (0%)	0 (0%)
50-75 lakhs	0 (0%)	0 (0%)	0 (0%)	0 (0%)
>75 lakhs	12 (100%)	12 (100%)	24 (100%)	12 (100%)
<b>PT</b>				
<17	8 (66%)	8 (66%)	16 (66.6%)	11 (91.6%)
>17	4 (33%)	4 (33%)	8 (33.3%)	1 (8.3%)
<b>INR</b>				
>1.5	0 (0%)	0 (0%)	0 (0%)	0 (0%)
<1.5	12 (100%)	12 (100%)	24 (100%)	12 (100%)
<b>GCS</b>				
0-5	3 (25%)	2 (16.6%)	5 (20.8%)	3 (25%)
6-10	8 (66.6%)	10 (83.33%)	18 (75%)	3 (25%)
11-15	0 (0%)	0 (0%)	0 (0%)	6 (50%)
<b>Time taken</b>				
0-10 min	2 (16.6%)	4 (33.3%)	6 (25%)	0 (0%)
11-20 min	8 (66.6%)	4 (33.3%)	12 (75%)	8 (66.6%)
>20 min	2 (16.6%)	4 (33.3%)	6 (25%)	4 (33.3%)

Table-1: Patient Characteristics

Tracheostomy indication	Ciaglia	Griggs	Combined	Open
Prolonged intubation	5 (41.6%)	7 (58.33%)	12 (50%)	2 (16.6%)
Airway protection	5 (41.6%)	2 (16.6%)	7 (29.1%)	4 (33%)
Airway Obstruction	0 (0%)	0 (0%)	0 (0%)	4 (33%)
Pulmonary toilet	2 (16.6%)	3 (25%)	5 (20.8%)	2 (16.6%)

Table-2: Indications for Tracheostomy:

Difficulty	No difficulty	Some Difficulty	Abandoned
Griggs (n=12)	9	1	2
Ciaglia (n=12)	8	3	1

Table-3: Difficulty Between Ciaglia And Griggs Methods:

collected using a semi structured proforma. Various parameters were assessed between open and percutaneous tracheostomy as well as the two groups of percutaneous tracheostomy. Analysis was carried out using SPSS version 17.0 using student t test and  $p<0.05$  was considered as significant.

## RESULTS

Our study was a prospective study on percutaneous tracheostomy and surgical tracheostomy done either in bedside ICU settings or in operation theatre. 36 patients were included in our study. There were 24 patients in the percutaneous tracheostomy group which was further divided into Ciaglia and Griggs group and 12 patients in the surgical tracheostomy group. Patient characteristics are shown in Table-1.

The most common age group was 61-70 years, youngest patient being 22 years and the oldest being 82 years. Out of the 36 patients there were 9 females and 27 males in our study. The indication for percutaneous tracheostomy in our study was mainly prolonged intubation in ICU patients ranging from 1 day to 21 days (Table-2).

Time taken was measured from the time of skin incision to successful placement of tracheostomy tube. Mean time taken in percutaneous tracheostomy was 14 minutes which was less than open tracheostomy (16.33 minutes), which is statistically insignificant. In the percutaneous tracheostomy group, Ciaglia single staged dilatation technique was faster than Griggs forceps dilatation, though the results were insignificant.

In our study, correlation between difficulty encountered in open and percutaneous tracheostomy was found to be insignificant. Two cases of Griggs method and one case of Ciaglia method were abandoned (Table-3).

Intra-procedural and post-procedural complications were analyzed. There were 17 complications in the percutaneous tracheostomy group and one in open tracheostomy group during the procedure and within a period of 2 weeks after the procedure. The results were not statistically significant (Table-4). We have found no significant difference in complications between Griggs and Ciaglia set used.

In our study we have found highly significant correlation between neck girth and complications. Also correlations between complications and thyroid notch -suprasternal notch distance were found to be insignificant (Table-5 and 6).

Out of the 24 percutaneous tracheostomies, 13 were done in ICU settings and 11 were done in OT settings. All the open tracheostomies were done in OT settings. We have found no significant correlation between complications, when procedures

were done in ICU and OT. Moreover complications were not significantly related to age, sex, and place of procedure and technique of procedure (Table-4).

## DISCUSSION

Advances in the ability to sustain critically ill patients have increased the need for tracheostomy in ICU patients. Open tracheostomy is time proven from the times of Chevalier Jackson.<sup>3</sup> But it has its own limitations, as it requires shifting of patients to Operation Theatre which may be unsafe for heavily compromised ICU patients. There is also an increased demand on operation theatre time, which is expensive and often in short supply. This has created an interest for less invasive, bed side, safe, rapid, cost effective and simple procedures.<sup>9</sup>

Ciaglia introduced a percutaneous tracheostomy procedure that used easy and straight forward Seldinger technique with progressive dilatation.<sup>4</sup> The potential advantages of this procedure, includes its technical ease, smaller incision and limited soft tissue dissection with fewer wound complications.<sup>10</sup> These advantages including a shorter procedure time and ability to perform the technique as a bed side ICU procedure has resulted in its wide acceptance as an alternative to surgical tracheostomy.

During the past two decades, the numbers of percutaneous tracheostomies has increased considerably with development of other techniques like Griggs forceps technique.<sup>12</sup> The feature of this tracheostomy is the use of a pair of modified Howard -Kelly forceps for blunt dilatation of the pretracheal and intercartilagenous tissue after insertion of the guidewire into the trachea.

'T-dagger' is a new percutaneous tracheostomy kit<sup>12</sup> introduced in India. The shaft of the T-dagger is smoothly curved at an angle of about 30 degree, with an elliptical cross section and accommodating number of oval holes. A 'J' tipped guidewire catheter is passed through a tunnel of the shaft and guide catheter to facilitate the formation of the stoma over it.

Rapitrac paercutaneous tracheostomy technique allows the insertion of a full size 7.0 (ID) or 7.5 (ID) cuffed tracheostomy tube into the trachea.<sup>13</sup> A specially designed percutaneous tracheostomy tool with inbuilt dilator is used to dilate the trachea. The tracheostomy tube is then inserted between the jaws of the dilator with a slight twisting movement.

Studies have compared the complications of the percutaneous technique with the open technique. The complications of the percutaneous technique have been classified into early<sup>9</sup> which include intra-procedural and those which occur within two weeks of the procedure. The late complications occur after 2 weeks of the procedure. Intra procedural complications are paratracheal insertions, loss of airway for more than 20 seconds, accidental decannulations, haemorrhage of more than 250 ml and pneumothorax.<sup>7</sup> Few studies also reported cardiac dysarrythmias.<sup>15</sup>

Complications	Percutaneous (n=24)	Tracheostomy	Combined	Surgical
	Ciaglia(n=12)	Griggs(n=12)	(n=24)	(n=12)
<b>Major</b>				
Paratracheal insertion	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Converted	1 (8.3%)	2 (16.6%)	3 (12.5%)	0 (0%)
Difficulty	3 (25%)	1 (8.3%)	4 (16.6%)	0 (0%)
Loss of airway	0 (0%)	1 (8.3%)	1 (4.2%)	0 (0%)
<b>Minor</b>				
Transient hypoxia	2 (16.6%)	4 (33.3%)	6 (25%)	0 (0%)
Subcutaneous emphysema	1 (8.3%)	1 (8.3%)	2 (8.3%)	1 (8.3%)
Bleeding moderate	0 (0%)	1 (8.3%)	1 (4.2%)	0 (0%)

**Table-4:** Intra Procedural and Post Procedural Complications of Percutaneous and Surgical Tracheostomy Group:

Type of Tracheostomy	Complication	Mean Neck Girth(cms)	Std deviation	P value
<b>Percutaneous</b>				0.006
	Nil	18	38.39	
	Hypoxia	4	33.63	
<b>Surgical</b>	Both	2	41.25	.124
	Nil	11	38.35	
	Emphysema	1	45.40	
P=0.006 highly significant				

**Table-5:** Comparison of Complications Vs Neck Girth in Open and Percutaneous Tracheostomy Group:

Type	Number	Mean(TN-SN) cms	Standard deviation	P value
<b>Percutaneous</b>				
	Complications	6	7.800	
	Open		1.4142	
Complications	1	9.000	1.4275	.835
Not significant				

**Table-6:** Comparison of Thyroid Notch –Suprasternal Notch (TN-SN) Distance Vs Complications in Open and Percutaneous Tracheostomy Group:

In our study we had 8 major and 9 minor complications in the percutaneous group. In the major complications we had 4 significant difficulties, 3 conversions, and 1 loss of airway in this group. In the patient in whom we had a loss of airway, patient suffered a cardiac arrest. Prompt resuscitation rescued the patient. Paratracheal insertion is one of the major complications in a difficult percutaneous tracheostomy. Paratracheal insertion is because of slippage of metal dilators off the calcified trachea or usage of soft guidewires which leads to kinking and development of false passages. Major haemorrhage of more than 250 ml can be seen in 0-4% of percutaneous tracheostomies as compared to surgical tracheostomies (0-3%).<sup>15</sup> We had one moderate haemorrhage in our series(8.3%). Other than injuries to major vessels, the percutaneous tracheostomy actually has a tamponading effect on small vessels and can also be used advantageously in coagulopathies.<sup>15</sup> Pneumothorax which occurs in 0-3% of cases as compared to 0.5-4% of surgical tracheostomies is due to neck extension and damage to cervical pleura. Cardiac dysrythmias may be because of hypoxia, hypotension or unrelated causes as these tracheostomies are done in very sick patients.<sup>15</sup> Accidental decannulation has been reported in 4% of percutaneous tracheostomies.<sup>9</sup> This complication is less common when compared to surgical tracheostomies because of lesser tissue dissection in PCTs. However if accidental decannulation does happen there may be difficulty in recannulation even at 7-16 days after tracheostomy

due to the small size of the wound.<sup>16</sup>

Inability to complete the procedure (1%) may occur at a significantly higher rate than surgical tracheostomy. Failures can be because of learning curve or dilator slippage over the calcified cartilages. Immediate conversion to ST is necessary in these cases. In our study one case in Griggs group in whom we lost the airway procedure was converted to surgical tracheostomy. Another case in the Griggs group had a vasovagal attack during the dilatation and stoma formation. This patient also had to be converted into bedside surgical tracheostomy. One case in Ciaglia group has to be converted because of the inability to successfully dilate the trachea with Ciaglia dilator. Late complications are related to cosmesis, wound infection and tracheal stenosis. Wound infection is related to tissue dissection. Avoidance of broad dissection and tissue disruption results in lesser chance of development of this complication when compared to ST.<sup>15</sup>

Early studies have revealed significantly more early major complications of PCT as compared to surgical tracheostomy.<sup>17</sup> Later studies<sup>9,18</sup> have revealed that early minor complications such as minor haemorrhage, subcutaneous emphysema are more common in percutaneous group as compared to surgical tracheostomy. Our study also showed more early minor complications in the PCT group as compared to open, though there was no significance. Late complications like wound infection, cosmesis and tracheooesophageal fistula are less

in PCT group (8%) when compared to ST group (13%).<sup>11</sup> When complication rates are compared as a whole (major and minor), there is no difference in intraprocedural complications between the two groups.

Many variables have to be taken into account when complications are compared between percutaneous tracheostomy and surgical tracheostomy. One of them is the place of tracheostomy. All our surgical tracheostomies were done in the Operating room. About half of our PCT's were done bedside. Comparison of complications between tracheostomies done in the ICU or otherwise did not show any difference. Studies<sup>16</sup> have shown that even though the overall complication rate for peri-operative complications were less in bedside tracheostomies than operation room tracheostomies (5% vs. 20%), no significant difference was found in complication rates of percutaneous tracheostomies and surgical tracheostomies done bedside. However there was an increased incidence of postoperative complications in the percutaneous tracheostomy group done bedside when compared to surgical tracheostomy group in this study.<sup>16</sup>

The other variable is type of percutaneous tracheostomy, some techniques of tracheostomy have a higher rate of complications than some others. Cooks Kit (multiple dilator technique) has a lower complication<sup>15</sup> than Rapitrac system. The Rapitrac set of schaffner et al<sup>13</sup> and the guidewire dilator forceps of the Griggs have poor performance record. The insertion of a sharp instrument into the trachea and blind dilatation is not safe surgical technique and may not be reproducible at a successful rate.<sup>15</sup> To date the Ciaglia technique with its avoidance of sharp tracheal instrumentation and gradual dilatation till placement of tracheostomy tube has been considered safer when compared to the other methods. Our small series of patients did not show any significant difference in complication rates between Ciaglia and Griggs methods of tracheostomy.

In our study the surgeons (otolaryngology consultants) of our teaching hospitals were using the percutaneous technique of tracheostomy for the first time in our institute. We had 17 perioperative complications in 24 patients, this would represent the learning curve of PCT in our department. The difference in complications of PCT reported by different groups<sup>16,18,19</sup> have incited researches to look for the learning curve for this procedure. In a study by Douglas D. Massick,<sup>16</sup> the complication incidence for first 100 PCT procedures were analyzed, it was found that out of the 63 perioperative complications, the first 20 had 34 complications. In this cohort there was an increased incidence of post operative complications (major haemorrhage, tube dislodgement and death), though the value did not reach statistical significance. Late complications like tracheal stenosis was higher in the first 50 patients when compared to the next 50. Another significant finding of the study was that suboptimal cervical anatomy contributed to complications independent of operator experience. Our study which includes our institutional experience by different surgeons also demonstrated this steep learning curve.

We had certain limitations to our study. In assessment of learning curve, we could not assess a single surgeon's learning curve since there were multiple surgeons involved. Moreover, the small number of patients decreased the power of our study. Randomization was not done between two study groups. Patients with unfavourable neck anatomy tended to go into the

surgical tracheostomy group indicating selector bias. Moreover, we could not study the late complications in our study.

## CONCLUSION

In conclusion percutaneous tracheostomy has a steep learning curve in a teaching institution. Our short study of 24 cases has brought out the peri-operative and post-operative complications associated with percutaneous tracheostomy. As it is a partially blind procedure even under bronchoscopic guidance, suboptimal cervical anatomy is a high risk for complications. We conclude that early experience of this procedure should be in operating theatre.

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# Prevalence of Low Mental Health Among Nurses in Medical Intensive Care Units

Bhirange Swapnil<sup>1</sup>, Rankhambe Harshali<sup>1</sup>, Chaware Snehal<sup>2</sup>

## ABSTRACT

**Introduction:** Professional nurses who work in ICU experienced more stressful conditions compared to those involved in other wards of hospitals. Excessive workloads, job factors, and organizational factors stand to be the leading causes of mental health problem in nurses. However, a little attention has been directed towards determining the prevalence of occupational stress and mental health problem in ICU nurses. The present study was intended to determine the prevalence of mental health problems among nurses working in the intensive care units in various private hospitals in Amravati city.

**Material and Methods:** The objective of this cross-sectional study was to determine the prevalence of mental health problems in ICU nurses working in various Private Hospitals. The mental health status of the nurses working in the ICU was characterized using the 28-item General Health Questionnaire (GHQ-28). 68 female ICU nurses completed the questionnaires. Statistical significance was analyzed using independent samples t-test as appropriate.

**Results:** The prevalence of somatic symptoms, anxiety, social dysfunction, and depression were 56.68%, 64.60%, 69.96%, and 14.18%, respectively. As per the independent samples t-test, somatic symptoms, anxiety, and social dysfunction had significant relationships with marital status ( $p = 0.01$ ), but no significant differences between mental health subscales and educational status, and working different shifts ( $p > 0.05$ ).

**Conclusion:** There was a high prevalence of low mental health among ICU nurses. There was a significant relationship between mental health and marital status. Future interventions to identify and reduce occupational stress are needed to develop the comprehensive health program to enhance nurses' levels of mental health.

**Keywords:** mental disorders, ICU nurses, marital status, educational status

## INTRODUCTION

The key to success in nursing care lies in the fact that the nurses must be sensitive enough to respond to even minimal changes in patients' health condition so that appropriate clinical assessment is done timely, accurately and expediently. This is possible only when affective states of nurses on duty are optimally aroused over different times of the day, which in turn thought to be conducive to enhance patients' safety.

It is becoming increasingly difficult to ignore the factors that are clearly important in stress induced by work, i.e., including long hours of working, the quality of the relationships between hospital workers, poor supervision, high workload, and poor work environment. The physical environment (including the factors like temperature, lighting, the levels of sound in hospitals etc.), in addition, has a great impacts on the levels of stress in the healthcare staff.<sup>1</sup> Occupational stress has a significant impact on workers' health and well-being, job satisfaction, their quality

of life and quality of family life, turnover, and absences from work.<sup>2</sup> In general, the prevalence of mental health problems among people was estimated to be 14 to 18%.<sup>3</sup>

Stress levels among professional nurses have increased due to the increased demands of clinical nursing in recent years. Previous studies have shown that there is an association of work demands and stress with adverse mental health like emotional exhaustion<sup>4</sup>, depressive disorder<sup>5,6</sup> and fatigue<sup>7,8</sup>, which found to result in sleep problems and absences from work due to sickness.<sup>4</sup>

Many nurses reported to experience high levels of occupational stress in their work environment. As an outcome of stressful workplaces and tasks, stress has effects on nursing behavior in hospital wards.<sup>3,1</sup> However, the results of the General Health Questionnaire (GHQ) among 870 nurses working in various hospitals in the south of England indicated that about 27% of hospital workers were suffering from occupational stress and various mental health problems.<sup>3</sup> Nurses in the intensive care unit are exposed to more traumatic events happening in their stressful working environment and reported to have experienced more stressful conditions than the nurses working in other wards of hospitals.<sup>9</sup> Higher levels of stress result in increased turnover rates and burnout among this working group.

The prevalence of mental health problems (anxiety and depression) among nurses is high. Excessive workloads, organizational factors and job factors are found to be the important leading causes of mental health problem in nurses.<sup>10,11</sup> However, far too little attention has been directed towards the determination of the prevalence of occupational stress and mental health problem in nurses working in ICUs. This study was intended to determine the prevalence of occupational stress and various mental health problems in ICU nurses working in private hospitals in Amravati city and to conclude the relationship between occupational stress and mental health.

## MATERIAL AND METHODS

This cross-sectional study was conducted to determine the prevalence of mental health problems in various Private Hospitals in Amravati City.

### Selection and Description of Participants

All registered female nurses employed in the private hospitals,

<sup>1</sup>Speciality Medical Officer, TNMC, Mumbai, <sup>2</sup>General Practitioner, Amravati, Maharashtra, India

**Corresponding author:** Swapnil Bhirange, Gajanan Nagar, Arvin Naka, Ward No. 08, Arvi Main Road, Wardha-442001, Maharashtra, India

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Variables		Somatic symptoms	Anxiety	Social dysfunction	Depression
Marital status	Single	45.04	58.71	64.5	10.32
	Married	60.86	66.71	71.93	15.57
Education Levels	Diploma	53.57	61.89	69.03	12.79
	Bachelor's degree or higher	57.33	65.18	70.14	14.45

**Table-1:** Prevalence of mental disorder subscales (%) according to marital status and education levels

Occupational stress	Education Level	Mean	SD	p-value*
Somatic symptoms	Single	45.03	5.63	0.000
	Married	60.86	6.57	
Anxiety	Single	58.71	4.78	0.000
	Married	66.71	7.12	
Social dysfunction	Single	64.50	4.50	0.000
	Married	71.93	7.77	
Depression	Single	10.32	3.85	0.180
	Married	15.57	16.21	

**Table-2:** Prevalence of mental disorders among nurses as per their marital status (\*Independent samples t-test; SD = standard deviation)

having intensive care units (ICU) of at least 3 beds to maximum possible number of beds in the Amravati city, were eligible to participate in this study. The nurses who had bachelor degree or were associate diploma holders of either nursing institutions or universities, and agreed to participate in this study, were included in the study. Any nurse with a qualification less than two years since completing their nursing program was excluded. The initial sample consisted of 80 female ICU nurses, 12 of whom did not complete the questionnaires.

### Technical Information

The 28-item General Health Questionnaire (GHQ-28) was used to characterize the mental health status of the nurses in the ICU. Numerous studies have investigated reliability and validity of the GHQ-28 in various clinical populations. Test-retest reliability has found to be high (0.78 to 0.9)<sup>12</sup> and both, interobserver and intraobserver reliability, have been reported to be excellent (Cronbach's  $\alpha$  0.9–0.95). High internal consistency has also been reported. The GHQ-28 has been reported to correlate well with the Hospital Depression and Anxiety Scale (HADS)<sup>13</sup> and also with the other measures of depression.<sup>12</sup>

This questionnaire has four subscales; each subscale consists of seven questions meant to evaluate anxiety, somatic symptoms, social dysfunction, and depression.<sup>14</sup> Mental health -related stress was rated using a 5-point Likert scale.<sup>3</sup> A high score suggests a severe mental disorder, and the lower score suggests no disorder. Demographical features, including age, education level, marital status and work experience, of the nurses in the ICU were collected with an appropriately designed form. The data for the study were collected using a questionnaire for the assessment of the mental health status among the nurses in the ICU. Ethical issues were considered. Written informed consent was taken.

### STATISTICAL ANALYSIS

Statistical analysis was done using independent samples t-test as appropriate, by Statistical Package for the Social Sciences (SPSS) software, version 20. The results were considered

significant at the level of  $\alpha = 0.05$ .

### RESULTS

The nurses in the present study were having the age ranging from 23 to 45 years, with an average of 28.99 years and with a standard deviation of  $\pm 4.89$ . About 82.24% of the nurses were holding Bachelor's degrees or a higher level degree, and about 17.64% of them were having a diploma-level education. The nurses who were married comprised 72.53% of the total number of participating nurses. 81% of the nurses had worked on rotating shifts, 10.29% had worked on permanent day shifts and 8.82% had worked on night shifts.

The most prevalent mental disorder in the nurses was found to be social dysfunction (69.96%), and the least prevalent mental disorder being the depression (14.18%). Among all the nurses, about 64.6% had anxiety symptom, those about 56.68% had somatic symptoms. In order to find out the relationships between marital status, mental disorders and education level, the score in each subscale were calculated and the independent samples t-test was applied. The results indicated that the prevalence in all subscales of mental health was greater in married nurses than in the nurses who were not married, and this difference was statistically significant ( $p < 0.05$ ). No significant difference was found between education levels and the mental health disorder subscales.

Table-1 shows the prevalence of mental disorders and its subscales according to education levels and marital status. Nurses having diploma-level educations were found to have higher somatic symptoms (80%) than in the nurses having more advanced educational levels. However, the other mental disorders were greater in the nurses holding Bachelor's degrees or higher level degrees.

Table-2 All mental disorder subscales, except depression, were greater in nurses who were married than those who were singles.

### DISCUSSION

This study was designed to study the prevalence of various mental health problems in nurses who work in ICU in various Private Hospitals in Amravati City. The results of the study indicated that the nurses on the fixed night shift schedule had much greater prevalence of somatic symptoms, anxiety, depression, and mental disorders than that in the nurses who worked the rotating shifts (Table-2). This finding was in agreement with previous findings of the study done among hospital nurses in Japan that showed a significant relationship ( $p < 0.001$ ) between mental disorders and shift work in nurses.<sup>15</sup> Assessment of mental disorders among nurses doing shift work in Shiraz, using the GHQ-28 questionnaire, showed that 45.4% of the reported nurses had experienced mental disorders. The highly prevalent mental disorders were anxiety (43.2%) and somatic symptoms (34.5%) and prevalence of depression and social dysfunction has been reported as 1.2% and 79.5% in

nurses who do shift work.<sup>16</sup> This study produced results that confirm the important findings of a previous work in this field. The investigation done among the nurses in Tabriz's teaching hospitals, considering the relationship between occupational stress, general health and burnout, revealed that 37.3% of the nurses suffered from significant mental health disorders, 30.5% of the nurses from somatic symptoms, 62.7% of the nurses from anxiety, 3.9% of the nurses from social dysfunction, and 16.9% of the nurses from depression.<sup>17</sup> This can be attributed to the heavy workload with less number of persons on duty, inadequate and poor quality of sleep, disputes among colleagues and also with the healthcare professionals and workplace violence.

The results also indicated that the prevalence of the mental health problem among married nurses was considerably greater than that in single/bachelor nurses working in the ICU (Table-1). The somatic symptom was noted to be the most prevalent mental disorder among married nurses (60.86% of the nurses). The results are consistent with the findings of other studies that found a significant difference between the nurses' marital status and depression and social dysfunction ( $p < 0.01$ ).<sup>16</sup> The results of another study showed that the schedule of shift work had a great impact on the levels of stress among workers.<sup>18</sup> This can be attributed to relatively low socioeconomic status and professional burden.

Mental disorders in nurses working in ICU who experienced high levels of stress were far greater than those experiencing low levels of stress. This result is in agreement with the findings of a previous study that showed a strong relationship between the development of mental disorders and occupational stress among nurses.<sup>19</sup> This may be due to disputes among colleagues and also with the healthcare professionals, poor nurse-patient relationship and workplace violence.

The factors that cause high prevalence of low mental health among nurses who work in the ICU must be identified and reduced and a comprehensive health program should be implemented in this field not only to reduce occupational stress but to enhance the level of nurses' mental health also, so as to improve the effectiveness and performance of the ICU.

Training programs to enhance communication skills and reduce stress could be beneficial in improving basic/intuitive communication strategies and also to promote safety as well as to improve health in the workplace.<sup>20,21</sup> Also an another important ergonomic recommendation is that night work should be reduced as much as possible. Schedule planners should avoid permanent night shift and rapid change over from night to day on the same day or from morning to night. The number of consecutive working days should be limited to 5-7. Every shift system should consider some free weekend including at least two successive full days off. Schedule planners must consider the time of recovery and rest breaks. Schedule should ideally and preferably be regular and predictable.<sup>22</sup>

## CONCLUSION

This study highlighted the important findings that the prevalence of low mental health among nurses working in the ICU was high. There was a significant relationship between marital status, shift work and mental health and their subscales. These results can be a roadmap to establish policies for hospitals in promoting the health and welfare of their staff members. Future detailed

interventions are needed to develop a comprehensive and appropriate health program in this field to reduce occupational stress and improve the level of nurses' mental health.

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# Internally Weighted Mandibular Denture: A Case Report

Ahzam Shaikh<sup>1</sup>, Smita A. Khalikar<sup>2</sup>, S.P. Dange<sup>3</sup>, Arun Khalikar<sup>2</sup>

## ABSTRACT

**Introduction:** Severely resorbed residual alveolar ridges pose a clinical challenge during prosthodontic rehabilitation. Residual ridge resorption leads to a decrease in denture bearing area which in turn will lead to a decrease in retention, stability and support of the planned complete denture prosthesis. Various treatment options have been described for rehabilitation of patients with a severely resorbed ridge.

**Case Report:** This article reports a case of severely resorbed anterior mandibular ridge for which an internally weighted mandibular denture was fabricated with a customized weighted metal base using putty index of the tooth arrangement as a guide. **Conclusion:** In cases of severely resorbed ridges, reinforcement of the denture with a customized metal framework with minimal metal display is an optimal treatment alternative to achieve the desired esthetic and functional outcome.

**Keywords:** Framework, Internally weighted, metal base, reinforce, resorbed ridge,

## INTRODUCTION

Metal bases and frame-works have been known for their use in reinforcing the mandibular denture base while managing unfavourable resorbed ridges. They improve the fracture resistance, dimensional stability, accuracy, weight and retention of the denture bases. Grunewald<sup>1</sup> introduced gold framework to compensate for the weight lost after tooth extraction and extensive resorption in resorbed mandibular residual ridges. Belfiglio<sup>2</sup> also advocated the use of metal bases to reinforce the complete dentures when a higher degree of dimensional change is expected during processing or when an increase in strength is needed. DeFurio and Gehl<sup>3</sup> described the use of chrome-cobalt as one of the most retentive base material for the foundation of maxillary complete dentures. Although the use of metal base dentures reinforced the prosthesis, they often irritate the underlying alveolar ridge and the post-delivery intaglio surface adjustments are difficult.<sup>4</sup> To overcome these disadvantages of a metal denture base, different authors have described different techniques to position and fabricate the internal metal bases during denture processing. Wormley and Brunton<sup>5</sup> described a technique to fabricate internally weighted mandibular dentures by molding softened sticks of wax into a triangular cross-section shape directly over the definitive cast to fabricate a metal bar. They incorporated plastic sprues projecting laterally at the facial and lingual sides of the wax pattern in a tripod configuration to suspend the metal bar during the denture processing. The technique reported by Hurtado<sup>6</sup>, consisted of fabricating a weighted metal base by using 4 cast metal tissue stops similar to the cast stops of distal extension partial removable prostheses. Kim et al<sup>7</sup> described a method for fabricating an internally weighted mandibular complete denture using a processed denture base and a plaster index of the preliminary tooth arrangement. The most recent technique described by Balch et al<sup>8</sup> described

the use of vertical posts extending from the framework into the definitive cast to maintain space beneath the framework during acrylic resin processing. The fabrication of internally weighted mandibular dentures requires accurate impressions and additional laboratory procedures while the cost of the alloys adds to the cost of the prosthesis. This article describes a case report wherein an internally weighted mandibular complete denture was fabricated with customized design and position of the metal base for an optimal esthetic and functional outcome and also allowed for conventional reline procedures.

## CASE REPORT

A male patient aged 69 years reported to the Department of Prosthodontics, Govt. dental College and Hospital with a chief complaint of broken lower denture. The patient gave a history of being a denture wearer for the past 3 years. He got his dentures replaced twice both times the reason being midline fracture of the lower dentures. Intraoral examination revealed that the anterior mandibular residual ridge was very severely resorbed as compared to the posterior residual ridge. The patient insisted on making a new set of dentures which won't get fractured. The patient was assessed and considered for an implant supported overdenture but due to the unwillingness of the patient to undergo any surgical procedures and age considerations it was decided to fabricate the mandibular denture reinforced with a metal framework.

A full-coverage preliminary mandibular impression was made by using stock impression trays and irreversible hydrocolloid. The maxillary final impression was made using a custom tray and zinc oxide eugenol impression paste and was poured in type 3 dental stone. As the mandibular ridge was severely resorbed anteriorly the lower impression was made using McCord's technique<sup>8</sup> (Figure-1). The occlusal vertical dimension was determined using trial bases with wax occlusion rims. Facebow record was then taken and the casts were mounted with the facebow and centric relation record. The trial dentures with denture teeth arranged were placed intraorally and evaluated clinically (Figure-1). The land area of the mandibular definitive cast was scored to make a putty index of the mandibular teeth arrangement. The mandibular master cast was duplicated onto which two sheets of modeling wax were adapted. Then as described by Graser<sup>9</sup> one sheet of wax was removed from the area which the metal framework would occupy. This was

<sup>1</sup>P.G. Student, <sup>2</sup>Associate Professor, <sup>3</sup>Professor, Government Dental College and Hospital, Aurangabad, India

**Corresponding author:** Dr. Ahzam Shaikh, Room no. 231, Dept. of Prosthodontics, Ghati campus, Govt. Dental College and Hospital, Aurangabad, Maharashtra, India.

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**Figure-1:** (a) Maxillary and mandibular final impressions. Mandibular final impression was recorded using McCord's technique. (b) Wax trial of the denture



**Figure-2:** Wax pattern of the framework on the refractory cast;  
**Figure-3:** Metal framework fabricated using putty index of the teeth arrangement



**Figure-4:** (a) Intaglio surface of the processed denture, (b) Postoperative view of the patient

then again duplicated to make a refractory cast. Spacer wax was adapted on this refractory cast in the slot prepared for casting according to the indexed denture teeth to provide optimal base fit and improve the esthetic outcome (Figure-2 and 3). Sprues were then fixed and casting was done. The cast metal insert was then adapted over the first thickness of baseplate wax (adapted on the master cast). Figure-3 shows the space available for the teeth and denture base. The trial denture base with the cast metal insert adapted on the master cast was then processed with high impact heat-polymerized acrylic resin. The prosthesis was then retrieved and polished for insertion. Figure-4 shows the intaglio surface of the processed denture.

## DISCUSSION

Severe resorption of the mandibular alveolar ridge may sometimes bring the need to construct a mandibular denture that is strong, stable and functional which can be met by a denture reinforced with a metal framework. The inherent strength of such a denture make it possible to meet the patient's special needs. The internally weighted mandibular denture fabrication

described here was fabricated using a combination of Graser's<sup>9</sup> technique and a modification of Kims<sup>7</sup> technique. We used a putty index instead of the plaster index used by Kim et al. It allowed for adequate restorative space to permit relief of framework from the definitive cast as evaluated by the putty matrix of the trial denture base positioned on the master cast. One study demonstrated that mandibular complete denture fractures decreased following internal metal reinforcement as long as adequate bulk of acrylic resin was present.<sup>10</sup> If sections of the denture above the internally suspended framework are too thin for adequate thickness of acrylic resin, then the mandibular complete denture's cameo surface can be modified and finished in metal so that strength is not compromised. The internally suspended framework is also indicated when edentulous ridge contours are irregular or significantly compromised, because all denture base adjustments remain in acrylic resin rather than metal. A disadvantage to this or any complete denture reinforcing framework is the added expense of the prosthesis for the patient.<sup>4</sup>

## CONCLUSION

In cases of severely resorbed anterior mandibular ridge, the reinforcement of the denture by a customized metal framework well adapted to the ridge is an optimal treatment alternative. This reinforcement will aid in resisting fracture of the resulting denture. The fabrication technique described in this article will help in achieving appropriate contour of the denture base with minimal metal display and may benefit the patient when implant placement or pre-prosthetic surgery is not an option.

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# A Rare Study of Electric Shock Associated Spinal Injuries: Prognosis and Outcome

Ravi Gaur<sup>1</sup>, Nimish Mittal<sup>2</sup>, Mrinal Joshi<sup>3</sup>, Krishna Dubey<sup>4</sup>

## ABSTRACT

**Introduction:** Electric shock associated with spinal injury is a rare type of trauma in the world with only few citations available for the same. In India, only a few case reports from various burn units are mentioned. To gain some insights on the magnitude of this problem in Indian context; we carried out this prospective study in our spine injury department to study the epidemiological data associated with spinal trauma secondary to electric shock and to study the neurological recovery patterns in electric injury leading to spinal cord injury.

**Material and Methods:** A study for demographic data collection along with neurological recovery patterns in such patients was conducted over a period of 21months from 1<sup>st</sup> October 2008 to 30<sup>th</sup> June 2010. All the patients having such type of injury were evaluated on ASIA scale and Lund and Browder chart for neurological assessment and assessing associated burn and marking entry and exit sites respectively. Radiological assessment with MRI was done to assess the vertebral injury, spinal cord injury and canal compression.

**Results:** No neurological improvement was noted in patients with such kind of injury over the period of one year follow-up suggesting the graveness of such type of injury. Associated findings of polyneuropathies were of no such significance, as paraplegia leads to complete loss of motor and sensory loss.

**Conclusion:** Complex form of trauma along with almost no recovery is the rule in cases of electric shock associated spinal trauma. Most of the families are devastated as nowadays trend for nuclear families is more pronounced even in rural area. Polyneuropathies found in such cases are not affecting the outcome as spinal injuries are severe and almost showing no recovery. Multiple level vertebral fractures were almost present in half of the cases suggestive of severity of trauma.

**Keywords:** Spinal injury, Electric shock, Vertebral fractures.

## INTRODUCTION

Electric injury associated spinal trauma is a very low incidence injury as only 2% of cases having electric injury are also having electric shock.<sup>1</sup> The investigator of the present study noted that the number of spinal injury associated with electric shock are quite prevalent in the Sawai Man Singh Hospital as compared to western counterparts and available international data does not show the exact picture of Indian context. The chief causes of accidents associated with electricity were clothes catching fire, falls, crushing and being struck by objects.<sup>1</sup> Risk factors included contact with moisture or working on damp ground. Literature on spinal cord damage after electrical trauma is scarce and the incidence, early diagnosis and treatment of this condition remain to be elucidated. In India; electricity is transmitted in AC form at 50 Hz at 220V, 440V, 11KV and 33KV. In industrial complexes 6.6KV is mainly used.<sup>2</sup> However, the long-term sequelae of the electrical injury might be more subtle, pervasive, and less well defined, and are particularly difficult

to diagnose, as the link between the injury and the symptoms can often go unrecognized by patients and their physicians.<sup>2</sup> Many who suffer electrical injury have considerable difficulty returning to work.<sup>3</sup> In an article on the delayed syndromes in patients with electrical injuries, it was speculated that exposure to electric fields is similar to the effects of irradiation.<sup>4</sup> So the present study aimed to study were to study the epidemiological data associated with spinal trauma secondary to electric shock admitted to Dept. of P.M. and R. during 1<sup>st</sup> Oct. 2008 to 30<sup>th</sup> June 2010 and to study the neurological recovery patterns in electric injury leading to spinal cord injury.

## MATERIAL AND METHODS

In this prospective study, 45 patients were recruited, who were admitted to as an inpatient spinal injury rehabilitation program in Department of Physical Medicine and Rehabilitation in Sawai Man Singh Hospital, Jaipur between 1<sup>st</sup> October, 2008 and 30<sup>th</sup> June, 2010. All acute spinal cord injury patients associated with electric shock, presented to our department were recruited in this study.

For epidemiological assessment, a clinical interview was carried out from patient and care givers. Diagnosis of spinal injury was based on Neurological assessment on American Spinal Injury Association (ASIA) scale and radiological evidence of vertebral injury or canal compromise on X-ray, CT scan or MRI.<sup>1</sup> To find out electric shock associated injuries, echocardiography (ECG), nerve conduction velocity (NCV) and lab investigations were also carried out as relevant to the injury and management. Electrical burn wounds were assessed on Lund and Browder chart and entry and exit wounds were identified and marked to identify path of current and associated lesion. Patients were periodically assessed every three month's period for neurological recovery patterns and rehabilitation needs up to a maximum duration of one year and minimum duration of six months. Consent was taken from the all the patient who were recruited in this study. The study was approved by the hospital ethical committee. Detailed history based on the memory of the patient was obtained regarding the site coming in contact

<sup>1</sup>Assistant Professor, Department of Physical Medicine and Rehabilitation, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, <sup>2</sup>Senior Resident, AIIMS, New Delhi, <sup>3</sup>Head of Department and Professor, Department of Physical Medicine and Rehabilitation, Sawai Man Singh Medical College, Jaipur, <sup>4</sup>Junior Resident Final Year, Department of Pathology, NIMS Medical College, Jaipur, India

**Corresponding author:** Dr.Ravi Gaur, H.No.-405, Dr. RMLIMS Faculty Residence, TC 40-41, Near Indian Oil Corporation Office, Vibhuti Khand, Gomti Nagar, Lucknow, UP-226010, India

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with the source of electricity and any associated burns like joule burns for assessment of site of entry and exit.

## STATISTICAL ANALYSIS

SPSS version 16.0 was used for analysis. Mean age of patients were calculated. Percentage of injuries were calculated to infer the results of the present study and compare with the available literature.

## RESULTS

Out of 2358 spinal cord injury patients admissions during the study period; 45 cases (1.91%) were enrolled as cases of spinal injury due to electric shock. All cases enrolled in the study were males. Out of 45, 43 (94%) cases are from rural area. Most of the patients were in between 20 -40 year of age group with a mean age of 32.59 years (table-1). The most common time of injury was between 5:00 A.M. to 5:00 P.M. (working hours) and no cases were reported who received the injury between 11:01 P.M. to 5:00A.M.

Only two patients were below 20 years; were working as line men/ electrician on temporary basis in government electricity board. One case was welder and got shock while checking connection of welding machine.

Most of the victims (73%) were educated up to secondary education, where as 17% were completely illiterate.

Most of the persons associated with this kind of injury were of low socio-economic group as 62% cases have income less than Rs.5000/Month (<100\$ / month) with family size of at least five persons. As opposite to the traditional belief, nuclear families (30 out of 43; 69.76%) are becoming more prominent in rural Indian society. In this study, average family size in nuclear families was 5.27 and for joint families was 10.93.

In the study group the most common type of injuries were dorsal spine injuries (28 out of 45; 62.22%) followed by cervical injuries (10 out of 45; 22.22%) (figure-1).

Mode of transportation to the hospital immediately after trauma was mainly jeep as ambulance facilities were scarce and costly. Average associated fall from height was 11.75 feet, which is suggestive that predisposing factors were deliberate reach to the electricity source by the affected persons. Hands were the most common sites of entry as they get injured while using tools (42/45; 93% cases). Right hand involvement was found greater than left hand which might be due to right hand dominance in people. In some cases tongue and upper back were also marked as site of entry of electricity. Most common exit site of electricity were legs (53%) followed by hands (22%) and then rare sites like upper back, abdomen etc. In four cases site of exit could not be

established (figure-2).

All the tetraplegic patients showed no signs of recovery with very high mortality (6 out of 12; 50%) at the end of completion of one year of study duration. At the end of study; a total of 34 out of 45 patients(75.55%) were recorded in ASIA 'A', 2 were recorded in ASIA 'B'(4.44%), one case each of ASIA 'C' and 'D' and ASIA 'E' included 7 cases (15.56%). None of patients recruited as ASIA 'A' improved. Only 2 patients out of

S. No.	Age	Cervical	Dorsal	Lumbar	No Bone Injury
1	0-20Yrs.	3	4	1	0
2	21-40 Yrs.	5	21	1	1
3	41-60 Yrs.	2	3	2	2
4	>60 Yrs.	0	0	0	0

Table-1: Age group- type of injury

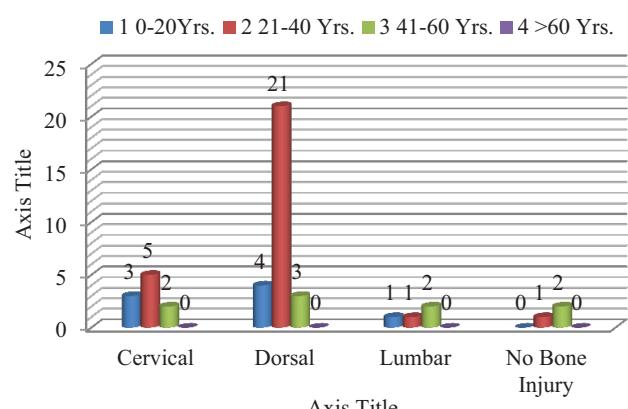


Figure-1 Associated Vertebral Injury

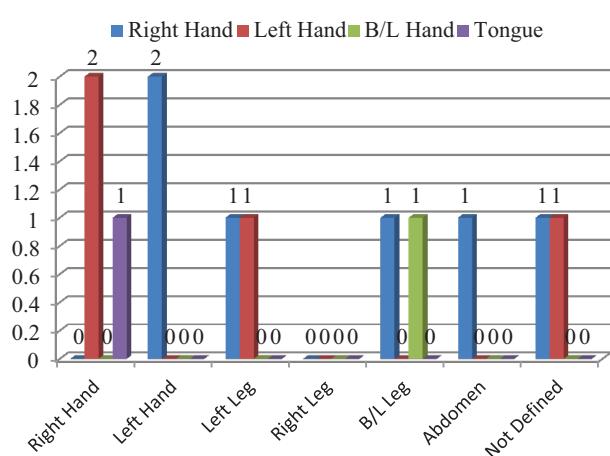


Figure-2: Site of entry/exit in cervical cases

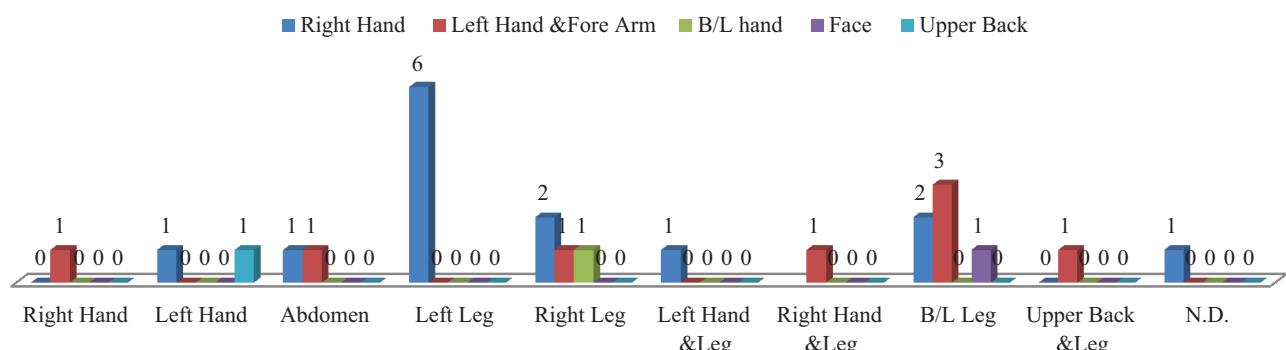


Figure-3: Site of entry/exit in dorso-lumbar cases

45 showed signs of partial recovery. One patient improved from ASIA 'B' to 'C' where as one another patient improved from ASIA 'D' to 'E' (figure-3).

Electricity also affects peripheral nerves suggested by presence of sensory and motor affection on Nerve Conduction Studies.

In all tetraplegic patients the site of entry was hands (11/12) or tongue (1/ 12) with exit sites was in opposite hand (41.67%), legs (33.33%) or not defined (25%).

In paraplegia, 16 cases out of 26 (61.53%) showed sign of entry in hands and site of exit in legs. Similarly 3 cases out of 26 (11.53%) were found with entry site in hand and multiple exit sites in hand and leg. One case showed site of entry on face with exit on bilateral legs. In another case entry site was found on upper back with exit site on left hand. In 2 cases, with entry site was on hands and the exit site was observed on abdomen. In one case entry site was on hand but no defined exit site was found. Two paraplegic patients out of 26 cases (7.7%) showed site of exit in opposite hand.

At the end of one year follow up, mortality was 11 (24.44%) which suggest that it is a grievous type of injury. In these eleven fatal cases, 6 cases were of cervical injury, 4 had dorsal injury and one case had no bone injury.

## DISCUSSION

Daniel P. Lammertse analyzed records of The Rocky Mountain Regional Spinal Injury System database at Craig Hospital and found 9 cases of spinal cord injury caused by electrical trauma out of 9363 SCI admissions over the period 1972–2003, representing slightly less than 0.1% of the cases. In our study this percentage was much higher (1.91%; 45/2358) suggesting different approach should be adapted to such problem in our country.

Koumbourlis AC proposed that there is no specific therapy for electrical injury and the management is symptomatic.<sup>5</sup> We completely agree to the fact as daily dressing of burn wounds, care as for acute spine injury patient along with early rehabilitation interventions while treating patients were the main guidelines followed.

EyadBaqain, Peter Haertsch, Peter Kennedy et al in their tertiary adult referral unit found only one third of cases associated with high voltage lines,<sup>6</sup> whereas in our study spinal injuries associated with high tension lines (11 KV/33 KV) accounted for 66.67% (30 out of 45 cases) while low voltage line related trauma was 33.33% (15 out of 45) cases.

Cherington M. proposed that Peripheral nerve lesions are uncommon in lightning-strike patients. By contrast, peripheral nerve injuries are common with generated electrical trauma.<sup>7</sup> In our study we agree that generated electricity causes affection of peripheral nerves but doesn't have significant impact on outcome as there is almost no neurological recovery after spinal injury in such cases.

Mary Ann Cooper in her study had two third of fatalities between the ages of 15 years and 40 years.<sup>8</sup> In our study too, the average age was 32.59 years and the age group of 21-40 years was the largest among the injured with 35 patients (35/45; 77.78%) between 15 years and 40 years of age. Dorsal injuries were the most prevalent in this age group (28 out of 45 patients; 62.22%) which lead to a paralytic life followed by cervical (10/45; 22.22%) and lumbar (4/45; 8.89%) injuries as none of

them recovered at the end of one year. In three patients no bone injury or SCIWORA (spinal cord injury without radiological evidence) could be defined as even magnetic resonance imaging was normal.

Most of the injuries occurred between 5:00 A.M. to 5:00 P.M. 38 out of 45 cases (≈85%) (working hours). Rest 7 cases were recorded in evening hours between 5:00 PM. To 11:00 P.M. No injury was recorded between 11:00 P.M. to 5:00 A.M.

R.C. Lee<sup>9</sup> described the biophysical injury mechanism in Electric shock trauma.<sup>9</sup> Upper limbs as well as upper chest and back were the most commonly affected area by burns. Major Burns were mostly arc or flash burns or when the clothes made of synthetic polyester or nylon fabric catches fire. Almost all cases (40/45; 88.89%) had at least joule burn or flash burn due to contact with electricity. Presence of contact points is diagnostic of an electrical injury beneath the skin. The skin appearance at the site of contact is often that of a well-defined charred wound that is depressed due to loss of tissue bulk.

Superficial electric burns have similar prognosis as burns from other causes but deep burns have delayed healing as compared to other causes of burns; because of the specific effect on nonviable tissue covered by healthy uninjured skin.

Sang HoonKo et al studied the relation between site of entry and exit to the level of injury. They found that, if site of entry is in head and neck area and exit site in lower limbs than the chances of paraplegia are more common. If both upper limbs and lower limbs are involved than chances of quadriplegia are more common.<sup>10</sup> In our study, the data reflects this is not always true. Hands were the most common sites of entry as they get injured while using tools or touching wires with bare hands (42 /45; 93% cases). Right hand involvement was found greater than left hand which might be due to common right hand dominance in most of the people. In one of the cases tongue was seen as the mark of entry wound, this happened with a carpenter who was trying to peel off electric wire with his teeth; he presented as a tetraplegic with no exit wound and he passed away due to sudden cardiac dysrhythmias. Most common exit site of electricity was legs (53%) followed by hands (22%) and then rare sites like upper back, abdomen etc. In four cases exit wound site was not seen or appreciable.

Brian James Daley et al also suggested that electric burn patients may present with bone fractures from either severe muscle contractions (eg, avulsion fractures) or as a result of falls. This was more commonly seen in upper limb long bones and in vertebrae.<sup>11</sup> In our study, multiple vertebral fractures were a common phenomenon (21/45; 46.67%). the largest group was dorsal spine injury (28/45; 62.22%) followed by cervical region (10/45; 22.22%) and lumbar spine injury (4/45; 8.89%). Three patients (3/45; 6.67%) had no bone injury. Out of these 28 cases of dorsal spine injury, 24 patients (24/28; 85.71%) had at least one fracture in D-4 to D-8 region. Two patients reported fracture of clavicle while one patient had fracture of mandible as associated injuries. Multiple rib fractures were also recorded. One paraplegic patient also had loosening of teeth.

Patients after spinal trauma secondary to electric shock had a poor prognosis. Most common causes of death in dorsal spine injury were pressure sores leading to cachexia which is associated with protein and blood loss and septicemia due to infections of these wounds. One patient with no bone injury had

very large flash burn (90%) and expired on third day due fluid loses from open burn wounds.

## CONCLUSION

Dealing with electricity at electric poles is most of the time associated with fall from height. Combined effect of injury by electricity along with fall from height leads to more complex form of trauma like multiple vertebral fractures with preference to dorsal region and almost no neurological recovery. This can be prevented most of the times while embarking on the electrical poles after wearing proper fall and electric shock preventive suits along with proper communication while dealing with high tension lines maintenance. Semi-skilled laborers without proper education are the main cause of such calamities. Early rehabilitation will definitely help the patient to overcome such catastrophe by proper health care and along with preparing the person and his family psychologically, physically and vocationally for maintaining the person in the main stream of society. As compared to the western data; in Indian scenario electric injury associated with spinal trauma is quite large in number and due to poor financial support giving proper rehabilitation becomes difficult.

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# A Study of Cardiovascular Autonomic Dysfunction in Type 2 Diabetes Mellitus Patients in a Tertiary Care Hospital

Angadi Sumaswi<sup>1</sup>, Goduguchinthia Lepakshi<sup>2</sup>, Nagatham Padmaja<sup>3</sup>

## ABSTRACT

**Introduction:** Diabetes mellitus is a major concern in India. Diabetes mellitus is a leading public health care problem in developing and developed world, with increasing incidence and long-term complications. Cardiovascular Autonomic Neuropathy (CAN) is a common but frequently overlooked complication of diabetes. So the present study was done to estimate the prevalence of cardiovascular autonomic dysfunction in type 2 diabetes mellitus patients and also the association between prolonged QTc interval and presence of cardiac autonomic neuropathy.

**Material and Methods:** 50 patients of type 2 diabetes mellitus who fulfilled the inclusion and exclusion criteria were studied between the period January and June 2015. Various cardiovascular autonomic function tests were performed on the patients and the patients were categorized as per Ewing's criteria. QT interval was measured in ECG and corrected for cardiac cycle length. (QTc)

**Results:** Early CAN was seen in 14%, Severe CAN in 14%, Definite CAN in 8% patients. Atypical CAN with other combination of abnormalities was seen in 32% patients. Tests were normal in 32% patients. Sympathetic dysfunction was seen in 48% patients. Parasympathetic dysfunction was seen in 60%. Combined parasympathetic and sympathetic dysfunction was seen in 40% patients. 8% had sympathetic dysfunction alone and 20% patients had parasympathetic dysfunction alone. Mean QTc interval of patients in this study was  $411.12 \pm 36.82$  msec. There was a statistically significant association between prolonged QTc interval and presence of CAN. ( $p < 0.05$ ).

**Conclusion:** Cardiovascular autonomic neuropathy is common in type 2 diabetic patients and can be recognized by simple bedside autonomic function tests. Prolonged QTc interval is an indicator for the presence of cardiovascular autonomic neuropathy in type 2 diabetic patients.

**Keywords:** Diabetes mellitus, cardiovascular autonomic neuropathy, QTc interval, Ewing's criteria.

## INTRODUCTION

Type 2 diabetes mellitus is the most common type of diabetes in the world constituting 90% of the diabetic population. Diabetes mellitus is a leading public health care problem in developing and developed world, with increasing incidence and long-term complications. The triad of neuropathy, retinopathy and nephropathy is characteristic of chronic diabetes mellitus.

Diabetic autonomic neuropathy is among the least recognized and understood complications of diabetes<sup>1-3</sup>, which can involve multiple systems, including the cardiovascular, gastrointestinal, genitourinary, sudomotor and metabolic system.

Cardiac Autonomic Neuropathy (CAN) results in damage to the autonomic nerve fibers that innervate the heart and blood vessels, resulting in abnormalities in heart rate control and vascular dynamics.<sup>3</sup> CAN results in increased incidence of silent myocardial infarction, cardiac arrest, sudden death, and inadequate response to stressful events, e.g., anesthesia and

surgery. Since CAN is asymptomatic most of the time, with symptoms appearing only in the late stages, recognizing CAN in the early stages helps to delay or arrest its progression. Thus, the present study was conducted to estimate the prevalence of cardiovascular autonomic dysfunction in type 2 diabetes mellitus patients and also the association between prolonged QTc interval and presence of cardiac autonomic neuropathy.

## MATERIAL AND METHODS

A cross sectional study of 50 type 2 diabetes mellitus patients, selected according to inclusion exclusion criteria, was done in Sri Ramnarain Ruia Government General Hospital, Tirupati during the period between January 2015 and June 2015.

### Inclusion criteria

1. Type 2 diabetes mellitus patients of age more than 18 years of both sexes.
2. Duration of diabetes for atleast 5 years.
3. Patients willing to give informed written consent.

### Exclusion criteria

1. Anemia
2. Alcohol consumption
3. Chronic renal failure
4. Use of beta blockers
5. Serum electrolyte abnormalities
6. Asthma or chronic obstructive pulmonary disease
7. Use of drugs that prolong QTc interval
8. Non complying patients who do not consent to participate in the study.

Careful history regarding symptoms of autonomic neuropathy was obtained and a general physical examination, detailed neurological examination and tests of autonomic function were done in all patients.

### Tests for assessment of cardiovascular autonomic function

The tests for the assessment of cardiovascular autonomic neuropathy were done as per standard protocols published in literature and as practiced in the AFT laboratory, AIIMS.

### Tests for parasympathetic function

1. Heart rate response to deep breathing
2. Heart rate response to Valsalva Maneuver (Valsalva ratio)
3. Heart rate response to immediate standing (30: 15 ratio)

<sup>1</sup>Post Graduate, <sup>2</sup>Professor and HOD, <sup>3</sup>Assistant Professor, Department of General Medicine, Sri Venkateswara Medical College, Tirupathi, Andhra Pradesh, India

**Corresponding author:** Angadi Sumaswi, MIG-324, APHB, Balaji Nagar Colony, Kukatpally, Hyderabad, Telangana, PIN-500072, India

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Test	No. of subjects (N=50)		
	Normal	Borderline	Abnormal
1) E-I difference	21 (42%)	11 (22%)	18 (36%)
2) Valsalva ratio	25 (50%)	12 (24%)	13 (26%)
3) 30:15 ratio	35 (70%)	9 (18%)	6 (12%)
4) BP response to standing	26 (52%)	15 (30%)	9 (18%)
5) BP response to sustained handgrip	26 (52%)	10 (20%)	14 (28%)

**Table-1:** Cardiovascular Autonomic Function Tests.

Pattern	Number (%)
Normal	16(32%)
Only sympathetic	4 (8%)
Only parasympathetic	10(20%)
Both (S+PS)	20 (40%)
Total	50(100)

**Table-2:** Pattern of autonomic dysfunction

### Tests for sympathetic function

1. Blood pressure response to standing
2. Blood pressure response to sustained hand grip

### Interpretation of test results

Test results were interpreted as per Ewing's criteria.<sup>4</sup>

*Normal* = All tests normal or 1 test borderline.

*Early* = One of the three heart rate tests abnormal or two borderline.

*Definite* = Two heart rate tests abnormal.

*Severe* = Two heart rate tests abnormal + one or both BP tests abnormal or both borderline

*Atypical*= Any other combination of abnormalities

### QTc prolongation

The QT interval was measured on an ECG recorded at rest (beginning of QRS complex to the end of T wave) and corrected for cardiac cycle length ( QTc) using Bazett's formula i.e. QTc = QT / √RR. A QTc interval more than 440 ms is said to be prolonged.

Other investigations done were Hb%, FBS, PPBS, HbA1c, Renal Function Tests (RFT), Serum electrolytes, Urine routine, Ophthalmic fundii examination, Chest X ray, ECG, 2D-ECHO. Before collection of data, all the subjects were briefed about the purpose of study and written informed consent was obtained. Ethical clearance was obtained from the Institutional Ethics Committee of the college.

### STATISTICAL ANALYSIS

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements were presented as Mean ± SD and results on categorical measurements were presented as proportions and percentages. Significance was assessed at 5 % level of probability. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Student's t-test was used to assess differences between continuous variables expressed as mean± SD. SPSS software (Version 17) was used for analysis.

### RESULTS

The age group of diabetic patients ranged from 37- 75 years. The mean age of type 2 diabetic patients was 55.48±10.75 years. The mean age of patients with CAN was 55.85±10.22 years and

that of patients without CAN was 54.69±12.11 years. 56% (28) of the study population were males and 44% (22) were females. The abnormal responses were most frequently found for heart rate response to deep breathing (36%) (table-1).

In this study, it was found that 32% (16) patients had no CAN. Positive tests of autonomic dysfunction were seen in 68% (34) patients. Only sympathetic dysfunction was seen in 8%(4) patients, only parasympathetic dysfunction in 20% (10) patients, both sympathetic and parasympathetic dysfunction in 40% (20) patients (table-2). Early CAN was seen in 14% (7), Severe CAN in 14% (7), Definite CAN in 8% (4) patients. Atypical CAN with other combination of abnormalities was seen in 32% (16) patients.

Patients with CAN had a statistically significant fall in SBP on standing than patients without CAN. They also had little rise in DBP on sustained handgrip than patients without CAN. Patients with CAN had statistically significant reduced heart rate variability (HRV) during deep breathing than patients without CAN. They also had significant difference in valsalva ratio and standing 30:15 ratio than patients without CAN (table-3).

Mean QT<sub>c</sub> interval of patients in this study was 411.12±36.82 msec. QTc interval was significantly prolonged in patients with CAN than in patients without CAN (table-4).

### DISCUSSION

Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease.<sup>5,6</sup> It is difficult to ascertain the exact prevalence of diabetic autonomic neuropathy, especially cardiac autonomic neuropathy since it is often asymptomatic or presents with vague symptoms. A total of 50 patients who were diagnosed to have type 2 diabetes mellitus based on ADA criteria were included in this study after considering the various inclusion and exclusion criteria.

In this study, 32% (16) patients had no CAN. Positive tests of autonomic dysfunction were seen in 68% (34) patients. Early CAN was seen in 14% (7), severe CAN in 14% (7), definite CAN in 8% (4) patients. Atypical CAN with other combination of abnormalities was seen in 32% (16) patients.

Mathur CP et al.<sup>7</sup> evaluated 50 diabetics for autonomic neuropathy by Ewing's criteria. Normal study was reported in 42%, early changes in 20%, definite in 30%, Severe in 4% and Atypical CAN in 4%. Pillai JN et al<sup>8</sup> evaluated 50 type 2 diabetes mellitus patients and found that 21 (42%) had severe autonomic neuropathy and 12 (24%) had early autonomic neuropathy by the autonomic function tests. In a study by Taha mahwi et al.<sup>9</sup> out of 150 cases, 106 cases had CAN. Early CAN in 35, definite CAN in 40, severe CAN in 31 patients. Agarwal et al<sup>10</sup> reported the prevalence of CAN in their study as 70%. Among them, early neuropathy was seen in 37%, definite neuropathy in 40%

AFT	Mean± SD	CAN		P value
		Absent	Present	
BP response to standing ( fall in SBP) in mmHg	10.80±6.94	5.75±1.61	13.18±7.22	<0.001,S
BP response to sustained handgrip (rise in DBP) in mmHg	14.40±5.27	18.38±2.22	12.53±5.26	<0.001,S
HR response to deep breathing (bpm)	13.77±5.60	18.87±2.85	11.38±4.94	<0.001,S
Valsalva ratio	1.18±0.10	1.27±0.06	1.14±0.08	<0.001,S
Standing 30:15 ratio	1.07±0.08	1.12±0.10	1.05±0.06	<0.01,S

**Table-3:** Interpretation of Autonomic Function Tests (unpaired student's t -test)

QT <sub>c</sub> Interval in MSEC (Mean±SD)	CAN	
	Absent	Present
411.12 ± 36.82	394.88 ± 28.91	418.76 ± 38.01
P=0.031, S		

**Table-4:** QT<sub>c</sub> interval and CAN (unpaired student's t- test)

and severe autonomic dysfunction in 22.9% patients.

The abnormal responses were more frequently found for heart rate response to deep breathing (36%) which was consistent with the study done by Mathur et. al.<sup>11</sup> (48%). BP response to standing and standing 30:15 ratio were also found to be less sensitive in this study. The study conducted by Barthwal et al<sup>12</sup> had detected heart rate response to deep breathing and valsava ratio to be the most sensitive while postural hypotension to be the least sensitive index. Domuschiev et al<sup>13</sup> also reported that heart rate response to deep breathing was most sensitive and was seen in 33.3% almost similar to the present study.

Tests of parasympathetic dysfunction were found to be most sensitive indicators of autonomic neuropathy. Sympathetic dysfunction was seen in 48% (24) patients. Parasympathetic dysfunction was seen in 60% (30). Combined parasympathetic and sympathetic dysfunction was seen in 40% (20) patients. 8% (4) had sympathetic dysfunction alone and 20% (10) patients had parasympathetic dysfunction alone. Study by Ramavat et al.<sup>14</sup> showed that 39.1% had parasympathetic neuropathy, 27% had sympathetic neuropathy, 19.2% had both parasympathetic and sympathetic neuropathy. Results in the present study are almost twice those found in this study. Only parasympathetic neuropathy was seen in 17.9% of type 2 diabetics, only sympathetic neuropathy in 6.5% of type 2 diabetic patients. The results of these categories are similar to the present study. In a study by AK Basu et al<sup>15</sup>, 50 type 2 diabetic patients were studied. Overall prevalence of CAN was 54%. Parasympathetic neuropathy was seen in 52% cases and sympathetic neuropathy was seen in 20% cases. Study by Jyotsna et al<sup>16</sup> revealed that parasympathetic dysfunction was found in 44.2% and sympathetic dysfunction in 51.9% diabetics. The study was conducted in 145 type 2 diabetes mellitus patients. It was found that sympathetic dysfunction was more prevalent than parasympathetic dysfunction.

Several studies have evaluated the correlation between prolongation of the QTc interval with the hypothesis that sympathetic dysfunction may prolong the interval. A 1992 consensus statement on autonomic testing portrayed Bazett's heart rate- QTc prolongation as a specific yet insensitive indicator of diabetic autonomic failure. Bellavere et al<sup>17</sup> in their study mentioned that diabetic cardiac autonomic neuropathy should be included among long QT syndromes.

Mean QTc interval of patients in this study was 411.12±36.82 msec. Patients who had CAN had a mean QTc interval of 418.76

± 38.01 msec while it was 394.88 ± 28.91msec in patients who did not have CAN. This implies that QTc interval was more in patients who had CAN and this difference was statistically significant ( $p = 0.031$ ).

Mathur et al. in their study of 50 diabetic patients confirmed that prolonged QTc is associated with cardiac dysautonomia ( $p < 0.01$ ). In a study by Pillai JN et al., diabetics with autonomic neuropathy had significantly higher QTc mean and QTc max values compared to diabetics without autonomic neuropathy and controls ( $P < 0.01$ ). In concordance with the above studies, the present study also showed significant association between cardiac dysautonomia and prolongation of QTc interval ( $p=0.031$ ).

The limitation of the study is that no clinical follow-up data is available and hence the influence of autonomic neuropathy on mortality including sudden cardiac death could not be assessed.

## CONCLUSION

Cardiac Autonomic Neuropathy thus is most frequently asymptomatic problem which can be identified by simple bed side tests. Early identification of Cardiac Autonomic neuropathy helps in effective prevention of cardiovascular disease related morbidity and mortality. QTc interval is a reliable indicator for the presence of Cardiac Autonomic Neuropathy.

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# Effects of Cigarette Smoking on Glomerular Filtration Rate in Apparently Healthy Individuals Studied at Gandhi Medical College and Hamidia Hospital Bhopal

T.N. Dubey<sup>1</sup>, Vikas Raikwar<sup>2</sup>, Preksha Dwivedi<sup>3</sup>

## ABSTRACT

**Introduction:** Glomerular hyperfiltration and albuminuria accompanied by early-stage diabetic kidney disease predict future renal failure. Cigarette smoking has reported to be associated with elevated GFR in cross-sectional studies and with renal deterioration in longitudinal studies. Study aimed to check the relationship between cigarette smoking and GFR in apparently healthy males, and to study effect of cigarette smoking on urinary albumin excretion.

**Material and methods:** 50 smokers and 50 non smokers were studied in Gandhi Medical College and hamidia hospital Bhopal from December 2014 to December 2015. Patient went a detailed clinical evaluation and laboratory investigation. Participants included in study were non hypertensive, non diabetic and without any prior or primary renal disorders.

**Results:** The present study included 100 smokers and 100 non smokers. The mean age of the studied patients was  $39.85 \pm 8.15$  among smokers and  $39.80 \pm 7.28$  among non smokers. Among smokers 49% smokers have proteinuria. Proteinuria was significantly associated with pack years among current smokers ( $p=0.011$ ). Smokers with  $>40$  pack years were found to be significantly associated with proteinuria. Among smokers 67% have high gfr. As compared to non smokers, current smokers have high GFR (mean= $120.06 \pm 18.53$ ) High GFR was significantly correlated in smokers with pack year $>40$  ( $p=0.025$ ). The average GFR in current smokers is  $120.06 \pm 18.53$ .

**Conclusion:** In our study it was found that current smokers have glomerular hyperfiltration and proteinuria as compared to non smokers. Glomerular hyperfiltration, proteinuria, high systolic and high diastolic blood pressure correlates significantly with pack years.

**Keywords:** Cigarette Smoking, Glomerular Filtration

## INTRODUCTION

Smoking has emerged as one of the major risk factor of renal injury but has not been extensively studied. Although smoking is related to ESRD in the long term<sup>1</sup>, the effect of cigarette smoking on renal function in early-stage kidney disease is unclear. Chronic kidney disease (CKD) causes a large number of morbidity and mortality, cardiovascular disease (CVD) being the most common cause of mortality among them. This rise is expected to continue, particularly in developing countries, where smoking and other cardiovascular risk factors are increasing substantially<sup>2,3</sup>, and will be paralleled by rising CKD- and ESRD-related costs.<sup>4,5</sup>

Detailed investigation has not been done, how smoking effects the kidney. In recent years, it has become apparent that smoking has a negative impact on renal function, being one of the most important remediable renal risk factors.<sup>6</sup>

In this study, we examined the effects of cigarette smoking on

renal function and albuminuria in apparently healthy participants who were not on antihypertensive and/or antidiabetic medication, and we investigated whether the relation between filtration rate of kidney (GFR) and smoking was modified by the renal functional, age, blood pressure, fasting serum glucose, and albuminuria

## MATERIAL AND METHODS

The present study included 100 smokers and 100 non smokers based on inclusion and exclusion criteria from December 2014 to December 2015 conducted in hamidia hospital Bhopal, India. The research work was approved by ethical committee, Barkatullah University. Eligible participants included for the current study were male aged between 20 to 50 years, who are current smokers, coming to hamidia hospital on OPD basis, having normal liver functions and were non hypertensive non diabetic. Those were excluded who had diabetes, hypertension, pulmonary disease and primary renal disorder at the time of presentation or diagnose later in the study.

The clinical examination consisted of relevant medical history, physical examination measurement like height and weight. Self reported questionnaire on life style characteristics such as smoking habit frequency of alcohol drinking. Blood sampling for the measurement of RFT, LFT, CBC, FBS, PPBS sand urinalysis r/m and dipstick urinalysis. Early morning blood samples were drawn. Serum creatinine was estimated by jaffe method. We calculated estimated GFR by using Gault Cock and Croft equation. Urine samples were collected as clean catch mid stream, early morning specimens. The result of dipstick urinalysis was interpreted as +1,+2,+3. After 5 minutes of rest BP was measured in a sitting room. BP was measured in supine position right arm with a standard sphygmomanometer.

## Measurement of Cigarette Smoking

The questionnaire about the smoking habit consisted of smoking status, average number of cigarettes smoked per day and duration of cigarette smoking for current smokers, and years since quitting for past smokers. Then participants were divided into two groups: non-smokers AND current smokers. The number of pack-years of exposure (that is, the number of

<sup>1</sup>Professor and Head of Department, <sup>2</sup>Post Graduate Student, <sup>3</sup>Assistant Professor, Department of Medicine, Gandhi Medical College and Hamidia Hospital, Bhopal, India

**Corresponding author:** Dr. Vikas Raikwar, Room No.03, E-Block, PG Boys Hostel, Gandhi Medical Collge, Bhopal-462001(M.P.), India

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packs of cigarettes smoked per day multiplied by the number of years smoked) is also calculated to see the long-term adverse effect of smoking on renal function.

### Outcomes

GFR was calculated and proteinuria was estimated. Glomerular hyperfiltration was diagnosed if estimated GFR was more 120 ml/min per 1.73 m<sup>2</sup>. Proteinuria was defined as 1+ or higher (30 mg/dl or higher) for dipstick examination.

### STATISTICAL ANALYSIS

The quantitative data expressed as standard deviations qualitative data were expressed in percentages. The data was analyzed by using chi square test and the difference in means were analyzed by using student T Test. Significance level for tests was set as (P< 0.05).

### RESULTS

The present study included 100 smokers and 100 non smokers. All were male. The mean age of the studied patients was 39.85 ±8.15 among smokers and 39.80±7.28 among non smokers. Maximum number of patient were in age group of 41 -50. Among smokers 49 % smokers had proteinuria and in non smokers 7% had proteinuria. Proteinuria was significantly associated with pack years among current smokers (p=0.011). Smokers with >40 pack years were found to be significantly associated with proteinuria (Table-1). Among smokers 67% have high GFR. As compared to non smokers, current smokers have high GFR (mean=120.06±18.53.). High GFR was significantly correlated in smokers with pack year>40 (p=0.025) (table-3). The average GFR in current smokers is 120.06±18.53. High systolic and diastolic blood pressure is found among current smokers as compared to non smokers (table-2).

### DISCUSSION

The present study included 100 smokers and 100 non smokers from December 2014 to December 2015 conducted in hamidia hospital Bhopal. Out of 100 current smokers (all male) ranging from 20 to 50 years (mean age=39.85±8.15), high GFR (>120ml/min/1.73m<sup>2</sup>) was found in 67% which is significantly correlated with pack years (p<0.01) as compared to non smokers. This data correlates well with Ekberg et al<sup>7</sup> who reported a significantly higher prevalence of glomerular hyperfiltration (41% vs. 18%) in the smokers than in the non-smokers. Among these current smokers, high GFR was significantly more common among smokers with pack year ≥40. (p=0.025) these result were also shown in the study done by Ishizaka N et al.<sup>8</sup> Cross-sectional in 7,078 Japanese male participants in whom they found high eGFR (>90.73ml/min/1.73 m<sup>2</sup>) current smokers consuming 20-39 cigarettes per day.

Among 100 current smokers, GFR was found to highest among 41 to 50 age group smokers. and age was insignificantly correlated with GFR (p=0.61). There was significantly higher prevalence of glomerular hyperfiltration (67% vs. 20%) among current smokers than in the non smokers, and is related to amount of cigarette smoking. Pintosestsma et al<sup>9</sup> Cross sectional study, in 7476 adults in a dutch community found elevated eGFR (>Mean±2SD) in current smokers consuming up to 20 cigarettes per day and in those consuming more vs. never smokers was 1.82 (1.31~2.53) and 1.84 (1.12~3.02) respectively

Pack year	U. Albumin				Total
	0	1	2	3	
1—20	26	5	2	0	33
	78.8%	15.2%	6.1%	0.0%	100.0%
21-40	21	21	8	3	53
	39.6%	39.6%	15.1%	5.7%	100.0%
>40	4	3	4	3	14
	28.6%	21.4%	28.6%	21.4%	100.0%
Total	51	29	14	6	100
	51.0%	29.0%	14.0%	6.0%	100.0%

P=0.003, High proteinuria was significantly more in cases with pack year >40.

Table-1: Correlation of pack year and urine albumine

Variables		Mean	± Std. Deviation
Age	Cases	39.85	8.15
	Controls	39.80	7.28
Hb	Cases	11.41	0.93
	Controls	10.84	0.87
S.Creatinine	Cases	0.62	0.12
	Controls	0.66	0.13
GFR	Cases	120.06	18.53
	Controls	115.19	16.42
SYS.BP	Cases	129.06	10.42
	Controls	128.66	8.14
DIA.BP	Cases	74.88	5.49
	Controls	73.30	5.10

Table-2: Variables and their means and standard deviation

Pack yr	GFR		Total
	>120	<120	
1—20	20	13	33
	60.6%	39.4%	100.0%
21-40	34	19	53
	64.2%	35.8%	100.0%
>40	13	1	14
	92.9%	7.1%	100.0%
Total	67	33	100
	67.0%	33.0%	100.0%

Table-3: Correlation of pack year with glomerular filtration rate (GFR)

adjusted for age, gender, BMI, BP, PG and alcohol. Similar results were obtained by Yoon HJ et al.<sup>10</sup> (Cross-sectional) in 35,228 Korean participants in a health screening program (III) Mean eGFR was significantly higher in current smokers than in former and never smokers.

Several mechanism may have played a role in contributing this association. Hyperfiltration is supposed to be an early manifestation of kidney disease. The nicotine induced increase in blood pressure and heart rate via sympathetic activation and vasopressin release probably explains this. Cadnapaphorchai et al<sup>11</sup> reported that nicotine increases vasopressin release by altering cervical parasympathetic tone.

Another key finding in our study was the relationship between cigarette smoking and proteinuria. We found that Out of total current smoker 49 % have proteinuria, which is compatible with results obtained by Zhang L et al.<sup>12</sup> 2008 (Cross-sectional) in 13,925 OR for albuminuria in current smokers vs. Non smokers adjusted for age, gender, obesity, DM, hyper tension

and hyperlipidemia. Proteinuria is significantly more common in current smokers ( $p<0.001$ ). We found that proteinuria was significantly more in current smokers with pack year  $\geq 40$  ( $P=0.03$ ). Out of total current smokers 10% have proteinuria with pack year  $\geq 40$  and is significantly correlated with pack years 32% of current smokers have proteinuria with pack years ranging between 21-40. This relationship was concordant with Ishizaka N et al.<sup>8</sup> Cross-sectional in 7,078 Japanese male participants in health screening (III) OR for albuminuria ( $\geq 30$  mg/gCr) in current smokers consuming 20-39 cigarettes per day and those consuming more was 1.56 (1.17~2.08) and 1.88 (0.99~3.55) respectively in comparison with never smokers adjusted for age, BP and FPG.

Mean systolic blood pressure among current smokers is  $129.06\pm 10.42$ , mean systolic BP among non smokers is  $128\pm 8.14$ . High systolic BP ( $>140$  mmhg) was significantly more common among smokers with pack years  $>40$  ( $p=0.001$ ). 18 % of current smokers have high systolic blood pressure.

Mean diastolic Blood pressure among smokers is  $74.88\pm 5.49$  which is significantly ( $p=0.0001$ ) higher as compared to non smokers mean  $73.30\pm 5.10$ . Out of total smoker 21.4% have high diastolic blood pressure ( $>90$  mmhg). High diastolic blood pressure ( $>90$  mmhg) is significantly more common in smokers with pack year  $>40$ , as compared to non smokers.

## CONCLUSION

In our study it was found that current smokers have glomerular hyperfiltration and proteinuria as compared to non smokers. Proteinuria and increased GFR can be considered as surrogate marker of chronic kidney disease in smokers. Thus, Even if ESRF is reached, smoking should be discontinued. Patients should be motivated to quit smoking, because it is the most effective and beneficial strategy against the whole spectrum of CKD.

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# Dentigerous Cyst: A Case Report in a 5 Year Old Child

Jasvir Kaur<sup>1</sup>, Neeraj Mahajan<sup>2</sup>, Amanpreet Singh<sup>1</sup>, Deepika Kapoor<sup>3</sup>

## ABSTRACT

**Introduction:** A dentigerous cyst is a developmental cyst of odontogenic origin, normally develops around the crown of unerupted or supernumerary tooth.

**Case report:** In this case report we are presenting a case of dentigerous cyst which involves permanent lateral incisor and canine in a five year old child, treated surgically by marsupialization technique.

**Conclusion:** The early detection of cyst by radiographs and histological evaluation and timely treatment in deciduous dentition can prevent unwanted effects like malocclusion, expansion and thinning of bone in permanent dentition.

**Keywords:** Dentigerous cyst, unerupted teeth, marsupialization.

## INTRODUCTION

A dentigerous cyst is a developmental cyst of odontogenic origin which develops around the fully-formed crown of an unerupted tooth.<sup>1</sup> These are discovered on routine radiographs, when a tooth has failed to erupt, a tooth is missing, teeth are tilted or are out of alignment.<sup>2</sup> These cysts are mostly found in mandibular third molar region followed by maxillary third molar region, maxillary canine and mandibular second premolar.<sup>1</sup> Radiographically, it is very difficult to differentiate between a normal enlarged pericoronal space and a cyst; if the width of this space has reached more than 2.5mm [and has an irregular outline] it is probably a dentigerous cyst.<sup>3,4</sup> This may be classified as central, lateral and circumferential type<sup>5,2</sup>. Impacted supernumerary teeth often develop dentigerous cysts.<sup>6</sup> They are the most aggressive of the cysts due to greater tendency than other jaw cysts to produce root resorption of adjacent teeth.<sup>7</sup> Histologically, it is composed of a thin connective tissue wall with a thin layer of stratified squamous epithelium lining. This case report shows a case of dentigerous cyst at an unusual place, mandibular canine region in a five year old child.

## CASE REPORT

A five year old child reported to the department of pediatric dentistry, Guru Nanak Dev Dental College and Research Institute, Sunam with chief complaint of decayed teeth and swelling on the right side of the face. On examination there were multiple carious lesions present and an intraoral swelling near the right canine region was found. (Figure 1) There was no pain but swelling was hard. Intraorally, there were missing 42 and rotated 41 and 83 was mobile. Patient was advised for an orthopantomogram and occlusal radiograph. Upon Radiographic examination a radiolucent lesion with thin borders, extending from apices of 41, 83, 71 and 72 and causing displacement of 41 and root resorption of 83 was present (Figure 2). A provisional diagnosis of dentigerous cyst was made.

The treatment modalities possible for cyst are enucleation or decompression/marsupialization methods depending upon Cyst size and site, involvement of dentition and surrounding

structures. In this case marsupialization was planned. After taking written consent and evaluation of medical history which was non contributory, surgery was done under general anesthesia. Incision was given, a flap was raised with the periosteal elevator. Tissue was removed and the cavity was cleaned with normal saline, cyst lining is placed in averted position and sutured to the surrounding mucosa to form an open cavity and filled by surgical pack. (Figure 3) Composite splinting of 41 and 73 was done. Specimen was sent for histological investigation. Histological Reports confirmed dentigerous cyst. Patient was advised for routine follow up and normal wound healing was taken place.

## DISCUSSION

Dentigerous cyst is the most common developmental odontogenic cyst of the jaws that encircles the crown of an unerupted tooth.<sup>2</sup> Previously known as follicular cyst; however, according to Browne et al dentigerous cyst is a better form. There are three radiological variations of dentigerous cyst (1) The central variant: crown is enveloped symmetrically, (2) in the lateral type cyst appears on one aspect of the crown, and in the (3) circumferential type the entire tooth appears to be enveloped by cyst.<sup>9</sup> Various authors have suggested that dentigerous cysts may develop by accumulation of fluid either between the reduced enamel epithelium and the enamel or between layers of reduced enamel epithelium.<sup>10</sup> It has been suggested by Main that the pressure exerted by an erupting tooth on an impacted follicle leads to the obstruction of the venous outflow and thereby results in rapid transudation of serum across the capillary walls, and thus there is increase in hydrostatic pressure of the fluid in turn separates the follicle from the crown.<sup>9</sup> It is generally seen that dentigerous cyst is less likely associated with more than one unerupted tooth is rare<sup>2,10</sup>. In the present case permanent mandibular canine and permanent lateral incisors were involved.

About 9% of dentigerous and 1% of radicular cysts occur in the first decade of life (Shear), while according to Donath, about 4% of dentigerous and less than 1% of radicular cysts appear in this life period.<sup>7</sup>

The differential diagnosis of dentigerous cyst include odontogenic keratocyst and primordial cyst and odontogenic tumors such as ameloblastoma, ameloblastic fibroma, and

<sup>1</sup>Senior Lecturer, Pediatric and Preventive Dentistry, BJS Dental College, Ludhiana, <sup>2</sup>Professor and HOD, Pediatric and Preventive Dentistry, GNDDC and RI, Sunam, India, <sup>3</sup>Lecturer, Pediatric and Preventive Dentistry, College of Medical Sciences, Bharatpur, Nepal.

**Corresponding author:** Dr. Jasvir Kaur, MDS, Senior Lecturer, Pediatric and Preventive Dentistry, BJS Dental College, Ludhiana

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**Figure-1:** Pre-operative intraoperative view



**Figure-2:** Orthopantomograph



**Figure-3:** Intra-operative view

adenomatoid odontogenic tumor.<sup>5,8,1</sup> Ameloblastoma is rare in children and Radiographically it is multilocular cyst like lesion, but may be unilocular with no particular features. Odontogenic keratocyst is also rare in children but more aggressive than dentigerous cyst. Occasionally a radicular cyst surrounding the crown of the developing permanent tooth bud, May also look like dentigerous cyst but radicular cysts are extremely rare in relation to the deciduous teeth and are small in size.<sup>4</sup>

## CONCLUSION

Depending upon Cyst size and site, involvement of dentition and surrounding structures treatment is planned accordingly.

Surgery is recommended for dentigerous cysts because it prevents the eruption of underlying permanent teeth. There are two surgical approaches for the treatment of large dentigerous cysts: Enucleation and Decompression. Enucleation technique is to treat larger cysts in paediatric patients, because of developing permanent tooth bud. Very satisfying results have been reported in children treating the cyst with marsupilization technique.

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# Assessment of Effect of Intensive Blood Pressure Therapy in Patients with Type 2 Diabetes Mellitus: A Clinical Study

Gopal Batni<sup>1</sup>

## ABSTRACT

**Introduction:** In diabetes mellitus patients, risk of cardiovascular disease is increased. Blood pressure in diabetic persons when assessed for risk of cardiovascular diseases, it was found that they exerted effect on major cardiovascular events among high-risk persons with type 2 diabetes. In support of this recommendation, there is lack of sufficient evidence in the literature. Therefore, we conducted this randomized clinical study to evaluate the effect of intensive blood pressure control in type 2 diabetes.

**Material and methods:** A total of 1025 patients with type 2 diabetes were included in the present study. A randomized intensive or standard glycemic control was assigned to all the participants. Patients with type 2 diabetes having glycated haemoglobin level of equal to more than 7.5% with history of cardiovascular disease were included in the present study. Patient with body mass index of more than 45, history of any other systemic illness or any known drug allergy were excluded from the present study. For participants in the intensive therapy group, visits to assess blood pressure were scheduled once a month for 4 months and every 2 months thereafter; for participants in the standard-therapy group, follow-up was done initially at 30 days time followed by quarterly per year check up. All the results were analyzed by SPSS software.

**Results:** Mean age of the patients undergoing intensive and standard therapy was 62.4 and 62.5 years respectively. Mean fasting glucose levels of the plasma in patients with intensive and standard therapy was found to be 177.1 and 172.8 mg/dl respectively. 195.2 And 190.5 mg/dl were the mean value of the serum total cholesterol levels in the patients undergoing intensive and standard therapy respectively. While comparing the mean cholesterol levels in two groups with patients undergoing intensive therapy having higher values in comparison to patients undergoing standard therapy, significant results were observed. No significant results were obtained while comparing the mean values for primary outcome in patients whereas while significant results were obtained while comparing the non-fatal stroke percentage per year in intensive therapy group and standard therapy group.

**Conclusions:** No strong evidence exists which could prove that of intensive blood-pressure controls can decrease the frequency of major cardiovascular events in diabetic patients.

**Keywords:** Blood pressure, Diabetes, Intensive

## INTRODUCTION

The risk of cardiovascular disease increases in diabetes mellitus patients by a factor of two to three at every level of systolic blood pressure.<sup>1</sup> On measurement of blood pressure (BP) in diabetic persons at risk of cardiovascular diseases, it was found to be below 120 mm Hg of systolic blood pressure which exerted effect on major changes occurring in the cardiac system among type 2 diabetic patients which are at higher risk as compared to other people.<sup>4</sup> In diabetic patients, recommendation of the seventh Report of the Joint National Committee on Prevention,

Detection, Evaluation, and Treatment of High Blood Pressure involves starting of the medicinal therapy in such patients to achieve systolic blood pressure of less than 130 mm of mercury.<sup>1-3</sup> There is, however, a paucity of evidence from randomized clinical trials to support these recommendations. Therefore, we conducted this randomized clinical study to evaluate the effect of intensive blood pressure control in type 2 diabetes.

## MATERIAL AND METHODS

A randomized clinical trial was conducted for the present study at 20 different tertiary health care centres. A total of 1025 patients with type 2 diabetes, based on inclusion exclusion criteria, were included in the present study. A randomized intensive or standard glycemic control was assigned to all the participants. Out of all the subjects included in the study, 550 were assigned to the placebo group along with simvastatin while remaining 475 were randomly assigned to intensive or standard blood control trials. Ethical approval was taken by the research committee of the committee of health care centre after giving in written the entire study protocol. All the patients were pre-informed about the research protocol and written consent was obtained from them. Criteria described previously in the literature were considered as standard in the present study for including patients in the present study.<sup>5</sup> Patients with type 2 diabetes having glycated haemoglobin level of equal to more than 7.5% with history of cardiovascular disease were included in the present study. Patient with body mass index of more than 45, history of any other systemic illness or any known drug allergy were excluded from the present study. All those subjects who had blood pressure of higher than 130 mm of mercury and lower than 180 mm of mercury and were on hypertensive drug therapy also came under inclusion criteria for present study.<sup>6</sup> Treatment strategies that are used to lower blood pressure were used in the current study. Approach described in the literature was used in the present study for the management of the blood pressure.<sup>4</sup> Assessment of the occurrence of self-reported symptoms of swelling or of dizziness on standing during the previous month was done at baseline and at 1, 3, and 4 years after randomization. For participants in the intensive therapy group, visits to assess blood pressure were scheduled once a month for 4 months and every 2 months thereafter; for participants in the standard-therapy group, follow-up was done

<sup>1</sup>Department of Medicine, Assistant Professor, RKDF Medical College, Bhopal, India

**Corresponding author:** Dr. Gopal Batni, Department of Medicine, Assistant Professor, RKDF Medical College, Bhopal, India

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initially at 30 days time followed by quarterly per year check up. Those factors were considered as potential adverse effects in which examination was done such as clinical and laboratory variables, including serum potassium and creatinine levels and estimated glomerular filtration rate.<sup>7</sup>

## STATISTICAL ANALYSIS

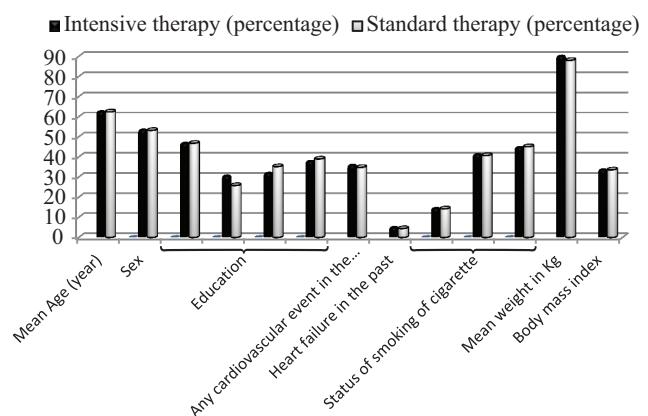
All the results were analyzed by SPSS software. Chi-square test and student t-test were used for assessing the level of significance. P-value of less than 0.05 was taken as significant values.

## RESULTS

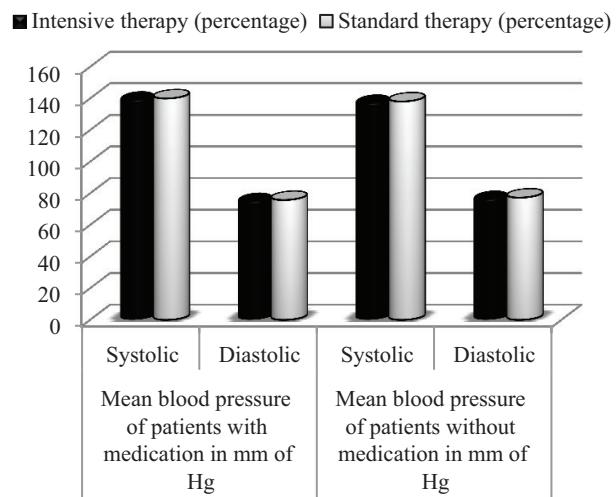
Figure-1 highlights the mean values for various details of demographic data and habit history of the patients. Mean age of the patients undergoing intensive and standard therapy were 62.4 and 62.5 years respectively. Majority of the patients in both the treatment therapy group were males. A significant major proportion of the patients in both intensive therapy group and standard therapy group had education of minimum of graduation. Mean weight of the patients was 90 kg in intensive therapy group and 88 kg in standard therapy group. Mean values for cardiovascular details of the patients with and without medication in the two study groups is shown in Figure-2. Mean systolic and diastolic pressure of patients without medication in intensive therapy group was 140.2 and 76.1 mm of Hg respectively. Mean systolic and diastolic pressure of patients without medication in standard therapy group was 140 and 75.8 mm of Hg respectively. Figure-3 shows the mean values for biochemical parameters of the patients on standard and intensive therapy. Mean percentage of glycated haemoglobin values in patients on standard therapy and intensive therapy were found to be 8.4 and 8.5 percent respectively. Mean fasting glucose levels of the plasma in patients with intensive and standard therapy was found to be 177.1 and 172.8 mg/dl respectively. 195.2 And 190.5 mg/dl were the mean value of the serum total cholesterol levels in the patients undergoing intensive and standard therapy respectively. Table-1 shows the p-value for the baseline characteristics of the patients. Significant results were obtained while comparing the mean cholesterol levels in two groups with patients undergoing intensive therapy having higher values in comparison to patients undergoing standard therapy ( $p$ -value < 0.05). Table-2 highlights the outcome of the patients at primary and secondary level. No significant results were obtained while comparing the mean values for primary outcome in patients whereas while significant results were obtained while comparing the non-fatal stroke percentage per year in intensive therapy group and standard therapy group.

## DISCUSSION

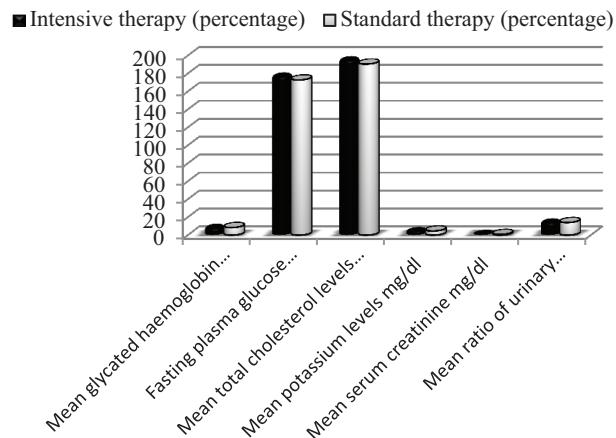
One of the most common metabolic diseases requiring measurement of sustained hyperglycaemia for its diagnosis is type 2 Diabetes mellitus. People with type 2 diabetes are at elevated risk for a number of serious health problems, including cardiovascular disease, premature death, blindness, kidney failure, amputations, fractures, frailty, depression, and cognitive decline.<sup>8</sup> After adjustment for other risk factors, an increase of 1% in the glycated hemoglobin level is associated with an increase of 18% in the risk of cardiovascular events, a rise in more than 10% of the death risk, and an increase of 37% in the risk of



**Figure-1:** Mean values for details of data of different demographic and habit history of the patients.



**Figure-2:** Mean values for cardiovascular details of the patients with and without medication



**Figure-3:** Mean values for biochemical parameters of the patients on standard and intensive therapy.

retinopathy or renal failure.<sup>9-11</sup> A reduction in the outcome of therapeutic strategies further lowering the glycated hemoglobin levels is suggested by the graded relationship between the glycated hemoglobin level and cardiovascular events and death. Some of the previous clinical trials support this hypothesis.<sup>8</sup> However; adequate testing of this hypothesis is still required in large scale. Hence, we conducted this randomized clinical study to evaluate the effect of intensive blood pressure control in type 2 diabetes.

Parameters		Intensive therapy (percentage)	Standard therapy (percentage)	p-value
Mean Age (year)		62.4	62.5	0.51
Sex	Male	53.3	53.2	0.45
	Female	46.7	46.8	0.62
Education	Less than high school	30.5	25.8	
	High school	31.8	35.2	
	Graduate	37.7	39.0	
Any cardiovascular event in the past		35.8	34.8	0.85
Heart failure in the past		4.9	4.4	0.15
Status of smoking of cigarette	Current	14.3	14.2	0.54
	Former	41.1	40.7	
	Never	44.6	45.1	
Mean weight in Kg		90	88	0.71
Body mass index		33.5	33.6	0.81
Mean blood pressure of patients with medication in mm of Hg	Systolic	140.2	140.0	0.41
	Diastolic	76.1	75.8	0.51
Mean blood pressure of patients without medication in mm of Hg	Systolic	138.2	138.1	0.45
	Diastolic	77.4	77.3	0.81
Mean duration of diabetes in years		9	10	0.81
Mean glycated haemoglobin level in %		8.5	8.4	0.09
Fasting plasma glucose levels mg/dl		177.1	172.8	0.09
Mean total cholesterol levels mg/dl		195.2	190.5	0.03*
Mean potassium levels mg/dl		4.6	4.6	0.81
Mean serum creatinine mg/dl		0.8	0.8	0.81
Mean ratio of urinary albumin to creatinine		14.5	14.0	0.41
*: Significant				

**Table-1:** Baseline characteristics of the patients.

Outcome		Intensive therapy (percentage / year)	Standard therapy (percentage / year)	p-value
Primary outcome		1.82	2.10	0.30
Secondary outcomes	Myocardial infarction (non-fatal)	1.15	1.30	0.35
	Stroke(non-fatal)	0.32	0.49	0.02*
	Death (cardiovascular cause)	0.55	0.47	0.84
*: Significant				

**Table-2:** Outcome of the patients at primary and secondary level

Inspite of the significant difference of mean systolic blood pressure between intensive-therapy group and the standard-therapy group, no significant reduction in the death rate or outcome of primary cardiovascular diseases is seen in intensive antihypertensive therapy was observed. Also, as far as secondary outcome is concerned, no significant benefit was observed. Intensive blood-pressure management did reduce the rate of total stroke and nonfatal stroke when compared statistically (p-value <0.05). Similar results were obtained by previous studies in the literature where results of two meta-analyses correlated with our results.<sup>12,13</sup> Arguedas et al conducted a clinical research to determine the association of decrease in blood pressure with reduction in mortality in diabetic patients. They searched the Databases of Abstracts of Reviews of Effectiveness (DARE) and the Cochrane Database of Systematic Reviews for related reviews. From the results, they concluded that no strong evidence exists in the patients of their study which could show a significant correlation of lowering of blood pressure with rate of mortality in diabetic patients.<sup>14</sup> Gerstein et al analyzed the long term effects of intensive lowering of blood glucose levels on the cardiovascular outcomes. They analyzed patients with type

2 diabetes and cardiovascular diseases and randomly assigned them with intensive therapy or the standard therapy to assess the cardiovascular risk factors. From the results, they concluded that in comparison to standard therapy, intensive therapy for more than three and half years showed a reduction of five year nonfatal myocardial infarction. At the same time, it also increased the 5 year mortality rate.<sup>15</sup> Gerstein et al conducted an investigation to assess that whether cardiovascular events are reduced in diabetic patients with intensive therapy to target normal glycated haemoglobin levels. They analyzed 10,251 patients of mean age of 62.2 years with a median glycated haemoglobin level of 8.1%. From the results, they concluded that in comparison with the standard therapy, the use of intensive therapy did not significantly reduction in major cardiovascular events when targeted normal glycated haemoglobin levels for 3.5 years.<sup>16</sup> Duckworth et al assessed the effect of intensive glucose control on cardiovascular events in patients with type 2 diabetes. They randomly assigned 1791 military veterans of mean age of 60.4 years who had a suboptimal response to therapy for type 2 diabetes to receive either intensive or standard glucose control. From the results, they concluded that

no significant effect of intensive glucose control in patients with poorly controlled type 2 diabetes is seen on the rates of major cardiovascular events.<sup>17</sup> Xie et al evaluated the effect of intensive blood pressure lowering on cardiovascular and renal outcomes. They searched the data bases for trials published between Jan 1, 1950, and Nov 3, 2015. From the results, they concluded that lowering of intensive blood pressure provided greater vascular protection than standard regimens.<sup>18</sup>

## CONCLUSION

From the observation found in the present study, it can be concluded that no strong evidence exist which could prove that of intensive blood-pressure controls can reduce the frequency of major cardiovascular events in diabetic patients. Further studies in future are recommended for better exploration of this area of medical field.

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# Dento Alveolar Hemorrhage following Laser Assisted Operculectomy: A Case Report

Sudhir Varma<sup>1</sup>, Manjusha Nambiar<sup>2</sup>, Salim Abu Fanas<sup>3</sup>, Ashok Mathew<sup>4</sup>

## ABSTRACT

**Introduction:** Lasers are widely used in dental procedures. The various lasers currently employed include Diode Laser, Er:YAG, CO<sub>2</sub> Laser and Nd:YAG. Of these the diode lasers are used routinely owing to their cost and technical specifications. The list of applications for diode laser in dentistry are immense, especially in the field of periodontology where it can be used for procedures such as gingivectomy, operculectomy, frenectomy, pocket decontamination and also in various implant procedures. The most valuable advantage of soft-tissue lasers over other surgical modalities is their ability to precisely cut and efficiently provide hemostasis, thereby reducing the chances of complications compared to conventional techniques.

**Case Report:** The present case reports an operculectomy performed in relation to lower left third molar in a 37-year old male patient using 980nm diode laser. Patient developed post-operative hemorrhage within 48 hours of the treatment and was successfully managed with careful follow-up and timely intervention.

**Conclusion:** Even though lasers have a haemostatic effect on the soft tissues, a probable complication of post-operative hemorrhage should be detailed to the patient prior to the surgery. As the etiological factors for post operative hemorrhage are varied and many, careful follow-up of the patient and timely intervention can help in successful management of the condition.

**Keywords:** Diode Laser, Operculectomy, Post-operative bleeding

## INTRODUCTION

Application of lasers in dentistry and especially periodontology are rapidly increasing today. Lasers offer several advantages over conventional scalpel surgery such as precise incision of tissues, coagulation intra-operatively and postoperative benefits. Semiconductor diode lasers [Gallium arsenide (GaAs), gallium-aluminum-arsenide (GaAlAs)] are portable compact surgical units with efficient and reliable benefits that are assigned according to economic and ergonomic consideration and offer reduced costs in comparison to other modern laser devices. Diode laser (wavelengths ranging from 810 to 980 nm) are used for various periodontal procedures such as gingivectomy, operculectomy, frenectomy, pocket decontamination and also in implant surgeries, based on the photothermal effect with an excision technique, or by ablation or vaporization procedures.<sup>1</sup> The present case reports an operculectomy performed using 980nm diode laser and the post-operative bleeding that ensued after 48 hours which was successfully managed with careful follow-up and timely intervention.

## CASE REPORT

A 37-year old male patient reported to the clinic with a chief complaint of severe pain in relation to lower left back teeth since 1 week. The pain was continuous in nature that aggravated mostly on eating. Clinical examination revealed an inflamed

pericoronal flap in relation to lower left third molar (Figure-1) associated with tenderness and unilateral submandibular lymph node enlargement. There was mild extra-oral swelling along with signs of trismus. Patient was on self-medication with analgesics to control the pain. Patient did not report any other significant medical or drug history.

OPG and IOPA of the involved area did not reveal any underlying pathology. Patient was put on a course of antibiotics (Tab Amoclov 625mg; amoxicillin and clavulanic acid and Tab Meterolag500 mg; Meteronidazole) and analgesics (Tab Brufen retard800mg) for 1 week. Patient was also instructed to perform salt water gargling and hot water fermentation.

After a week, the patient reported for the treatment of the infected operculum. The advantages and disadvantages of both conventional operculectomy i.e with a surgical scalpel and laser assisted operculectomy were explained to the patient and the latter was chosen by the patient.

**Laser assisted Operculectomy:** Informed consent was taken from the patient prior to the procedure. Operculectomy was performed with a diode laser 980nm (DenMat, USA) under local anaesthesia (2% Lidocaine HCl) adhering to optimum laser safety protocols. Lasing was carried out with a 200μm fiber tip at 1W pulsed mode initially with the pulse width set at 500msec. This was mainly done to provide the tissues sufficient relaxation time. Following this, lasing was continued for 1 minute at 3W continuous mode. Total time taken for the procedure was 2 minutes with 10 seconds interval in between (Figure-2). Copious irrigation with saline was performed to remove the debris and the area was cleaned using a sterile gauze dipped in betadine. Patient was advised to take analgesics for 2 days following the procedure and was instructed to avoid any hard or spicy food.

After 48 hours, continuous bleeding from the treated site was reported by the patient over a phone call. The patient was instructed to keep an ice pack over the bleeding site. However, the bleeding continued and the patient visited the emergency department of a local hospital and was given Inj. Dicynone 250 (Etamsylate) to control the bleeding. The patient reported to the clinic on the following day.

<sup>1</sup>Assistant Professor, <sup>2</sup>MDS, <sup>3</sup>Dean and Professor, Department of Periodontics, <sup>4</sup>Lecturer, Department of Oral Medicine and Radiology, College of Dentistry, Ajman University of Science and Technology, Al-Fujairah, UAE

**Corresponding author:** Dr Sudhir Varma, Department of Periodontics, Assistant Professor, College of Dentistry, Ajman University of Science and Technology, P.O Box 2202, Al-Fujairah, UAE

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Intra oral examination revealed persistence of minor bleeding from the treated site even at 72 hours (Figure-3). The area was copiously irrigated with saline. The patient was instructed to continue the Dicynone 500 mg tablets (Etamsylate), one tablet every 6 hours for 5 days and to avoid hard food for the next 2 days. The patient was kept under daily follow-up till complete resolution of the bleeding occurred at one week. The patient was advised to perform routine blood investigation and the results did not reveal any underlying bleeding or coagulation disorders. Complete healing occurred at one month post-operatively (Figure-4).

## DISCUSSION

The chief advantage of laser assisted soft tissue surgeries is that it provides a bloodless surgical field and is a right tool for adequate haemostasis. Diode lasers in a range of 810 to 980nm wavelength is used in both continuous and pulsed mode in soft tissue surgery with the excision, vaporizing and ablative mode.<sup>1</sup> Using the right laser on the inflamed operculum makes difference in post surgical healing depending on the type of laser used.<sup>2</sup> Studies by Pirnat<sup>3</sup> demonstrated the cutting ability of the soft tissue diode laser with a depth of 2–6mm into the tissues with the sealing of small blood and lymphatic vessels as a result of the heat generated thereby eliminating bleeding and edema. A diode laser of 980nm wavelength in both pulsed and continuous wave mode was used in the present case.

Operculectomies are sometimes a suitable alternative for relieving pain when compared to third molar extractions, depending on the condition of the existing third molar, its relation to the surrounding structures and its angulation.<sup>4</sup> Post operative hemorrhage is a rare and life threatening complication, the incidence of which has been reported to be between 0.1% and 6.5%.<sup>5</sup> Very few articles in literature has mentioned the cause of postoperative hemorrhage following routine operculectomies and almost none have reported the event after laser assisted operculectomy. However, the only valid reason which could be emphasised for the bleeding observed in the present case is that temperature rise in tissue is directly proportional to the power output, spot size, pulse width and operator hand movements.<sup>6</sup> Postoperative bleeding may have varied etiologies, including slipping of ligatures and reopening of previously cauterized veins.<sup>7,8</sup> Predisposing factors such as retching and bucking during recovery and perioperative increased blood pressure are considered the most significant for causing post operative hemorrhage.<sup>9</sup>

Few studies have focused on prevention and risk factors of postoperative hemorrhage after operculectomy and most of the studies did not identify perioperative risk factors for the development of hemorrhage.<sup>10</sup> This is the first case to the authors' best knowledge that reported bleeding after routine laser assisted operculectomy, which was adequately managed with timely intervention and medication.

## CONCLUSION

As the etiological factors for post operative hemorrhage are varied and many, careful follow-up of the patient and timely intervention are necessary. Studies to evaluate the role of various laser parameters on soft tissues are required. Even though lasers have a haemostatic effect on the soft tissues, a probable complication of post-operative hemorrhage should be



**Figure-1:** Pre operative view of inflamed pericoronal flap in relation to 38; **Figure-2:** Persistent bleeding at 72 hrs after Laser assisted Operculectomy.



**Figure-3:** Postoperative view after 1 week following Laser assisted Operculectomy; **Figure-4:** Post-operative view at 1 month.

detailed to the patient and updated on the consent form.

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# Whether Poor Thoompson Score Predicts Need of Expensive and Specialized Nicu Care

Vikas Agarwal<sup>1</sup>, Kushal Agrawal<sup>2</sup>, Mohd. Sadique<sup>2</sup>

## ABSTRACT

**Introduction:** Infrastructure required for maintaining such high-risk patients such as ventilatory support, inotropic support and intensive monitoring is still lacking at most periphery centers in our country so present research was done with the aim to study the need of ventilatory support, inotropic support, anti convulsive medication and glucose infusion support in term asphyxiated neonates with history of asphyxia and Thompson score >10 within 48 hours of life.

**Material and methods:** Ours is a Retrospective cohort study conducted at Tertiary neonatal intensive care unit. Study was conducted from October 2015 to March 2016 on 61 term neonates with history of delayed cry at birth admitted in NICU, LLRM medical college Meerut. Outcomes measured were need of ventilatory support (CPAP or intubatory support), need of inotropic support, anti convulsive medication, need for glucose infusion.

**Results:** Thompson score >10 within 48 hours of life had following results- On ventilatory support- Sensitivity 65.6% (95% C.I- 46.8%-81.4%); Specificity 42.3% (95% C.I- 23.4%-63.1%); Likelihood Ratio (+) - 1.14 (95% C.I- .752- 1.72); Likelihood Ratio (-) - 0.813 (95% C.I- .422-1.57). On ionotropic support- Sensitivity 80% (95% C.I- 44.4%-97.5%); Specificity 41.7% (95% C.I - 27.6% -56.8%); Likelihood Ratio (+)- 1.37 (95% C.I 0.927-2.03); Likelihood Ratio (-)- 0.48 (95% C.I -1.33-1.73). On anti convulsant medication- Sensitivity- 81% (95% C.I- 58.1%-94.6%); Specificity - 48.6% (95% C.I- 31.9%-65.6%)P; Likelihood Ratio (+)- 1.58 (95% C.I- 1.08- 2.3); Likelihood Ratio (-) 0.392 (95% C.I- 0.153- 1.00). On GIR support- Sensitivity- 100 % (95% C.I- 29.2%- 100%); Specificity- 40 % (95% C.I- 27%- 54.1%); Likelihood Ratio (+)- 1.67( 95% C.I- 1.34- 2.07); Likelihood Ratio (-) 0.

**Conclusion:** Thompson score < 10 within 48 hours of life was good indicator that asphyxiated newborns will not be needing inotropic or GIR support.

**Keywords:** Neonate, ventilator, GIR support, inotrope, anti convulsant

## INTRODUCTION

Hypoxic-ischemic brain injury of the neonates remains a significant problem throughout the world. In India as per NNPD 2002, incidence of Apgar score <7 at 1 minute was found in 8.4%, Apgar score <7 at 5 minutes was found in 2.4% of births. Mortality associated with perinatal asphyxia was 28.8% of all neonatal deaths in India. Hypoxemia is defined as the 'diminished amount of oxygen in the blood supply' and cerebral ischemia as the 'diminished amount of blood perfusing the brain'; Ischemia is pathologically more significant as it leads to decrease in glucose levels in the brain which causes neuronal defect.<sup>1</sup> Asphyxia is the result of an impairment of exchange of the respiratory gases oxygen and carbon dioxide. Thus, in addition to hypoxia, asphyxia leads to additional damage by

producing increase in carbon dioxide levels in the body which leads to acidosis and increased cerebral blood flow resulting in a number of metabolic and physiological adverse effects (CBF).<sup>1</sup> Pathogenesis of Hypoxia – Ischemia may have acute or chronic progression. Neonatal encephalopathy is a disease with an evolving progression associated with deterioration of the neurological signs and symptoms (seizures and impaired conscious state) in the first 24 hours and slow improvement over next few days.

Thompson et al<sup>2</sup> in 1997 introduced a clinical grading system to describe the neurological abnormalities directed at developing quantifiable scores with good reproducibility.

The score consists of a clinical assessment of nine signs-

**LOC (level of consciousness):** The assessment of LOC is as described originally by Sarnat and Samat(3). The neonates are classified as Normal if they are staring with normal spontaneous movements and are Hyper alert if exaggerated responses to minimal stimuli are present. Stu

**Fits (clinically apparent seizures):** The score increases with increasing frequency of seizures.

**Posture:** This is assessed again as described by Sarnat and Samat (3) But in Thompson method an additional score of 1 has been given to the infants who present with intermittent bicycling movements of the limbs together with fisting (which is defined as flexion of thumb which is adducted and opposed across the palms)

**Moro. Grasp, Suck:** (the primitive reflexes: Moro reflex, palmar grasp and suck reflex) - These reflexes are normal in the mildly affected infant, poor or partial in moderate HIE and absent in severe HIE.

**Respiratory rate:** In severely affected neonates respiratory rate may decrease to apnea and require ventilator support

**Fontanelle tension:** The progression in scoring for fontanelle tension is from normal to full to tense/ bulging fontanelle.<sup>3-6</sup> How the intervention might work

Hypoxic Ischemic encephalopathy was originally described by Amiel Tison in 1969.<sup>7</sup> Numerous diagnostic methods have become available to diagnose and assess the extent of the cerebral damage caused by perinatal asphyxia. Though accurate, these diagnostic tests like MRI scanning, CT scanning,

<sup>1</sup>Associate Professor, <sup>2</sup>Third Year Resident, Department of Pediatrics, LLRM Medical College, Meerut, India

**Corresponding author:** Dr. Vikas Agarwal, Associate Professor, LLRM Medical College, Meerut, India

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cranial ultrasound and Doppler ultrasound are still prohibitively expensive and difficult to access.

Sarnat and Samat (3), groups affected infants into one of three categories: mild, moderate and severe. The criteria of categorization of neonate into moderate or severe is at times subjective which makes it difficult for easy differentiation and also it leads to variable outcomes in neonates classified as moderate asphyxia Application of this grading system is also time consuming and requires some pediatric expertise. Thompson scoring is fast and reliable method of scoring with inter-observer reliability coefficient of 0.87.<sup>7,8</sup>

As reported by NNPD (2002-2003) Bag and mask ventilation was required in 6.3% and chest compressions was required in 0.8% of newborns. Paucity of data in assessing the sensitivity, specificity, positive predictive value and negative predictive value of Thompson scoring for requirement of ventilatory support, inotropic support etc. prompted us to conduct this retrospective cohort study to better arm clinicians at periphery centers to rapidly prognosticate a patient using Thompson scoring and can assist in timely referral of patients to better equipped neonatal units.

## MATERIAL AND METHODS

We conducted a retrospective cohort study at a Tertiary newborn care center with 61 term newborns between October 2015 to march 2016. All enrolled full term ( $> 37$  weeks) inborn babies had been admitted to NICU for post resuscitative care during that time period. Demographics and pertinent medical history of mother were retrieved from delivery details. During the neonates stay in NICU, babies were closely monitored and complete recording for requirement of assisted ventilation, episodes of hypoglycemia, seizures, bleeding manifestations and clinical deterioration were documented. Resident doctor on duty did Thompson scoring initially at 6th hour of life then after 24 hours. We retrieved the data from previous files and formed a cohort of enrolled neonates, based on inclusion exclusion criteria, in the time period from October 2015 to march 2016.

### Inclusion criteria

- All in born full term babies ( $> 37$  weeks defined by modified ballard scoring) with APGAR score less than 4 at 5 minutes or with complain of delayed cry.
- All term babies with history of perinatal asphyxia.
- All term babies with clinical signs of perinatal asphyxia.

### Exclusion criteria

- Preterm babies.
- Severe congenital anomalies.
- Newborn with coagulopathy.
- Newborns of mothers on drugs like phenytoin, warfarin, and phenobarbitone, MgSO4.
- Newborns with severe sepsis or meningitis.

### Primary outcomes

- Need of ventilatory support in neonates with Thompson score  $> 10$  within 48 hours of life

### Secondary outcomes

- Need for Inotropic support in neonates with Thompson score  $> 10$  within 48 hours of life.
- Need for Anti convulsant medication in neonates with Thompson score  $> 10$  within 48 hours of life

- Need for Glucose infusion for Hypoglycemia in neonates with Thompson score  $> 10$  within 48 hours of life

Sensitivity is the ability of a test to correctly classify an individual as 'diseased'. The ability of a test to correctly classify an individual as disease-free is called the test's specificity. Positive Predictive Value is the percentage of patients with a positive test who actually have the disease. Negative predictive value is the percentage of patients with a negative test who do not have the disease.<sup>9</sup>

## STATISTICAL ANALYSIS

Microsoft office 2007 was used for making tables. Descriptive statistics like mean and percentages were used to infer results. Data was interpreted at 95% confidence interval.

## RESULTS

In the need for ionotropic support arm of our study we found that Thompson score  $> 10$  within 48 hours gave a sensitivity of 80% (95% C.I- 44.4%-97.5%) and specificity of 41.7% (95% C.I- 27.6%-56.8%) with negative predictive value 90.9% (95%, C.I-70.8%-98.9%). So our study shows that a patient with a Thompson score of  $< 10$  within 48 hours will not need ionotropic support in 90.9 % of cases (table-1).

In the need for ventilatory support arm of the our study we found that Thompson score  $> 10$  within 48 hours gave Sensitivity of 65.6% (95%, C.I-46.8%-81.4%) and specificity of 42.3 (95% C.I- 23.4%-63.1%). Negative predictive value of 50% ( 95% C.I- 28.2%- 71.8%) and PPV of 58.3% (95% C.I - 40.8%-74.5%) for need of ventilatory support. So we concluded that Thompson score  $> 10$  within 48 hours is not a good indicator of need of ventilatory support in the patient (table-2).

In the need for Anti Epileptic drugs arm of our study we found that Thompson score  $> 10$  within 48 hours had sensitivity of 81% (95% C.I - 58.1%-94.6%), specificity of 48.6% (95% C.I-

Prevalence	55%	42%	68.3%
Sensitivity	65.6%	46.8%	81.4%
Specificity	42.3%	23.4%	63.1%
Roc area	0.54	.412	0.668
Likelihood ratio(+)	1.14	0.752	1.72
Likelihood ratio(-)	0.813	0.422	1.57
Odds ratio	1.4	0.489	4.01
Positive predictive value	58.3%	40.8%	74.5%
Negative prdictive value	50%	28.2%	71.8%
(95% Confidence interval)			

**Table-1:** Ventilatory support for thompson score  $> 10$  within 48 hours of life

Prevalence	17%	8.6%	29.4%
Sensitivity	80%	44.4%	97.5%
Specificity	41.7%	27.6%	56.8%
Roc area	0.608	0.46	0.757
Likelihood ratio(+)	1.37	0.927	2.03
Likelihood ratio(-)	0.48	0.133	1.73
Odds ratio	2.86	0.606	-
Positive predictive value	22.2%	10.1%	39.2%
Negative prdictive value	90.9%	70.8%	98.9%
(95%Confidence interval)			

**Table-2:** Ionotropic support for thompson score  $> 10$  within 48 hours of life

31.9%-65.6%), Positive predictive value of 47.2% (95% C.I- 30.4%-64.5%) and Negative predictive value of 81.8% (95% C.I - 59.7%-94.8%) which means that Thompson score >10 within 48 hours had good sensitivity and the clinician should closely observe for seizure episodes especially subtle seizures in newborns with Thompson score of >10 within 48 hours. And as the Negative predictive value is >80% it shows that patients with Thompson score <10 will not need Anti convulsive medication (table-3).

Hypoglycemia is a common complication of hypoxia- ischemia (Boardman et al 2015).<sup>10</sup> Intensive Management of persistent hypoglycemia is by institution of glucose infusion which is an intensive modality. In the need for Glucose infusion arm of our study we found that Thompson score >10 within 48 hours had sensitivity of 100% (95% C.I- 29.2%-100%), specificity of 40% (95% C.I- 27%-54.1%), positive predictive value of 8.33% (95% C.I- 1.75%-22.5%) and negative predictive value of 100% (95% C.I- 84.6%- 100%). This means that Thompson score <10 at 48 hours was 100% predictive of not requiring glucose infusion in the patient (table-4).

## DISCUSSION

Most experts agree that HIE is not a single clinical event but is a disease process which is evolving over time. The clinical signs and symptoms of the insult are a reflection of the biochemical and molecular changes occurring in the brain following the initial insult. MRI studies have shown that the initial area affected by the asphyxia is usually less extensive and the size of the lesion progresses over the first few days after injury.<sup>4</sup> Both Diffusion weighted imaging and MR spectroscopy show similar progression of the CNS involvement with brain injury initially being localized to Putamen and Thalamus and later involving extensive areas of the brain.<sup>5-10</sup>

In animal models it has been proven that apoptosis induced

by experimental hypoxia-ischemia has prolonged role and apoptosis causing mediators like caspase are present in high levels as late as 7 days after initial insult.<sup>11</sup> The initial hypoxic-ischemic injury results in an area of infarction. The penumbra continues to show adverse changes in the form of neuronal necrosis or apoptosis (programmed cell death) even after the hypoxic insult is over.<sup>6</sup> The area which can be later involved and the time taken for the changes to occur is still unclear.

Also it is very well known that due to electro-clinical dissociation in newborns many times electric seizure activity in the brain may not have any or may have very subtle clinical manifestations which can be easily missed if the clinician is only monitoring for seizure activity.<sup>12</sup> Optimal management of HIE in newborns includes adequate resuscitative measures in the delivery room, with regular monitoring and management of seizure acitivity and supportive for complications like hyperthermia, hypoglycemia etc.<sup>8</sup>

What all this means for a clinician is that even if a neonate presenting with history of asphyxia does not have any clinical features suggesting extensive cerebral brain damage, regular monitoring of the neonate should be done using objective clinical scoring method like Thompson scoring. Magnetic resonance spectroscopy is one of the few diagnostic tests, which can accurately prognosticate neonate with asphyxia episode, but these tests are expensive and are rarely available in periphery centers. Also management of such patients needs high technical expertise. So in view of the lack of diagnostic testing we conducted our study to arm the clinician with data which can help him confidently apply Thompson scoring to decide whether a particular neonate would be requiring further intensive support and help make better informed judgment regarding timely referral of the patient.

## CONCLUSION

Perinatal Asphyxia in neonates is a cause of significant mortality and needs timely management with sophisticated methods and machines which are not readily available at a peripheral centre. What our study adds is that Thompson score is a rapid scoring method with little inter observer variability which can assist physicians in accurately prognosticating an asphyxiated neonate and do timely referral to a tertiary care centre.

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Prevalence	36%	24%	49.9%
Sensitivity	81%	58.1%	94.6%
Specificity	48.6%	31.9%	65.6%
Roc area	.648	.529	.767
Likelihood ratio(+)	1.58	1.08	2.3
Likelihood ratio(-)	.392	.153	1
Odds ratio	4.03	1.18	13.6
Positive predictive value	47.2%	30.4%	64.5%
Negative prdictive value	81.8%	59.7%	94.8%
(95%Confidence interval)			

**Table-3:** Anti convulsant medication for thompson score >10 within 48 hours of life

Prevalence	5.2%	1.1%	14.4%
Sensitivity	100%	29.2%	100%
Specificity	40%	27%	54.1%
Roc area	0.7	0.635	0.765
Likelihood ratio(+)	1.67	1.34	2.07
Likelihood ratio(-)	0	-	-
Odds ratio	-	0.485	-
Positive predictive value	8.33%	1.75%	22.5%
Negative prdictive value	100%	84.6%	100%
(95% Confidence interval)			

**Table-4:** GIR support for thompson score >10 within 48 hours of life

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# To Study Outcome of Intramedullary Nailing in Grade I and II (Gustilo- Anderson) Compound Diaphyseal Fractures of Tibia

Akhilesh Kumar<sup>1</sup>, Narendra Singh Kushwaha<sup>2</sup>, Shailendra Singh<sup>3</sup>, Kumar Shantanu<sup>3</sup>, Shah Waliullah<sup>3</sup>, Vineet Sharma<sup>4</sup>

## ABSTRACT

**Introduction:** Open fractures of the tibia are among the most common of serious skeletal injuries. They are slow to heal and frequently cause permanent sequelae if not managed timely and with precision. Our work presents the outcome of closed intramedullary nailing in grade I and II (Gustilo Anderson) compound diaphyseal fracture of tibia.

**Material and Methods:** The study group comprised of 28 patients who underwent surgical treatment with closed locked intramedullary nailing. All patients were followed for period of one year from August 2014 to July 2015 in prospective manner. Functional result was compared as per Ketenjian and Shelton Criteria modified by Yokoyama et al.

**Results:** In our study we observed that the mean age of the patients was  $28.64 \pm 7.917$  years, mean time surgery interval was found to be  $14.54 \pm 6.304$  hours. Mean time for full weight bearing was  $14.43 \pm 3.191$  weeks and mean union time was  $15.43 \pm 3.726$  weeks. Infection was found in 10.7% (n=28) of patients in which two (7.14%) patients had superficial infection and in one (3.57%) case deep infection was seen. Final assessment as per Ketenjian and Shelton Criteria modified by Yokoyama et al. done and observed excellent to good result in 89.28% of total patients and fair to poor in 10.72%.

**Conclusion:** Thus it was concluded that in Grade I and Grade II tibial diaphyseal fracture, closed intramedullary interlocked nailing is an excellent procedure, gives satisfactory results with proper alignment, good range of motion, and low infection rate leading to proper union and less patient morbidity.

**Keywords:** open tibial fractures, closed intramedullary interlocked nailing, functional result.

## INTRODUCTION

Open diaphyseal fractures of long bone of lower limb are most complex, challenging and controversial orthopedic injuries. The ultimate aim of open fracture treatment is to prevent infection, achieve bony union and restore function.

Ramon Gustilo<sup>1</sup>, in his landmark study in 1976, has laid down the foundations of open fracture management: thorough debridement and irrigation, fracture stabilization, early soft tissue coverage and rehabilitation.

This management protocol as well as his scheme of open fracture grading revolutionized open fracture treatment, are now accepted internationally and to date, remain to be clearly defined as the core principles and the very essence of current treatment.

The management of diaphyseal fractures is evolving and progressing. New reduction and fixation concepts are emerging based on better understanding of the biology of fracture repair and of the role of the soft tissues in the healing process.<sup>2</sup> Restoration of length, axial alignment, and rotation is essential,

but anatomical reduction of every fracture fragment is not very essential.<sup>3</sup> Classically open fractures are managed by conservative means and various types of external fixator.<sup>4</sup> External fixators lead to various complications like, infection (pin tract), nonunion, inadequate fixation and these patients generally require secondary surgical procedures.<sup>5-7</sup>

In past few decades intramedullary nailing in open fractures has been advocated and practiced by many surgeons<sup>8-11</sup> but still it remains a matter of debate.

In context of this debate, we conducted a prospective study on intramedullary fixation of grade I and II compound diaphyseal fractures of tibia. Intramedullary nailing has been proven to be the method of choice for fixation of these fractures and as it fulfills the objective of stable fixation with minimal tissue damage resulting in better and quicker fracture union, early rehabilitation and at the same time decreasing hospital stay of patient.<sup>12-14</sup> The present study was aimed to analyze outcome of grade I and Grade II (Gustilo Anderson)<sup>15</sup> open diaphyseal fractures of tibia treated with Intramedullary nailing.

## MATERIAL AND METHODS

A prospective study of 28 patient with compound (Gustilo grade I and II) diaphyseal fractures of tibia were included in study treated at the department of Orthopaedic Surgery, King George's Medical University INDIA, U.P., Lucknow from August 2014 to July 2015.

Data was collected from the patient admitted through Orthopedics OPD and Trauma centre in King George's Medical University, Lucknow and satisfying the inclusion criteria: 1) Open diaphyseal (Gustilo Anderson) Grade 1 and 2 fracture of lower limbs, 2) Age >16 year-<60 year, 3) Injury surgery interval <24 hours, 4) Patient giving informed consent. Patients not giving informed consent and not satisfying above criteria were excluded from study.

All the selected patients were treated with debridement and intramedullary interlocking nail. The patient were followed up at regular interval of 4-6 weeks for one year. Check X-rays were taken at every visit and patient was assessed

<sup>1</sup>Junior Resident, <sup>2</sup>Associate Professor, <sup>3</sup>Assistant Professor, <sup>4</sup>Professor and Head of Department, Department of Orthopaedic Surgery, King Georges Medical University, Lucknow, India

**Corresponding author:** Dr Narendra Singh Kushwaha, Associate Professor, Department of Orthopaedic Surgery, King Georges Medical University, Lucknow, India

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clinicoradiologically for fracture union. Functional result was compared as per Ketenjian and Shelton Criteria modified by Yokoyama et al.<sup>16,17</sup>

## STATISTICAL ANALYSIS

The results are presented in mean $\pm$ SD and percentages. Data was evaluated based on the descriptive statistics. Microsoft word 2007 was used to generate tables and graphs.

## RESULTS

In our study 28 patients of Grade I and II open fracture of tibia were followed in prospective manner. Average age for fracture shaft tibia was  $28.64\pm7.917$  years (Table-1). Vehicular accident in 21 (n=28) patients was observed to be the main cause of fracture in the study (75%) and more common in males (82.14). Grade II injury 64.28% (n=28) was found to be more common than grade I (35.72%).

In the study mean time injury surgery interval was found to be  $14.54\pm6.304$  hrs (Table-2). Majority of patients operated by tibial interlocking nail were started with partial weight bearing within 4 weeks and full weight bearing as tolerated by patient. Maximum patient were able to bear full weight between 12-16 weeks with mean ( $\pm$ S.D) of  $14.43\pm3.191$  weeks.

The union of the fracture was assessed by standard radiological and clinical criteria.<sup>18,19</sup> Due to presence of nail we could not give stress to the fracture site, hence loss of pain on walking was considered as clinical indicator of union.<sup>20</sup> Mean union time was found to be  $15.43\pm3.726$  weeks (Table-3). Range of motion of knee was achieved to the normal limits in all the patients with mean of  $129.00\pm3.590$  degree. 90% of the patients achieved near normal range of ankle movement, dorsi flexion ( $>20^\circ$ ) and plantar flexion ( $>30^\circ$ ). Post operative complications like compartment syndrome, neurovascular deficit, thromboembolism, shortening, stiff knee joint, was not observed in any of the patients. Superficial infection was observed in 7.14% (2) patients, while deep infection in 3.57% i.e. 1 patient only. Delayed union was observed in 3 patients. Anterior knee pain was observed in 14.28% (i.e. 4 pat.) of total cases in the study. Implant failure in form of broken nail or screw was not seen in any case.

## DISCUSSION

In our study on 28 patients, the majority of the patients were in the age group of 21-40 years. There were 22 (78.57%) patients in this age group. The mean age of the patient was  $28.64\pm7.917$  years. Younger age group were more prone as they are the persons who were physically active, engaged in increased various outdoor activities and thus sustaining high-velocity injuries. Our results are supported by study of Bonatus et al<sup>21</sup>, in which the average age was 30.3 years and Court Brown et al.<sup>22</sup> (1990) noted the average age to be 32.4 years. Our study should males predominance with 17 male patients (85%) which is in agreement with the similar study of Hooper et al<sup>23</sup> (male predominance 80%) and the study of Abdelaal et al<sup>24</sup> (80%). The incidence of males is higher because of their more outdoor activities, while women confined themselves to the domestic activities.

In our study majority of fractures i.e. 21(75%) occurred due to road traffic accidents. This finding is supported by Lawrence et al<sup>4</sup> study showing 90% incidence. Court Brown et al<sup>22</sup> study,

Age (Years)	No. of patients	%
16-20	4	14.28
21-30	16	57.14
31-40	6	21.42
41-50	2	7.14
51-60	0	0.00
Mean ( $\pm$ S.D.)		
$28.64\pm7.917$		

Table-1: Age wise distribution.

Duration	No. of patients	%
0-6hrs	04	14.28
6-12 hrs	08	28.57
12-24 hrs	16	57.14%
Mean $\pm$ SD		
$14.54\pm6.304$ hrs		

Table-2. Injury Surgery interval.

Time in weeks	Fracture of Tibia (n=28)	Percentage (%)
10-15 weeks	11	39.28
16 -20 weeks	12	42.85
>20 weeks	3	10.71%
Mean $\pm$ SD		
$15.43\pm3.726$ weeks.		

Table-3: Mean union time for fracture tibia.

also showed that the commonest mode of injury was road traffic accidents. This high incidence in our country can be attributed to the poor road traffic sense and poor quality of roads.

Among all fractures 64.28% belonged to grade II. In cases of compound fracture injury surgery interval plays an important role, as delay beyond golden period can lead to complications.<sup>25</sup> In our study maximum patients had been operated after the golden time period interval of 6 hours with mean time of  $14.54\pm6.304$  hours. This delay could be the reason, because our institute is a tertiary referral centre where patients come after a primary management outside and lack of awareness of people for the presence of tertiary centre.

Depending on fracture pattern early partial weight bearing was started as early as tolerated by patient because mechanical loading of injured bone is conducive to its healing.<sup>25</sup> The mean time of full weight bearing was  $14.43\pm3.191$  weeks.

In our study we promoted early weight bearing as it promotes healing and early union.<sup>26</sup> In our series of tibial interlocking nail mean union time was found to be  $15.43\pm3.726$  weeks and in 1 case sufficient union was not achieved by 20 weeks so secondary procedure was done in form of fibulectomy and bone marrow infusion. Ekeland et al<sup>27</sup> observed average union time of 16 wks and Vaquero et al<sup>28</sup> of 21 weeks. Our study is also supported Puno et al.<sup>29</sup>

Early physiotherapy in form of quadriceps drill exercises, knee and ankle range of motion exercises are key in postoperative management of tibial interlocking nail as they help in achieving near normal range of motion if started as early as possible and this is evident in our study. Range of motion at the knee joint in our study was with the mean of  $129.00\pm3.590$  degree as compared to Bluent Daglar et al<sup>30</sup> mean of knee flexion angle ( $134^\circ$ ) in 90% ankle range of motion was found to be within

Results	No.of patient (N=28)	%
Excellent • No notable abnormality	21	75
Good • Occasional pain with prolonged use • Joint motion 75% of normal • Trivial swelling • Normal gait	4	14.28
Fair • Pain with ordinary activity • Joint motion 50% of normal • Small amount of swelling • Slight limp	2	7.14
Poor • Constant pain • Joint motion <50% of normal • Any visible deformity • Limp, gait on cane or crutches	1	3.57

**Table-4:** Ketenjian and Shelton Criteria modified by Yokoyama et al.

normal limit.

In our study early antibiotics were instituted in all patients and incidence of infection was found to be 10.7% (3) of patients. Our study is supported by study of Bone and Johnson which showed infection of 4.7% in grade I and 10.5% in grade II, court Brown et al<sup>20</sup> which showed infection of 3.8% in grade I and 9.5% in grade II, Tenser A et al<sup>31</sup> who also reported 13% infection rate.

In our study 2 had superficial wound infection. This responded to the usual oral broad spectrum antibiotics and daily dressings of the wound. One patient had deep infection. Regular dressing, oral antibiotics and guarded weight bearing was continued till the fracture united (24 weeks) and later patient was managed by exchange antibiotic coated intramedullary nailing.

Anterior knee pain is the common complication in intramedullary tibial nailing. In our study, was seen in four cases (14.28%) as compared to the study of Joshi D et al<sup>32</sup> 10.71%. Toivannen et al<sup>33</sup> also noted anterior knee pain to be common in tibial intramedullary nailing.

In our study Post operative complications like compartment syndrome, neurovascular deficit, thromboembolism, shortening, stiff knee joint, rotational instability, Implant failure in form of broken nail or screw was not observed in any of case.

In our study, final assessment was based on the functional scale of Ketenjian and Shelton, which was modified by Yokoyama et al,<sup>19,20</sup> (Table-4) As per criteria among the 28 patients 89.28% (25) had excellent to good result, and 10.72% had fair to poor results, compared to Joshi D et al<sup>32</sup> which showed 85% of excellent to good and 15% of fair to poor result and Abdelaal et al<sup>24</sup> had 85.4% excellent to good result and 14.6% had fair to poor results using same criteria.

## CONCLUSION

Thus our study proves that in Grade I and II open tibial shaft fracture intramedullary interlocked nailing is an excellent procedure leading to proper union with a slight delay but allowing early weight bearing and less patient morbidity. It provides strong fixation, rotational stability and earliest return to

functional status, as the rate of healing is good with this method.

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# A Clinical Study of Wheezing Child

SK. Nazeer Ahmed<sup>1</sup>

## ABSTRACT

**Introduction:** Wheezing or noisy breathing is one of the common symptoms with which children are consulted in the pediatric out-patient or admitted into hospital for investigation and treatment. In view of the multiplicity of conditions that cause wheezing, the present study is undertaken to study the common causes of wheezing or noisy breathing in children.

**Material and Methods:** The present study was conducted among children who presented to the hospital with history of noisy breathing, wheezing, breathlessness were included in the study.

**Results:** The common cause of wheezing in children is bronchial asthma but bronchiolitis in infants (16.6%) and tropical eosinophilia (8.3%) round worm infestation (8.3%) in older children constituted large percentage. Maximum number of children with bronchial asthma were between 5-9 years (70%). In bronchiolitis cases, all children came with the history of wheezing (breathlessness). The common presenting symptom of children with foreign body was wheezing with repeated respiratory infections and dyspnea. The consistent signs were signs of obstructive emphysema with Bag-pipe sign and rhonchial fremitus and expiratory thud. In the present series there were 10 cases of worm infestation with wheezing attacks. Other cases included respiratory infections like acute laryngo Tracheo-Bronchitis, primary complex, bronchopneumonia cases.

**Conclusion:** Though the common cause of wheezing was Bronchial Asthma, other causes like bronchiolitis in infants, Tropical eosinophilia, and round worm infestation in elder children were responsible for Asthma like attacks.

**Keywords:** Bronchial Asthma; Bronchiolitis; Respiratory infections; Wheezing

## INTRODUCTION

Wheezing or noisy breathing is one of the common symptoms with which children are consulted in the pediatric out-patient or admitted into hospital for investigation and treatment. Wheeze is a characteristic harsh breathing, audible at times without the aid of stethoscope, due to partial obstruction of upper respiratory tract including trachea, bronchi and bronchioles either due to extrinsic and intrinsic of factors and is characterized by expiratory dyspnea and prolonged respiration.<sup>1</sup> For many it is thought to be synonymous with bronchial asthma, but 'all that wheezes is not asthma'.<sup>2</sup> Wheezing is a symptom of many pathological conditions, the aetiology of which has to be investigated for proper management of the case. Apart from Bronchial asthma other causes like tropical eisonophilia, acute respiratory infections like Bronchiolitis and helmenthic infestation must be thought of.<sup>3</sup> Wheeze that is localized and lateralized (unilateral) is always secondary to obstruction of one of the bronchi either due to foreign body in the lumen or extrinsic pressure by enlarged lymphnode, tumour, or anomalous blood vessel.

In view of the multiplicity of conditions that cause wheezing, the present study is undertaken to study the common causes of

wheezing or noisy breathing in children.

## MATERIAL AND METHODS

The present observational longitudinal study was conducted in Owaisi Hospital and Princesses Esra Hospital, which are allied hospitals for Deccan College of Medical sciences, Hyderabad, from December 2006 to November 2007. All children who presented to the OPD and IPD with history of noisy breathing, wheezing, breathlessness were included in the study. All Children <2months and >14 years and breathlessness due to CVS, CNS causes were excluded from the study. The criteria used for the diagnosis of bronchiolitis were severe dyspnea with signs of respiratory muscles acting, without any positive history of asthma or eczema, temperature or normal or slightly more than normal (not beyond 100 F), wheeze and diminished breath sounds. The criteria for diagnosis of tropical eosinophilia was an increase in absolute eosinophila count more than 2000/cmm without any known detectable cause for eosinophilia. Those cases presented with history of repeated respiratory infections and wheezing, careful auscultation revealed that wheezing was unilateral and localized. Rhonchial fremitus was palpable on one side only. At times rhonchi were heard on both sides of chest but they were transmitted sounds because of thin chest wall.

## STATISTICAL ANALYSIS

Obtained data was arranged according to characteristics and was expressed as a number and percentage of respondents and were analyzed using the SPSS Version 17 software.

## RESULTS

Table-1 shows that the common cause of wheezing in children is bronchial asthma but bronchiolitis in infants (16.6%) and tropical eosinophilia (8.3%) round worm infestation (8.3%) in older children constituted large percentage.

**Analysis of the in-patient cases with bronchial asthma:** Maximum number of children with bronchial asthma were between 5-9 years (70%). Males constituted larger percentage (58.33%). Male: Female ratio was 32:25 (7:5). Amongst the cases of bronchial Asthma, most of the children belonged to middle socio-economic status (table-2).

**Family history:** 24 cases (40%) gave a definite positive history of bronchial asthma in the family. Details revealed that in 15 cases (25%) asthma was present on paternal side, while in 9 cases (15%) the disease was present on maternal side. However in 3 cases (5%) family history of asthma in the siblings and

<sup>1</sup>Assistant Professor, Department of Pediatrics, Narayana Medical College Nellore, India

**Corresponding author:** Dr. Nazeer Ahmed., M.D, 3/1329 Nawabpet, Setti Gunta Road, Nellore, Andhra Pradesh, 524002, India

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in all of them either father or mother, grand-father or mother, uncle or aunt was suffering from bronchial asthma. This shows that if more than one sibling is suffering from asthma one of the parents or grant parents usually must be suffering from asthma.

**Eczema:** 9 cases (15%) gave a definite history of eczema during early childhood before the asthmatic attacks started. In 3 cases (5%) eczema was presented along with asthmatic attacks.

**Seasonal attacks:** Seasonal attacks were present in 24 cases (40%). Winter was the common season where in 25% cases used to have repeated attacks of wheezing while in 9 cases (15%) the attacks were common during the months of February to April (spring), cases probably are due to Pollen allergy.

**Infection:** Infection was one of the important factor which was precipitating asthmatic attacks. Signs of infection like, fever, congestion of throat, leukocytosis were present in 33 cases (55%). These are the cases which were referred as having "Asthmatic bronchitis". In these cases antibiotics were used in addition to bronchodilators for the treatment of acute attack.

**Allergy:** In 9 cases (15%) signs of allergy like rhinorrhea, sneezing preceding wheezing; pale oedematous nasal mucous membrane, eosinophilia in the nasal smear and blood were present. However because of the lack of facilities skin testing was not done.

**Food Factors:** In 8 cases there was definite correlation between consumption of certain food factor and asthmatic attacks. This was tested after the attack was treated in the hospital, the suspected item or substance was served in the food, and in 13.3% bases the following food substances precipitated or aggravated attacks (table-3).

**Exercise:** In 2 cases (3.3%) wheezing was initiated on running or physical exertion. In these two cases where there was no organic lesion in the heart. After the exercise, when auscultated these children had typical asthmatic breathing which used to persist for 2-5 hours.

**Investigations:** Polymorpho nuclear leukocytosis was present in 33 cases (55%). In 12 cases (20%) there was definite blood eosinophilia of more than 10% but less than 2000 cells/cmm absolute eosinophilia count. That is in 80% cases even during acute attack eosinophilia was not present.

**Radiological Features:** During acute attack 34 cases (56.6%) were showing emphysematous lungs. The emphysematous changes disappeared after acute attack subsided, in 24 cases (40%) while in 10 cases (16.6%) they persisted even after attack. Increased bronchovascular markings were noted in 30 cases (50%) while 6 cases (10%) present with bronchopneumonic changes and one case of pneumothorax.

**Analysis of the in-patient cases with bronchiolitis:** Total number of cases of bronchiolitis were 20. Among the 20 cases, 13 were males while 7 were female children. The common age was between 7 – 12 months (50%) (table-4).

The table-5 summarized the presenting symptoms and signs in bronchiolitis cases All most all children came with the history of wheezing (breathlessness). 7 cases complained of nocturnal cough and 4 cases (40%) presented as difficulty in breathing. 2 cases had liver enlargement. 1 case showed significant lymphadenopathy and mantoux test was negative.

Absolute eosinophilic count varied from 2000/cmm to 9192/cm. X-Ray chest was normal in 3 cases. 7 cases showed increased

Aetiology	No. of cases	Percentage
Bronchial Asthma	60	50.0%
Bronchiolitis	20	16.60%
Tropical Eosinophilia	10	8.30%
Round-worm infestation with repeated wheezing	10	8.30%
Acute Laryngo-tracheobronchitis	7	5.81%
Primary Complex	5	4.15%
Brochopneumonia	4	3.32%
Foreign body	3	2.5%
Rickets with costochondral beading	1	0.83%

**Table-1:** Analysis of the in-patient cases from the aetiological points of view

Age	Cases	Percentage
1-4 Years	14 Cases	23%
5-9 Years	42 Cases	70%
10-12 Years	4 Cases	7%
Socio-Economic Status		
Socio economic status	Cases	Percentage
High S.E.S.	21 Cases	35%
Middle S.E.S.	24 Cases	40%
Low S.E.S.	15 Cases	25%

**Table-2:** Demographic distribution of bronchial asthma cases

Egg	2 Cases	Custard apple	1 Case
Banana	1 Case	Sugar	1 Case
Fish	1 Case	Chocolate	2 Cases

**Table-3:** Food Allergies in Bronchial Asthma Cases

Age	Cases	Percentage
2-3 Months	2	20%
4-6 Months	4	20%
7-12 Months	10	50%
1-2 Years	4	20%

**Table-4:** Age wise distribution of bronchiolitis patients

Presenting signs and symptoms	No. of cases
Dyspnea and tachypnea	20
Irritability and excessive crying	14
Intercostal retraction	20
Suprasternal retraction	5
Xiphisternal Retraction	5
Temperature:	
Normal	15
More Than 99 degree F	5
Tachycardia	14
Significantly palpable liver	12
Palpable spleen	3
Definite signs of congestive heart failure	8
Throat swab for culture:	
No Organs (Probably Viral)	18
Streptococci	1
H. Influenza	1
Radiological feature: Emphysema	18

**Table-5:** Presenting signs and symptoms in bronchiolitis

Case No.	Age and Sex	Definite H/o. F.B.	Presenting Symptoms	Duration	Positive Physical Signs,	Type of F.B.
I	5 Years Male	+	Wheezing and Repeated Respiratory Infections	1 Month	Unilateral Rhonchi wheeze –signs obstructive emphysema of right lower lobe bag-pipe sign positive	Beatle nut
II	6 Years Male	+	Wheezing and barking cough	3 Months	Bag-pipe sign positive signs of obstructive emphysema left lower lobe	Custard apple seed
III	3 Years	-	Progressive dyspnea and cough	2 Days	Positive bagpipe size –Wheeze+ obstructive emphysema right lower lobe.	Small Stone

Table-6: Cases Of Foreign Body

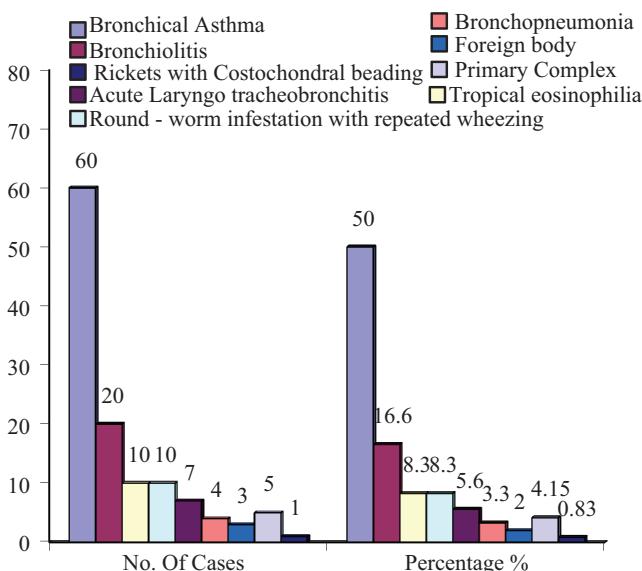


Figure-1: Analysis of the in-patient cases from the aetiological points of view

broncho vascular markings while 4 cases (40%) showed typical perihilar and basal mottling.

Table-6 shows cases Of foreign body. The common presenting symptom was wheezing with repeated respiratory infections and dyspnea. The consistent signs were signs of obstructive emphysema with Bag-pipe sign and rhonchial fremitus and expiratory thud. The common site of foreign body was right lower lobe bronchus – the 2 foreign bodies were non-radioopaque while one was radio-opaque (small stone). All the cases responded dramatically to bronchoscopic removal of foreign body but for one case where crepitations persisted for three months after removal foreign body but there were no signs of bronchiectasis.

#### Round Worm Infestation

In the present series there were 10 cases of worm infestation with wheezing attacks. All the 10 cases were being treated as Asthma. But on investigation, stool examination revealed ova of round worm. Out of the 10 cases, 6 cases were males, while 4 cases were female children. Two children gave history of passing round worms. 4 children gave history of pain in abdomen and 3 children gave history of pica. All these children were passing round worm ova. 2 children in addition had giardiasis and one child had ankylostomiasis. Blood examination in 6 out of 10 cases showed eosinophilia (varying from 500-1500 cells/cmm of absolute eosinophilia count). These children were treated with ALBENDAZOLE followed after 15 days, stool examination was repeated after 1 month. In 9 cases ova disappeared after

treatment and in 8 cases Asthmatic attacks disappeared. In only one case of ascariasis, there were signs of bronchopneumonia with an absolute eosinophilia count of 1420 cells/cmm. Thus fitting probably into "Loeffler's Syndrome", All the cases of ascariasis with Asthma like attacks responded well to antihelminthic treatment. So these cases were included under the heading of Round worm allergy and Asthmatic attacks.

#### Other Cases

Under this heading were included respiratory infections like acute laryngo Tracheo-Bronchitis, primary complex, bronchopneumonia cases. One case was having marked costochondral beading (rickets) so as to cause pressure on the lung parenchyma and the child was prone to respiratory infection and wheezing attack. The X-ray chest was showing pulmonary plethora and fine reticular appearance. This probably is due to frequency of respiratory infections causing narrowing of bronchial lumen and wheezing attacks.

#### DISCUSSION

Wheezing is a very common respiratory symptom during childhood. Epidemiological studies have reported that almost one-third of all children wheeze at least once in the first three years of life, with nearly 50% of all children having at least one wheezing episode by the age of 6 years.<sup>4</sup>

The present study found that the common cause of wheezing in children is bronchial asthma but bronchiolitis in infants (16.6%) and tropical eosinophilia (8.3%) round worn infestation (8.3%) in older children constituted large percentage. Heyman PW et al<sup>5</sup> compared a large number of the wheezing children aged 3 to 18 years and reported that viral infections were the dominant risk factor for wheezing among children hospitalized before 3 years of age. Prasad S et al<sup>4</sup> determined the severity of Vitamin D deficiency and its association with recurrent wheeze in children less than 3 years of age and concluded that Vitamin D deficiency was associated with increased risk of recurrent wheezing.

The present study is a selective one because those cases which could be followed were included in the study. Many of the cases, for example Bronchial Asthma cases were referred along with diagnosis. Acute respiratory infections like Bronchopneumonia and laryngo-tracheobronchitis in younger children can present with the complaint of wheezing for the relatively small bronchi can get easily narrow by inflammatory oedema and mucous secretions. In the present study, maximum number of children with bronchial asthma were between 5-9 years. Males constituted larger percentage (58.33%) with male:female ratio of 7:5. The prevalence of asthma in boys is almost double that of girls with then ratio ranging from 1.3:1 to 3.3:1 as quoted by various workers.<sup>6,7</sup> Most of the asthmatics have the onset

of wheezing usually by 5 years of age. A 20 year follow up study was conducted by Blair<sup>8</sup> to study the natural history of childhood asthma and found that 30% of all asthmatics have their first episode of wheezing in first year of life, 57% by 2 years of life and 84% of all by 5 years of life.

Viral infections are the major factors in precipitating an asthmatic in 40 percent of cases.<sup>9,10</sup> The predominant viruses causing this infection included respiratory syncytial virus, parainfluenza virus, corona virus and rhinovirus. Food allergy in asthma is a controversial subject and difficult to prove. Attributed food allergies have been observed in 19.75 percent of the children, predominantly to grapes, banana, guavas, citrus fruits, ice-cream, chocolate fried food, tomatoes etc, but correlation is not proved. Pollen and molds in 7.5 percent of children while house dust, cold air, passive smoking, cockroach, debris, cologne spray, mosquito coil smoke, were found to be triggering factors in 6.3 percent of patients<sup>10</sup>

In the present study, those cases where wheezing was localized or confined to one half of the chest, when investigated the cause was either in the lumen such as foreign body or pressure on the wall of bronchus by enlarged lymphnodes of primary complex. The upper the site of obstruction like larynx, trachea, more is the inspiratory dyspnea, thus producing harsh vibratory high pitched shrill, crowing noise, which is known as 'stridor'. Inspiratory dyspnea is associated with expiratory distress because during expiration due to increased intrathoracic pressure, the bronchiolar lumen further narrows. The more peripheral the obstruction to the airway the more is the difficulty expressed during expiration resulting in hissing sound which is known as wheezing.<sup>11</sup> Thus obstruction to the airway whether upper or lower the difficulty in breathing is experienced, both during inspiration and expiration. However because of the natural recoiling during expiration greater effort is needed during the act. Expiratory thoracic muscles compress the lower chest, abdominal muscles contract pushing diaphragm up in an attempt to squeeze the air out of the lung resulting in raised intrapulmonary pressure, the air now escapes under high pressure through the narrowed bronchial lumen producing cooy sound.<sup>12</sup>

Children have small air passages and abundant lymphatic tissue. Most of their diseases are inflammatory or allergic and therefore nose, throat and bronchi are easily obstructive.<sup>13</sup>

## CONCLUSION

Though the common cause of wheezing was Bronchial Asthma, other causes like bronchiolitis in infants, tropical eosinophilia, and round worm infestation in elder children were responsible for Asthma like attacks.

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# Correlation of Serological, Biochemical and Molecular Viral Markers with Histological Parameters in Chronic Hepatitis B for Assessment of Response to Therapy

Rigvardhan<sup>1</sup>, Kavita Sahai<sup>2</sup>, Gurvinder Singh Chopra<sup>3</sup>, Rakhi Negi<sup>4</sup>, Atul Kotwal<sup>5</sup>

## ABSTRACT

**Introduction:** Hepatitis B virus (HBV) infects more than 350 million people worldwide. The presence of continuing viral replication correlates with continuing disease activity and is associated with Hepatitis B e antigen (HBeAg) and hepatitis B virus DNA (HBV-DNA) in serum. Subsequently, the patient may undergo a spontaneous or therapy induced remission, which is accompanied by loss of HBV-DNA and HBeAg. This prospective study was undertaken to correlate all the above parameters so as to have an insight to monitoring of therapy in chronic hepatitis B (CHB).

**Material and methods:** 66 patients of CHB were enrolled and were followed up for 24 months. Blood samples were collected for aspartate aminotransferase (AST), alanine aminotransferase (ALT), hepatitis B surface antigen (HBsAg), Anti-hepatitis B core antigen (HBcAg), HBeAg and HBV-DNA. Liver biopsies were done in all individuals. Immunohistochemical staining for HBsAg and HBcAg were done where indicated. The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software.

**Results:** There was a statistically significant improvement in the biochemical, serological and virological profile of the patients after therapy. However, the necroinflammatory activity showed improvement but was not statistically significant. Immunohistochemistry showed good correlation with viral load.

**Conclusion:** HBV-DNA is the most reliable marker to assess seroconversion followed by HBeAg. IgM-anti HBc positivity during or post-therapy denotes continuing necroinflammatory activity. Histology shows improvement but was not significant in our study.

**Keywords:** Chronic hepatitis B, therapy, serological and viral markers, histology

## INTRODUCTION

Serendipity led to the identification of Australia antigen, now known as hepatitis B surface antigen (HBsAg).<sup>1</sup> Hepatitis B Virus (HBV) is a major health problem in Asia and sub-Saharan Africa.<sup>2,3</sup> Progression to long term infection occurs in 15-40% of cases resulting in chronic hepatitis B (CHB).<sup>4,5</sup>

The natural history of CHB includes a Hepatitis B e Antigen (HBeAg) positive, immune tolerant phase which progresses to a HBeAg-positive immune-reactive phase, HBeAg-negative inactive HBV carrier state, HBeAg-negative CHB phase and HBsAg negative phase (occult infection).<sup>6</sup> The HBV can be detected serologically by HBV DNA in the serum.<sup>7</sup> Histopathological changes include necroinflammatory activity and fibrosis, which can be correlated with various parameters.<sup>8</sup> Suppression of viral replication is critical to reduce the risk of complications from HBV. In a large-scale, long-term follow up study of chronic HBV infection, elevated serum HBV DNA

levels were found to be the strongest single risk factor for progression to cirrhosis.<sup>9</sup> Periodic serological and viral markers studies are required during antiviral therapy to assess treatment response. As complications occur after decades of infection and often long after treatment has been initiated, various surrogate markers are used to ascertain treatment benefit.<sup>10</sup> These include serum aminotransferase levels, HBeAg or anti-HBe, HBsAg or anti-HBs, serum HBV DNA level and liver histology. Numerous definitions have been used to assess response to antiviral therapy such as biochemical response, virological response, histological response and complete response (biochemical and virological response with loss of HBsAg).<sup>11,12</sup> Recent studies favor using durable HBV DNA suppression as the primary measure of therapeutic success.<sup>9,13</sup>

The aims and objectives of this study were:

1. To determine changes in serum aspartate aminotransferase (AST) and ALT levels and serological profile (HBsAg, Anti hepatitis B core (HBc) IgM and HBeAg) in CHB with therapy.
2. Quantitative determination of HBV DNA in plasma and its correlation with serology with therapy.
3. Determination of histology in liver biopsies in all cases and correlation of above parameters with immunohistochemical detection of HBsAg and HBcAg in the biopsies from patients with CHB.

## MATERIAL AND METHODS

**Patient selection:** In this prospective study, 66 cases of CHB were followed for 24 months. Sample size was determined by the number of patients who were followed for a period of two years and for whom almost complete data was available. History of any concomitant illness was taken into consideration but was not an exclusion criterion. Informed consent and Institutional ethical clearance was obtained. Patients were treated with lamivudine with or without peg-interferon. All the patients were

<sup>1</sup>Associate Professor, Department of Pathology, <sup>4</sup>Assistant Professor, Department of Biochemistry, Command Hospital (Central Command), Lucknow, <sup>2</sup>Professor, Department of Pathology, <sup>5</sup>Professor, Department of Community Medicine, Army College of Medical sciences, Delhi Cantt, Delhi, <sup>3</sup>Professor, Department of Microbiology and Molecular Biology, Christian Medical College and Hospital, Ludhiana, India

**Corresponding author:** Dr Rigvardhan, Associate Professor, Department of Pathology, Command Hospital (Central Command), Lucknow – 226002; India

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were evaluated for:

**Biochemical parameters:** AST and ALT were measured using ERBA kits in opERA system (BAYER) in accordance with principle based on International federation of clinical chemistry. Quality control measures were strictly followed.

**Serological parameters:** HBsAg, HBeAg and IgM-anti HBc were performed by enzyme immunoassay (Milano, Italy). Positive and negative controls were run simultaneously to check the validity of test.

**Molecular viral marker:** Extraction of DNA was done using AccuPrep Genomic DNA Extraction Kit (BIONEER) which is a column-based assay. Quantitative PCR assays were carried out using HBV RG Real-ArtTM reagents in Rotor-Gene 2000 instrument where fluorescence labeled oligonucleotide probe bind specifically to the PCR amplicate and fluorescence intensity during the course of Real time PCR enables verification as well as quantification of the accumulating product. Samples with more than  $10^5$  copies/ml were considered positive.

**Histological evaluation:** Specimens were fixed in 10% buffered formalin, processed by routine methods, embedded in paraffin and sections cut to 3-4 um in thickness. Sections were subjected to hematoxylin and eosin stain and reticulin stain. Scores were accorded as per modified Knodell-Ishaak scoring system.<sup>14</sup> Immunohistochemical (IHC) staining was done in selected cases for HBsAg and HBcAg with monoclonal antibodies (ready to use kit manufactured by SEROTEC (USA).

Interpretation of IHC staining:

- (a) HBsAg: strong brown staining of cytoplasm or membranous or both pattern of staining.
- (b) HBcAg: strong brown staining of nucleus, cytoplasm or mixed pattern.

## STATISTICAL ANALYSIS

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean $\pm$ SD (Standard deviation). Wilcoxon assigned rank test was used to test the significance of two means. The level of significance "p" value was considered statistically significant if  $<0.05$ .

## RESULTS

In this study, all the patients were males. 45% were in age group 20-30 years, 42 % in 31-40 years, 10.6% in 41-50 years and 2.4 % in 51-60 years. Mean age was 33.5 ( $\pm 6.75$  SD) years.

### Biochemical Profile

**A. AST profile:** Before treatment, mean AST value was  $73.83 \pm 89.37$  SD IU/L (Range= 15 to 494 IU/L) which reduced to a mean of  $42.43 \pm 25.29$  SD IU/L (Range= 17-139 IU/L). AST profile is summarized in Table-1. Amongst these 32 cases had normalized, 12 remained static, 16

cases improved but did not normalize whereas 06 cases worsened. This reduction in the post-treatment AST levels shows statistical significance (p value = 0.0042).

**B. ALT profile:** The mean value of ALT was  $122.8 \pm 159.6$  SD IU/L (Range= 15 to 696 IU/L) which reduced to  $62.27 \pm 66.6$  SD IU/L (Range= 17-409 IU/L). ALT profile is summarized in table-1. As compared to pre-treatment levels- 25 cases had normalized, 11 remained static, 12 cases had worsened and 18 cases improved but did not normalize. The reduction in the post-treatment value exhibits statistically significant reduction ( p value = 0.0018).

### Serological profile

**A. HBsAg:** As per patient selection criteria, all cases were HBsAg positive. Post therapy, 16 cases (24.2%) became HBsAg negative whereas 50 cases (75.8%) continued to remain positive. Statistical correlation by Wilcoxon assigned ranks test shows a Z value of – 4.0 and p value of 0.002.

**B. HBeAg:** In this study, 42 cases (63.6%) were positive whereas 24 (36.4%) cases were HBeAg negative. After therapy out of 42 HBeAg positive cases, 35 (83.3%) cases became HBeAg negative, whereas 07(16.7%) cases remained HBeAg positive. Those cases, which were HBeAg negative continued to remain negative post-treatment. Statistical correlation by Wilcoxon assigned ranks test shows a Z value of – 5.96 and p value of 0.000.

**C. IgM anti-HBc:** In 52 cases, where IgM anti-HBc was carried out, 19 (36.5%) were positive and 33 (63.5%) were negative. Of the 19 cases, which were IgM- anti-HBc positive, 10 (52.7%) became negative whereas 09 (47.3%) cases continued to remain positive. Out of 33 cases which were IgM anti-HBc negative, 31 (94%) continued to remain negative whereas 02 (6.0%) became positive. Statistical correlation by Wilcoxon assigned ranks test shows a Z value of – 4.79 and p value of 0.001.

**D. Molecular viral marker:** Out of 66 cases, HBV-DNA was positive in 61 (92.4%) cases and only 05 (7.6%) cases were negative. Among HBV-DNA positive cases, the mean viral load was 701,239, 942. 5-copies/ ml. After therapy, 38 (62.3%) became negative whereas 23 (37.7%) remained positive. Amongst 05 cases, which were HBV-DNA negative, 01 (20%) case became positive, rest 04 (80%) remained negative. Statistical correlation by Wilcoxon assigned ranks test shows a Z value of – 5.86 and p value of 0.000. Post therapy, the mean HBV-DNA level reduced to 234,644,954.5-copies/ ml in HBV-DNA positive cases. The serological and molecular viral marker profile is summarized in table-2.

### Histological profile

The scoring was done as per modified Knodell-Ishaak (KI)

	Pre-treatment profile				Post-Treatment Profile			
	upto 40	41-80	81-160	>160	0-40	41-80	81-160	>160
AST (normal upto 40 IU/L) n=66	32	20	06	08	40	14	07	05
ALT (normal upto 40 IU/L) n=66	22	20	11	13	36	15	08	07

Table-1: AST and ALT profile

system, 34 (51.5%) cases were in the subgroup 0-4, 21 (31.2%) in the subgroup 0-8 and 11 (16.6%) in the subgroup more than 8. Amongst the category with KI score of 0-4, post therapy liver biopsy was done in 13 cases of which six cases improved, 04 cases remained the same whereas 03 cases worsened. Amongst the category with KI score 5-8; post therapy liver biopsy was done in 07 cases of which 06 cases improved whereas 01 case worsened. In the category with KI score of more than 8, post therapy liver biopsy was done in 05 cases of which 04 cases improved whereas 01 case worsened. Thus, overall 16 (64%) cases improved, 05 (20%) cases worsened whereas 04 (16%) remained static (table-3). Statistical correlation by Wilcoxon assigned ranks test shows a Z value of -1.595 and p value of 0.111.

### Immunohistochemistry profile

1. HBsAg: Two patterns of staining were noted - Cytoplasmic (Figure-1A) and cytoplasmic + Membranous (Figure-1B). Cytoplasmic positivity was seen in 23 (48.9%) of cases. The mean KI score in these cases was 3.6/22. Cytoplasmic and Membranous positivity was seen 20 (42.6%) cases with mean KI score of 5.3/ 22. These cases also had high viral load with mean HBV-DNA levels of 902,947,705.7-copies/ml. Negative staining for HBsAg was seen in 4 (8.5%) cases.
2. HBeAg: Three patterns of staining were noted
  - (a) Nuclear staining (figure-1C): This pattern was seen in 13 (50%) cases that were HBeAg positive. HBeAg negative cases did not show this pattern.
  - (b) Nuclear and cytoplasmic pattern (figure-1D): This pattern was observed in 10 (37.5%) HBeAg positive cases and was associated with high levels of HBV-DNA (mean=1,349,657,212.7 copies/ml). These cases had a mean KI score of 8/22. This pattern was not seen in HBeAg negative cases.
  - (c) Only cytoplasmic pattern of staining was seen in 02 (7.6%) HBeAg negative cases. Mean KI score was 4.3/22. This pattern was not seen in HBeAg positive cases. 03 (12.5%) HBeAg positive cases and 19 (92.4%) HBeAg negative cases did not stain for HBeAg.

## DISCUSSION

Focus of hepatitis B research is development of more effective therapies aimed at inhibiting HBV-DNA synthesis and in eliminating ccc DNA.<sup>1,10</sup>

### Biochemical profile

In this study, best response was seen in cases with pre-treatment ALT more than 160 IU/L where out of 13, 06 (46.2%) cases normalized and 07 (53.8%) improved but did not normalize. In this subgroup, 07 cases were HBeAg positive before therapy, all became HBeAg negative with therapy. ALT levels were higher in HBeAg positive cases compared to negative cases with higher necroinflammatory score but they responded well to treatment. Normalization of the ALT level during therapy is thought to reflect improvement in necroinflammation. Serial measurement of ALT levels may also reveal emergence of antiviral resistance.<sup>15,16</sup> Assessing treatment response using serum ALT has limited predictive value as in early trials of lamivudine

	Pretreatment profile		Post-treatment profile	
	Positive	Negative	Positive	Negative
HBV-DNA n=66	Positive	61	23	38
	Negative	05	01	04
HBeAg n=66	Positive	42	07	35
	Negative	24	00	24
IgM anti-HBc n=52	Positive	19	09	10
	Negative	33	02	31
HBsAg n=66	All Positive		52	14

Table-2: Serological and molecular viral marker profile.

n=25	Improved ( $\geq 2$ pts)	Same	Worsened
0-4	06	04	03
5-8	06	nil	01
>8	04	nil	01

Table-3: Histological response

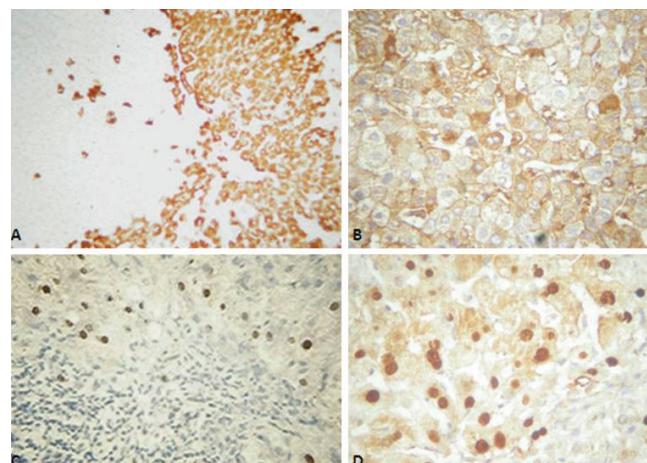


Figure-1: Cytoplasmic (A) and cytoplasmic + membranous (B) pattern of HBsAg immunohistochemistry staining. Nuclear (C) and nuclear + cytoplasmic (D) pattern of HBeAg immunohistochemistry staining.

therapy not all patients who achieved biochemical response (70%) had improvement in necroinflammatory score (56%).<sup>17,18</sup> In a recent study of more than thousand CHB patients, significant number of patients with persistently normal ALT levels (<40 IU/L) had significant fibrosis or inflammation on biopsy.<sup>19</sup> The decrease in response rates with time can occur due to accumulation of YMDD mutants (Substitution of Isoleucine for Methionine at position 552) a virological breakthrough, which are always persistent.<sup>20</sup>

### Serological profile

In our study, HBsAg seroconversion was seen in 16 cases. HBsAg seroconversion is most durable treatment endpoint but correlates poorly with therapy.<sup>10</sup> It occurs in less than 2% of patients taking nucleoside analogues for one year and 3 to 8% of patients receiving interferon or peg interferon.<sup>11</sup> As HBsAg seroconversion is more durable than HBV DNA suppression alone treatment cessation is possible only after this has been achieved.

In our study, HBeAg seroconversion was seen in 35 (83.3%) out of 42 cases. HBeAg has been advocated as an indicator of active underlying liver disease and high degree of infectivity. In contrast, the clearance of HBeAg from sera is associated

with reduction in viral replication and normalization of transaminases.<sup>16,21</sup> Long term lamivudine therapy even after HBeAg seroconversion has shown additional benefit where relapse rate following cessation of therapy were 13% at one year and 16% at two years, suggesting that long-term therapy might increase the durability of response.<sup>22</sup>

Cases, which were HBeAg negative before therapy, continued to remain so in our study. None of the large prospective studies have reported any case becoming HBeAg positive with therapy who were negative before treatment.<sup>10,23</sup>

IgM anti-HBc is an indirect marker for acute phase of hepatitis and in the "window period", it is the only marker available for detection of HBV infection.<sup>1,24</sup> In our study, we found that among IgM anti-HBc positive cases, 09 (47.3%) continued to remain positive. Among IgM anti-HBc negative cases, 02 (6%) became positive. Thus, total 11 cases were positive after therapy. Out of these, liver biopsy was done in 03 cases, all of whom showed worsening of KI score compared to pre-treatment KI score.

Colleredo et al using semi-quantitative assessment of IgM anti-HBc showed that antibody titer below 0.2 has 75% predictive of a mild necroinflammatory activity and rules out severe activity (29% sensitivity and 91.6% specificity) whereas antibody titer between 0.2 to 0.5 and more than 0.5 was associated with moderate and severe necroinflammatory activity, respectively. They also concluded that although necroinflammatory activity correlates with IgM anti-HBc levels, stage of fibrosis was unrelated to IgM anti-HBc antibodies.<sup>25</sup> Quantitative hepatitis B core antibody level may be a novel biomarker for predicting treatment response in HBeAg-positive patients receiving therapy.<sup>24</sup>

#### Molecular viral marker profile

HBV-DNA is the hallmark of active viral replication as it has been found in the liver biopsies of cases which were HBsAg and HBeAg negative serologically. Molecular hybridization techniques have demonstrated HBV-DNA in liver biopsies in cases, which were anti-HBe positive and HBsAg negative.<sup>26</sup>

In our study, HBV-DNA seroconversion was seen in 38 (62.3%) HBV-DNA positive cases. In cases which were HBeAg and HBV-DNA positive before therapy, 23 (59%) cases became HBV-DNA negative whereas 16 (41%) cases remained HBV-DNA positive. Amongst cases, which were HBeAg negative but HBV-DNA positive before therapy, 15 (68.2%) cases became HBV-DNA negative whereas 07 (31.8%) cases continued to remain HBV-DNA positive. Thus overall, we found HBV-DNA seroconversion of 62.3%.

Serum HBV DNA level estimation at various time points during therapy play an important role in determining the course of therapy. Recent studies suggest that initial viral kinetics during therapy can predict the sustained virological response in CHB.<sup>27</sup> Regarding cases, which became HBeAg negative but remained HBV-DNA positive are those which are associated with circulating HBV genomes harboring mutations in the precore promoter i.e. A to G substitution at position 1896.<sup>28</sup>

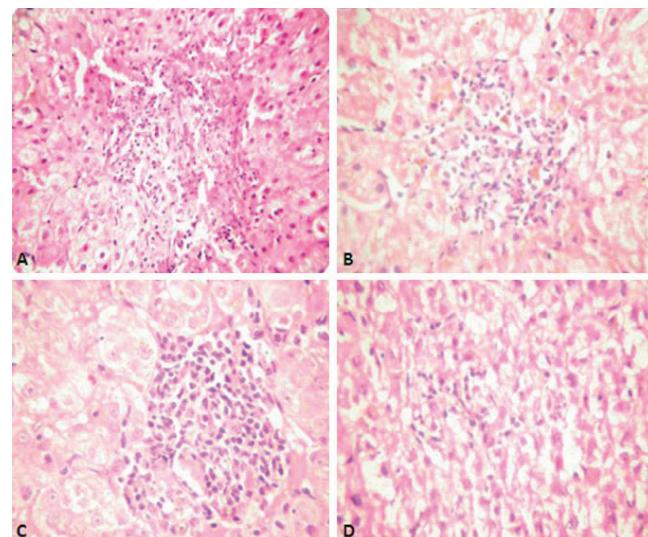
A major problem of anti-viral therapies is the emergence of drug resistance conferred by mutations in the YMDD motif of HBV-DNA reverse transcriptase. The prevalence of YMDD mutations increases with longer duration of antiviral therapies and this has been detected in 20% of immunocompetent patients per year of treatment.<sup>20,28</sup> In our study, HBV-DNA positivity post-therapy is

also probably due to emergence of mutant strains.

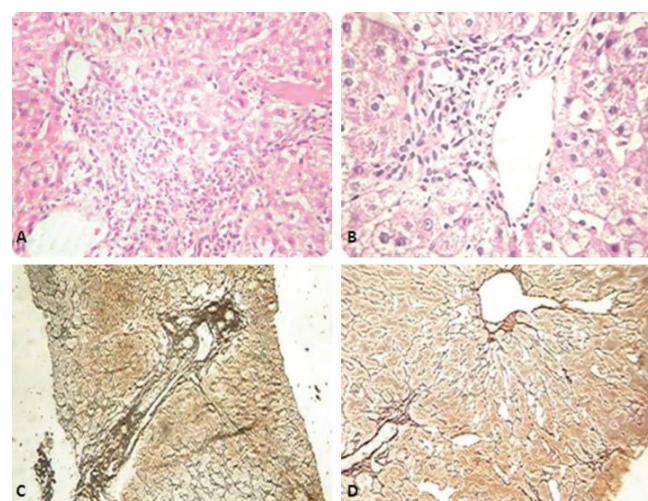
#### Histological profile

We used modified Knodell-Ishaak scoring system which includes interface hepatitis and bridging necrosis, lobular inflammation, portal inflammation and fibrosis. Histological response is defined as an improvement in the histology activity index (HAI) of 2 points or more or improvement in the fibrosis score.<sup>10</sup> Post therapy, the improvement was seen in interface hepatitis (figure-2 A,B), lobular inflammation (figure-2 C, 1D) as well as in portal inflammation (figure-3 A,B). Of the cases that improved, extent of fibrosis also improved in 07 (43.7%) cases (figure-3 C,D).

In HBeAg positive and HBV DNA positive cases, improvement was seen in 10 cases, worsening in 04 cases while 01 case remained static. Amongst the cases, which worsened histologically, 03 cases continued to remain HBV-DNA positive after therapy whilst HBeAg seroconversion was seen in all cases. 02 of the cases, which worsened after treatment, were found to be HIV positive. Other two cases, which worsened



**Figure-2:** Improvement in interface hepatitis (A-pre-treatment; B-post treatment) and lobular inflammation (C-pre-treatment; D-post treatment) with therapy.



**Figure-3:** Improvement in portal inflammation (A-pre-treatment; B-post treatment) and fibrosis (C-pre-treatment; D-post treatment) with therapy.

histologically, may be cases of some other chronic infection or reaction to drugs. The case, which became HBV-DNA negative with therapy but worsened histologically, might be harboring HBV-DNA mutants, which could not be detected during routine screening using conventional primers.

In cases, which were HBeAg negative but HBV DNA positive before treatment, improvement was seen in six cases, worsening in 01 case and 03 cases remained static. The case, which worsened, was HBV-DNA positive after therapy.

### Immunohistochemistry profile

We found that cytoplasmic + membranous pattern for HBsAg and nuclear +cytoplasmic pattern for HBcAg was associated with high viremia and increased necroinflammatory activity.

03 HBeAg positive and 19 HBeAg negative cases did not show positive staining for HBcAg. This can be explained on the basis of sequencing analysis of integrated viral DNA which suggested that the HBsAg gene remains intact whereas the HBcAg gene gets either deleted or rearranged resulting in impaired synthesis of HBcAg in the liver with integrated HBV-DNA.<sup>29</sup>

Ramalho et al found significant correlation between intrahepatic HBcAg expression with HBeAg and HBV-DNA ( $p<0.001$ ) with highest levels of HBV-DNA found in the cases with nuclear and cytoplasmic pattern of staining (mean=  $10^6$  viral genomes/ml). They also found significant link between HBV-DNA and membranous pattern of HBsAg staining ( $p=0.001$ ).<sup>30</sup>

In our study, lack of HBcAg staining in HBeAg negative cases can be explained on the basis that the accumulation of viral nucleocapsid antigen in the cytoplasm is caused by defective maturation and/or secretion of this antigen. According to pathogenetic theory, the immune response to HBeAg (membrane bound nucleocapsid antigen) is responsible for liver damage, while the immune response to free HBcAg has no apparent antiviral effect since the nucleocapsid is always masked within the HBsAg envelope of the virion.<sup>30</sup> In HBeAg negative carriers with precore mutations, there is a less severe liver damage than those with wild type mutations.<sup>31</sup> Furthermore, the data suggests that HBcAg expression is not associated with integrated form of HBV-DNA and HBsAg staining can be seen in integrated as well as episomal forms of HBV-DNA.<sup>29</sup>

### CONCLUSION

Based on above findings, we conclude that HBV-DNA seroconversion is the single most reliable marker for assessing therapy-induced response. HBeAg seroconversion is a good marker for predicting therapy response but is not as reliable as HBV-DNA seroconversion. Presence of IgM anti-HBc after therapy signifies continuing necroinflammatory activity. Pre-treatment high ALT levels along with HBeAg positivity predict a successful therapeutic response. Histological profile shows improvement with therapy, although the overall histological response was not statistically significant in our study.

In IHC, membranous + cytoplasmic pattern of HBsAg and nuclear + cytoplasmic pattern of HBcAg signifies high viral load and marked necroinflammatory activity.

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# Clinico-radiological Risk Factors Associated with Post Stroke Vascular Cognitive Impairment

Dubey T N<sup>1</sup>, Dhiran Arpit<sup>2</sup>, Sejwar Anil<sup>3</sup>

## ABSTRACT

**Introduction:** Cognitive impairment due to cerebrovascular disease is termed “Vascular Cognitive Impairment” (VCI) and forms a spectrum that includes Vascular Dementia and milder forms of cognitive impairment referred to as Vascular Mild Cognitive Impairment. The aim of this study was to determine the clinical, neuro-imaging and laboratory predictors of post stroke cognitive impairment.

**Material and methods:** We prospectively evaluated 100 stroke patients for 3 months after incident stroke for development of VCI. Patients with VCI comprised of those with Vascular mild cognitive impairment (VMCI) and vascular dementia (VaD).

**Results:** Out of 100 patients, 54 patients (54%) had VCI, out of which 36 patients(36 %) had VMCI and 18 patients (18%) had VaD. The risk factors which were significantly associated with VCI was hypertension, diabetes mellitus, prior stroke, dyslipidemia, urinary Incontinence, baseline stroke severity score, high LDL level, strategic site lesion and higher ARWMC score. Post stroke VCI was unrelated to type and location of stroke, there was no difference by sex. The VaD and VMCI group did not differ on any specific cerebrovascular risk factor.

**Conclusion:** Cognitive decline is common after stroke. Post stroke VCI is related to various clinical, radiological and laboratory risk factors. Better knowledge of these risk factors will increase the effectiveness of preventive and therapeutic strategies.

**Keywords:** Vascular cognitive impairment, stroke, risk factors.

determine the clinical, neuro-imaging and laboratory predictors of post stroke cognitive impairment.

## MATERIAL AND METHODS

This study was a prospective observational study conducted in Medicine Department of Gandhi Medical College and Hamidia Hospital Bhopal from November 2014 to October 2015 after taking ethical clearance from ethical committee and informed consent was taken from the patients before participating.

### Inclusion criteria

Patients who were consecutive acute stroke patients either ischemic or hemorrhagic admitted in hamidia hospital.

### Exclusion criteria

- 1) Patients with aphasia
- 2) Patients with reduced level of consciousness
- 3) Patients with stroke associated with tumors, trauma, subarachnoid hemorrhage
- 4) Patients with transient ischemic attack
- 5) Patients with severe hearing and visual impairment
- 6) Previously diagnosed case of Dementia/cognitive impairment Mental Retardation
- 7) Patients with history of psychosis or other psychiatric and neurological disorder
- 8) Brain ischemia due to cardiorespiratory arrest
- 9) History of any neurosurgical operation
- 10) Patients not willing to participate in study.

We prospectively evaluated 100 consecutive stroke patients for 3 months after incident stroke for development of VCI. Patients with VCI comprised of those with Vascular mild cognitive impairment(VMCI) and vascular dementia (VaD).

### Methods

A standard assessment was done at admission and 3 months after stroke; this included clinical, and cognitive assessments, blood investigations, ECG, MRI/CT, 2D ECHO, Carotid Doppler and MMSE (mini mental state examination). Association Internationale pour Recherche et l'Enseignement en Neurologie (NINDS-AIREN) criteria was used for vascular dementia.

**Demographic and clinical characteristics-** Included was age, sex, educational level, socioeconomic status, occupation, family history of dementia, smoking habits, hypertension, diabetes mellitus, hypercholesterolemia, atrial fibrillation [AF], ischemic heart disease [IHD], history of alcohol intake, transient ischemic attacks, prior stroke and any other systemic

<sup>1</sup>Professor and Head of Department, <sup>2</sup>Resident(3rd year), <sup>3</sup>Assistant Professor, Department of Medicine, Gandhi Medical College, Bhopal, India

**Corresponding author:** Dr. Arpit Dhiran, 7/23, Old Subhash Nagar, Bhopal 462023, India

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illness. All patients were subjected to cardiac examination included an electrocardiogram (ECG) and echocardiography of the heart. Clinical features like urinary incontinence, sensory abnormality, gait abnormality, bulbar features, peripheral signs of atherosclerosis and blood pressure was noted. Stroke severity was assessed by the national institute of health stroke scale(NIHSS).

Laboratory measurements included was blood Sugar on admission, renal and liver functions and lipogram (serum total cholesterol [TC], triglycerides [TG], low-density lipoprotein cholesterol [LDL-c], highdensity lipoprotein cholesterol [HDL-c]), complete blood picture.

**Neuroimaging characteristics:** A noncontrast CT brain / MRI was done for all patients. The following radiological data were collected: Presence of hemorrhage, infarct subtypes, number, laterality of lesions and strategic site of the lesion that was defined as the lesions involving areas like hippocampus, thalamus, caudate, globus pallidus, anterior limb of internal capsule. Age related white matter changes (ARWMC) were evaluated in all the patients on CT based upon ARWMC scale.

**Cognitive assessment:** Higher mental functions was clinically evaluated, for which Mini-Mental State Examination (MMSE), a widely used scale for the screening test for dementia is

used. It consists of a variety of questions grouped into seven categories, each representing a different cognitive domain or function (orientation to time, orientation to place, repetition of words, attention, calculation, recall of words, language, visual construction). Memory assessment was done by asking questions (immediate-same as attention, recent-same as recall, remote- previous life events). To determine whether patient had pre-stroke cognitive decline, a reliable proxy accompanying the patient was interviewed, retrospectively, as to whether patient exhibited any signs of cognitive impairment in the form of memory impairment, apraxia, aphasia, agnosias, executive dysfunction before stroke and interference with daily activities because of them. Cognitive assessment was again done at follow up after 3 months to study cognitive impairment.

## STATISTICAL ANALYSIS

All statistical analysis were done using the statistical package for social sciences for windows and Microsoft excel. P value  $\leq 0.05$  was considered to be statistically significant. Categorical data was analysed by chi-square test and student t test was used to compare means of two different groups.

## RESULTS

In this study, the frequency of patient's having post stroke

		Patient group				Significance			
		NOVCI(n=46)		VCI(n=54)					
		Count	Row N %	Count	Row N %				
Sex	Female	15	40.5%	22	59.5%	0.70	0.401		
	Male	31	49.2%	32	50.8%				
Low education	Absent	24	55.8%	17	41.5%	4.397	0.037		
	Present	22	38.6%	37	62.7%				
Socio economic status	Low	26	41.9%	36	58.1%	1.08	0.298		
	Middle	20	52.6%	18	47.4%				
Handedness	Left	1	14.3%	6	85.7%	3.05	0.081		
	Right	45	48.4%	48	51.6%				
Hypertension	Absent	18	64.3%	10	35.7%	5.23	0.022		
	Present	28	38.9%	44	61.1%				
Diabetesmellitus	Absent	30	55.6%	24	44.4%	4.32	0.038		
	Present	16	34.8%	30	65.2%				
Alcohol	Absent	36	43.4%	47	56.6%	1.36	0.244		
	Present	10	58.8%	7	41.2%				
Smoking	No	31	43.7%	40	56.3%	0.54	0.463		
	Yes	15	51.7%	14	48.3%				
Tobaccochewer	No	31	47.7%	34	52.3%	0.21	0.644		
	Yes	15	42.9%	20	57.1%				
Ischemic heart disease	Absent	42	48.3%	45	51.7%	1.40	0.237		
	Present	4	30.8%	9	69.2%				
Dyslipidemia	Absent	31	55.4%	25	44.6%	4.486	0.034		
	Present	15	34.1%	29	65.9%				
Prior stroke	No	38	52.1%	35	47.9	3.99	0.046		
	Yes	8	29.6%	19	70.4%				
Familydementia	No	43	47.3%	48	52.7%	0.64	0.424		
	Yes	3	33.3%	6	66.7%				
Atrial fibrillation	Absent	33	47.8%	36	52.2%	0.30	0.585		
	Present	13	41.9%	18	58.1%				
Urinary incontinence	Absent	43	51.8%	40	48.2%	6.63	0.01		
	Present	3	17.6%	14	82.4%				
Sensory abnormality	Absent	36	43.9%	46	56.1%	0.81	0.369		
	Present	10	55.6%	8	44.4%				

Table-1: Comparison of risk factor profile in VCI and NO-VCI group

vascular cognitive impairment (VCI) is 54% (54/100), 18% (18/100) of the patients had VaD (vascular dementia), 36% (36/100) of the patients had VMCI (vascular mild cognitive impairment), 46 % (46/100) of the patients had NO VCI (no vascular cognitive impairment) (Table-1).

In our study, out of 100 patient there are 63 males and 37 females, although the VCI (Vascular cognitive impairment) occurred more frequently in females, the difference was not statistically significant. In our study mean age of patients having no vascular cognitive impairment is  $62 \pm 5$  years, mean age of patients having mild vascular cognitive impairment is  $63 \pm 6$  years, mean age of patients having vascular dementia (VaD) is  $65 \pm 6$  years.

The percentage of the patient's having low socioeconomic status is more in patient's having vascular cognitive impairment (VCI) as compared to those who don't have any cognitive impairment but the difference is not statistically significant ( $p=0.298$ ). In

our study, patients with vascular cognitive impairment (VCI) had significantly lower educational status ( $p=0.036$ ), in terms of years of formal education, as compared to those who did not develop vascular cognitive impairment (VCI).

Amongst the various risk factors hypertension, diabetes mellitus, prior stroke, dyslipidemia, ischemic heart disease, tobacco chewing, smoking and family history of dementia were more frequently seen in VCI (vascular cognitive impairment) group than NO-VCI group. However only Hypertension ( $p=0.022$ ), diabetes mellitus ( $p=0.038$ ), dyslipidemia ( $p=0.034$ ), prior stroke ( $p=0.046$ ) were significantly associated with development of Vascular cognitive impairment.

In this study, after statistical analysis the clinical parameters which were significantly associated with development of vascular cognitive impairment are urinary incontinence ( $p=0.01$ ), systolic blood pressure ( $p=0.049$ ), and baseline stroke severity score ( $p=<0.001$ ). Though the clinical parameters like gait

		Patient group				Significance			
		NOVCI (N=46)		VCI					
		Count	Row N %	Count	Row N %				
Gait abnormality	Absent	39	45.9%	46	54.1%	0.003	0.955		
	Present	7	46.7%	8	53.3%				
Bulbar features	Absent	40	44.4%	50	55.6%	0.88	0.349		
	Present	6	60.0%	4	40.0%				
Peripheral signs atherosclerosis	Absent	36	50.7%	35	49.3%	2.18	0.14		
	Present	10	34.5%	19	65.5%				
ECG	Normal	31	55.4%	25	44.6%	4.486	0.034		
	Abnormal	15	34.1%	29	65.9%				
Echo2d	Normal	22	50.0%	22	50.0%	0.51	0.477		
	Abnormal	24	42.9%	32	57.1%				
Typestroke	Ischemic	44	47.8%	48	52.2%	1.54	0.214		
	Hemorrhagic	2	25.0%	6	75.0%				
Hemisphere involved	Non-dominant	17	51.5%	16	48.5%	1.33	0.515		
	Dominant	22	40.7%	32	59.3%				
	Both	7	53.8%	6	46.2%				
Type of lesion	Single	28	53.8%	24	46.2%	2.68	0.101		
	Multiple	18	37.5%	30	62.5%				
Strategic site lesion	Absent	39	56.5%	30	43.5%	9.92	0.002		
	Present	7	22.6%	24	77.4%				
Age	Upto 60 yrs	23	51.1%	22	48.9%	2.52	0.283		
	61-70 Yrs	21	45.7%	25	54.3%				
	71-80 Yrs	2	22.2%	7	77.8%				

Table-2: Comparison of mean of various risk factors in two groups.

	Patient group				Significance			
	NOVCI		VCI					
	Mean	Standard Deviation	Mean	Standard Deviation				
Age	62	5	64	6	1.96	0.052		
Systolic BP	148	28	158	29	1.96	0.049		
Diastolic BP	83	9	88	16	1.58	0.117		
Total cholestrol	135	32	142	50	0.80	0.425		
LDL	156	45	173	52	1.98	0.041		
HDL	44	3	43	3	1.29	0.20		
Triglyceride	179	77	157	49	1.71	0.091		
Blood sugar admission	141	45	151	48	1.05	0.297		
NIHSS	5	2	7	3	3.55	0.0006		
	No VCI		VCI		P Value			
Median arwmc score (range)	1.5 (0-12)		4.5(0- 15)		0.001			

Table-3: Comparison of mean of various risk factors in two groups.

abnormality, peripheral signs of atherosclerosis and atrial fibrillation are more frequently found in VCI group but the difference was not statistically significant.

The laboratory parameters which were significantly associated with VCI group included high LDL level ( $p = 0.041$ ), and abnormal ECG ( $p = 0.034$ ). The parameters like high blood sugar on admission, high triglyceride level, high cholesterol level were frequently found in VCI group but are not statistically significant (Table-2,3).

## DISCUSSION

Vascular Cognitive impairment is commonly seen condition after stroke. Many researches had done on cognitive impairment after stroke, mostly in western countries with relatively scarce data from developing countries. In this study, the frequency of VaD was 18% whereas that of VMCI was 36%. Previous studies revealed similar rates of post stroke dementia, Khedr et al.<sup>11</sup> reporting a rate of 21%. Sachdev et al<sup>12</sup> reporting a rate of 21.3%, Pohjasvaara et al.<sup>13</sup> (31.8%) and Barba et al.<sup>14</sup> (30%). The variations in rates of PSD in might be the result of different criteria which are used for diagnosing VaD. In the present series, patients who developed VCI had lower educational status as compared to patients who did not develop VCI. This may be due to the fact that those with higher level of education have more cognitive reserve. Many other studies have reported similar observations. Patients in VCI group were older than those in No-VCI group, although this difference was not significant. Many previous studies revealed that vascular cognitive impairment commonly develops in patients with higher age. In our study, patients who developed VCI were more likely to have diabetes mellitus, hypertension, prior stroke, urinary incontinence, abnormal ecg, and high systolic blood pressure, LDL levels and more NIHSS score on admission. Pohjasvaara et al.<sup>13</sup> found that total cholesterol, dysphasia, gait impairment, urinary incontinence were significantly associated with post stroke dementia. Khedr et al.<sup>11</sup> found that hypertension, ischemic heart disease, and family history of dementia were significantly associated with post stroke dementia. Hebert et al.<sup>15</sup> found that diabetes, hypertension, apolipoprotein E were found to be associated with vascular dementia. They also found that patients with VaD more frequently had higher LDL and lower HDL levels. Amongst the neuroimaging features, presence of strategic site lesion and higher ARWMC scores were significantly associated with development of VCI, but there was no correlation with type of stroke (ischemic) and laterality of stroke with VCI. Sachdev et al.<sup>12</sup> found no significant association between laterality of stroke and VCI. However, they reported that patients with post stroke cognitive impairment had significantly higher load of total as well as periventricular white matter hyperintensities (WMH). Many other studies supported that dementia occurred more frequently in strokes involving dominant hemisphere. On statistical analysis, the parameters which were significantly associated with VCI are low level of education ( $\leq 10$  years of formal education), hypertension, diabetes mellitus, dyslipidemia, prior stroke, urinary incontinence, abnormal ecg, higher LDL level, higher systolic blood pressure, strategic site lesion, higher ARWMC score and baseline stroke severity (NIHSS) score. The difference between two groups (VMCI and VaD) in various parameters was not statistically significant. This

study had several limitations. First, we excluded a fair number of patients for various reasons which may led to underestimation of the prevalence of post stroke cognitive impairment. Secondly, follow-up duration in this study was limited to 3 months.

## CONCLUSION

Post-stroke cognitive impairment is commonly seen and is associated with considerable morbidity. Both ischemic and hemorrhagic strokes may result in cognitive impairment. The risk factors for development of Vascular cognitive impairment following stroke in this study are lower educational status, Hypertension, Diabetes Mellitus, Dyslipidemia, Prior stroke, Urinary incontinence, High systolic blood pressure, NIHSS score, LDL level, abnormal ECG, strategic site lesion and greater severity of age related white matter changes.

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# Maxillofacial Imaging in Forensic Science: A Newer Approach

Moazzam Jawaid<sup>1</sup>, Ali Amir<sup>2</sup>, Kamil Shahnawaz<sup>3</sup>, Yumna Qamar<sup>4</sup>, Piyush Upadhyay<sup>3</sup>, Jyotsana Singh<sup>2</sup>

## ABSTRACT

Forensic science has emerged as quite interesting as well significant speciality gainig a lot of interest and importance from world of law professionals. One of the reason for its rise as a speciality is the introduction of maxillofacial imaging. The maxillofacial radiographic techniques has been found out to be quite important in human identification. Forensic maxillofacial radiology includes the conduction, interpretation, and reporting of radiological examinations and procedures connected to the courts and the law. The inclusion of the maxillofacial radiologist provides invaluable information in forensic consultations and medico legal investigations. This paper has been formulated to evaluate the role of dentomaxillofacial radiography in forensic science where radiographic methods may be used to determine identity using the teeth, root structures andfrontal sinuses. Recent imaging techniques, such as computed tomography and magnetic resonance imaging are being incorporated in this speciality.

**Keywords:** Forensic science, maxillofacial radiology, forensic odontology.

## INTRODUCTION

Forensic science is a branch of scientific that include method of collection and examination of evidence in a judicial setting and is accepted by the court and the general scientific community. It is a branch of science that involves the application of dental sciences in the identification of dead individuals by comparing ante- and postmortem records.<sup>1</sup>

From 66 AD till date, identification on the basis of teeth has significantly contributed tin identification of dead individuals, the first case being accepted by the law in the year 1849.<sup>2</sup> In children, analysis of the number of teeth that has erupted play a role in the estimation of age at death, as well as, to the identification procedure of unknown skeletons. The attempt is made to compare the properties and characteristics of unknown skeletons with the person whose identity is being analyzed. So,in this manner the disappeared child can be identified. However, it also contribute in the age evaluation of living children with unknown identity, suspected of crime or violence with aggravating circumstances, by the police.<sup>3</sup>

In the 21<sup>st</sup> century despite massive advancement in science and technology, human race is still facing problems due to natural disasters (earthquakes, tsunamis), medical breakthroughs, crime, and violence accounting for the loss of numerous lives. The significance of personal identification of dead people in such situation become quite important is for personal, social, and legal purposes. Forensic science deals with the identification of the dead using numerous techniques. Forensic odontology has proved to be quite significant in human identification. Methods like rugoscopy, bite marks, palatal rugae, photographs, lip prints, etc. are used for identifying the individuals.<sup>4</sup>

Generally these methods depend solely on the examination of the soft tissues,so it become very necessary to preserve them.

This become a problem when thee body parts get burnt, lacerated and traumatized. In the human body, teeth and facial bones are hard structures and are unaffected by the decompositional/destructional forces well even under extreme forces and/ or temperature variations. The specific anatomical features of the teeth are captured easily on the radiographs so they become an invaluable tool in forensic sciences. Radiographic identification has long been in use and the technique is efficient, comparatively easy, records can be obtained in both living and dead.<sup>5</sup> It has an added advantage that it is less expensive as compared with the DNA analysis. They can play an important role in solving the medicolegal cases with the help of sound knowledge of all these special imaging techniques which will enhance the scope of maxillofacial imaging in personal identification.<sup>6</sup>

## HISTORY

The case of dental identification was first reported in an 80-yearold John Talbot in 1453. Dr. Paul Revere is being credited as the first expert of forensic odontology. He was able to identify the body of Dr. Joseph Warren with the help of silver and ivory bridges. The earliest use of forensic odontology was used in U.S. Court. In a very interesting incident a person crime was confirmed by crushed fragments of mineral teeth fused to gold. Criminal was then hanged. L'Art Dentaire en Medicine Legale was the first dissertation on forensic odontology written by Dr. Oscar Amoedo in 1898. Since then several studies has been performed in this regard. Chantilly. Welty and Glasgow in 1946 in order to further enhance the forensic odontology introduced the use of computers and they created a computer system in which the information about the teeth of 500 people were stored in 1 minute.<sup>7,8</sup> Kieser-Nielsen assessed the uniqueness of teeth mathematically. Sogannaes et al. (1982) compared the bitemarks of twins by using computer application and found out the bitemarks were different and unique . Sweet and Pretty conducted a study to conclude that the size, shape and pattern of the incisal or biting edges of upper and lower anterior teeth are specific to an individual. Analysis of bite mark evidence through video analysis was utilized in a California court. David et al. are being credited to involve scanning electron microscopy in bite mark analysis.<sup>9</sup> In todays era of modern technology newer

<sup>1</sup>Post Graduate Student, Department of Oral Medicine and Radiology,

<sup>2</sup>Post Graduate Student, Department of Public Health Dentistry, <sup>3</sup>Post Graduate Student, Department of Conservative and Endodontics, Institute of Dental Sciences, Bareilly, <sup>4</sup>Post Graduate Student, Department of Orthodontics, Z.A.D.C. AMU, Aligarh, India

**Corresponding author:** Moazzam Jawaid, Room No. 125, New Resident Hostel, Institute Of Dental Sciences, Bareilly, Uttar Pradesh, 243001, India

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methods has been designed.

## DENTAL IDENTIFICATION PROCEDURES

The premortem and post-mortem properties of a person in the teeth are unique. They can be analyzed for the purpose of forensic identification. Dental experts can examine the teeth and maxillofacial bones for the purpose of identification in trauma patients. The helpful evidence may be tooth chips, broken teeth, recent tooth loss indicating antemortem trauma to the mouth. These injuries can be attributed either as a result of non accidental or accidental trauma. By analyzing the regressive changes of teeth like attrition and other structural changes the arthropological age of the deceased person can be identified. Tooth has been used as quite reliable evidence in personal identification of living or dead persons using the specific features of the jaws and the teeth. Several researchers have advocated the uniqueness of tooth. Many scientists believe that tooth impression is more usable evidence than the bite marks, which are believed to be more specific than DNA. The genetic make-up may be same in both the twins but the dental impression may be different.<sup>10</sup>

## FRONTAL SINUS RADIOGRAPHIC ANALYSIS

### Sex Determination And Personal Identification

There are usually two frontal sinuses, located in the posterior part of the superciliary arcs. They are found to appear between the external and internal faces of the frontal bone. The anatomical features of frontal sinus include presence of septum which have the tendency to deviate from the midline. The significance of frontal sinus in forensic sex determination lies in their unique pattern. The research people strongly believe that two frontal sinus can never be same. It has been found that they are as much unique in a person as fingerprints. Even twins are considered to have different frontal sinuses.<sup>11,12</sup> Frontal sinus radiographs may be used because it is commonly exposed in sinus series investigations. It has been suggested that the frontal sinuses have the potential to be used in correctly identifying sex.

Radiographs of individuals taken by Caldwell technique with frontonasal support are evaluated. CBCT can also be used to obtain the images. It has been mentioned in several studies that frontal sinus have different patterns among males and the females. Schuller in 1943 conducted several radiological studies on morphological variations of the frontal sinus and found that

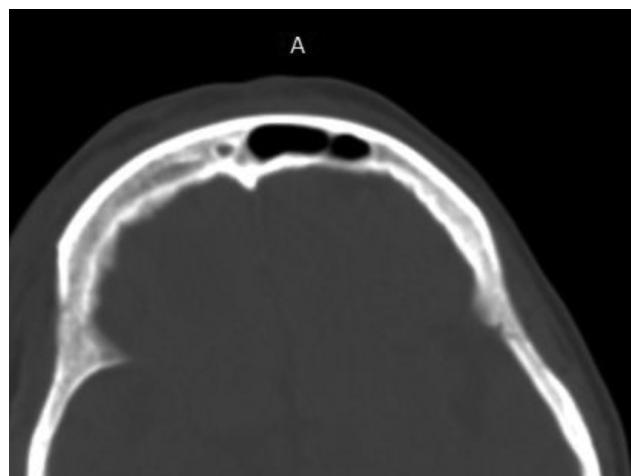


Figure-1: Frontal Sinus as observed in Axial section CBCT

the size of frontal sinus is greater in the males as compares with the females.<sup>13</sup> Ponde et al., had also given the same conclusion from his own radiological studies.<sup>14</sup> Another study showed the same result i.e the mean area of frontal sinus in males are found out to be greater than the females. Brown carried out a study and found that the sagittal diameter is more in males than in females. Similar finding was observed by Camarago et al.<sup>15</sup> However in another study it was observed that the right and the left sagittal diameters of frontal sinuses in males were greater than those for females but the differences were not statistically significant. The difference in the morphogenetic features of cranium in the males and females are quite evident. The main reason for this difference is the genetic make up irrespective of other factors like difference in nutritional status, hormonal changes and the muscular changes.<sup>16</sup> Such attributes can explain why the frontal sinus of male is larger than that of female.

## PANORAMIC RADIOGRAPHS IN AGE AND GENDER IDENTIFICATION

### Gonial Angle, Ramus Height And Bicondylar Width

A significant number of studies has been performed on panoramic radiographs to measure three mandibular parameters, gonial angle, ramus height and bicondylar width.<sup>17-19</sup> Some studies have shown widening of gonial angle with advancement of age.<sup>20</sup> Among the several studies conducted for measurements of landmarks on panoramic radiographs the most accurate and reliable measurable value was found out to be that of gonial angle.<sup>21</sup> Females were found to have a significant higher value of gonial angle than their male counterpart; which was similar to the results obtained by Ghosh et al.<sup>22</sup>

This study was carried out with the endeavour to establish the fact that measurable mandibular parameters in orthopantomograms such as gonial angle, bicondylar width and ramus height, can be used to establish a correlation with an individual's age and gender in dentulous subjects in Far North Queensland. The study design included the involved the use of 2699 randomly selected panoramic radiographs of subjects belonging to the ages of 19-69 years. The analysis of each panoramic radiograph was done with the purpose of measuring and recording the above three parameters. The findings were tabulated into appropriate age and gender groups and subjected to statistical analysis.

Females, on the other hand, were shown to have a significantly larger gonial angle than males. From previous studies it can be generalized that gonial angle increases with age, whilst bicondylar width and ramus height were shown to decrease with age. It was concluded that the assessment of mandibular morphology through radiographic measurements may be useful in estimating an individual's age and gender when comparing to a known population standard.<sup>23</sup>



Figure-2: Orthopantogram showing Gonial angle and ramus height

### Demirjian's Method

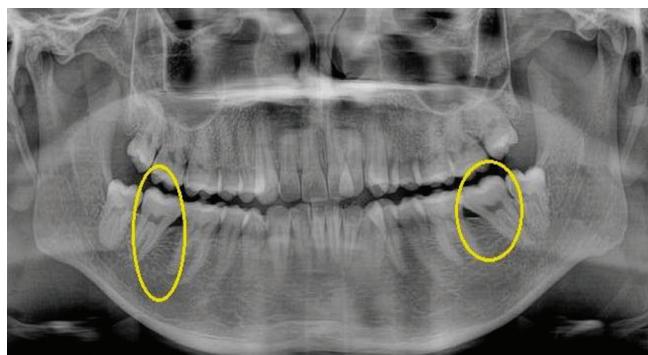
Among the various commonly used methods for age estimations on panoramic radiographs, the one that has been extensively used is Demirjian's method which is simple and practical. The advantage lies in the explanation of the stages of tooth development thereby the differences in age estimation by the different observers as by the same observer is very less.<sup>24</sup> Furthermore, it is non-invasive and can be done in-vivo. As the third molar is associated with a high incidence of congenital absence, so the modifications of Demirjian's method as suggested by Orhan et al., has been described.<sup>25</sup>

Olze et al. in their study on mineralization of wisdom teeth in Caucasian, Mongoloid and African population samples found significant differences in the reaching of a particular stage of mineralization amongst different populations, which indicate the need for population-specific investigations.<sup>26</sup>

Acharya A.B has been credited to utilize Demirjian's criteria to assess the third molar development by analysing the OPGs of 221 Indian subjects belonging to the age group of 15-21 years. He came to the conclusion that a significant one fourth population of India has been wrongly analyzed for age estimation and have been placed in wrong age groups.<sup>27,28</sup>

### Mandibular Second Molar Calcification Stages

There are two most common methods for assessment of the dental development. First one is the analysis of tooth eruption while the second one is the analysis of analysis of tooth calcification.<sup>29</sup> Since it is generally advised for orthopantomogram for patient undergoing orthodontic treatment, hence skeletal development assessment using the different calcification stages of mandibular molars will provide an added advantage over the hand wrist radiographs. If the routine radiographs will be used then there will be no added radiation exposure to the subjects. The study was conducted to investigate (1) the relationships between the stages of mandibular second molar calcification and skeletal maturity; and (2) whether second molar calcification stages can be used as a reliable diagnostic tool to determine skeletal maturity. The study design included panoramic radiographs and lateral cephalograms of 300 subjects (137 males and 163 females) belonging to age groups from 9 to 18 years. The dental maturity was evaluated using the Demirjian Index, while the skeletal maturity was evaluated using the Cervical Maturity Index (CVMI). It can be concluded that a highly significant association exists between DI and CVMI. Mandibular second molar DI stages are reliable indicators of skeletal maturity.<sup>30</sup>



**Figure-3:** Mandibular Second Molar calcification stages on Orthopantomogram

### LATERAL CEPHALOGRAMS

#### Stature Estimation For Personal Identification

Stature is unique for a person. It can be applied for personal identification when there is no complete skeleton present for analysis. In that case the stature of the remains of skeleton which is available can be used for the personal identification. It is also important to establish a method to evaluate the stature based on dead body remains obtained. It can be based on the information regarding the specificity of the population to which the dead body remains belong. For this purpose, measurements of 4 distances between cephalometric landmarks of the mandible namely Co-Co (bicondylar distance); Go-Go (bigonial distance); Co-Go (condylion-gonion distance); Go-Gn (gonion-gnathion distance) and the stature in 56 subject including both the males and females subject from Caucasian Italian population on the lateral cephalograms. It was found that the parameters were significantly correlated. This can conclude that by such measurements the stature of the mandible of a population can be found out and helpful in forensic sciences.

#### MRI

Arthur Conan Doyle's fictional detective Sherlock Holmes had great interest in the fact whether the injuries were pre-mortem or the post-mortem. It is of quite important value in real forensic investigations. It is very necessary to differentiate whether the fracture is pre mortem or antimortem because it gives information regarding the sequence of events leading to the death of the patient. Then it provides information about the cause of fracture. Over the last decade, cross-sectional imaging techniques such as CT and MRI have been introduced in the practice of forensic medicine and the field of forensic radiology has evolved significantly. The main advantages of CT and MRI over ongoing procedure autopsy are the simplified and accurate maintenance of findings related to forensic. Besides these are non-invasive approach.

Another advantage of advanced forensic imaging is that they provide additional information about vital reactions. The previous literature revealed a case of an accident involving the flying activity that proved fatal. The victim got electrocuted followed by severe burning and falling from a great height. On the basis of clinical imaging findings of bone marrow oedema in acute fractures, it was concluded how the death took place that is the speed flyer death took place due to electrocution, not due to the fall and that the fractures were post-mortem in nature. In this way the sequence of events that lead to the death of the person was finalized. Here it was easy to conclude that death took place due to high power electric wire. More research is needed to find out whether oedema in bone marrow in acute fractures is a reliable significant sign.

### DIGITAL RADIOGRAPHY IN PERSONAL IDENTIFICATION

There are various methods of digital radiography present about which literature is present. The basic mechanism of image acquisition by digital radiography involve the following steps: 1) radiographic images digitization with the aid of a scanner, video camera or, yet with images acquisition directly from a x-ray machine 2) the next step involve image processing by mean of software, this feature involve comparison of images

by means of interposition or subtraction.<sup>26,27</sup> These modern techniques allow an accurate analysis of the spatial relations of teeth roots and supporting structures on ante- and post-mortem images.<sup>28</sup> Hence, without having extra exposures there can be proper comparision made between the pre-mortem and the ante-mortem images by using the digital radiography.<sup>29</sup> It has been observed that there is some wrong information provided by this technique. The main reason maybe the difference in geometry of the pre-mortem and post-mortem radiographs. The above mentioned correction is essential to remove the discrepancy in the process of image subtraction.<sup>30</sup>

## COMPUTED TOMOGRAPHY IN FORENSIC IDENTIFICATION

Three-dimensional computed tomography (CT) is a useful imaging method in the process of human identification, and presents innumerable advantages in this field as compared with the traditional radiographic projection. Firstly, there is negligible superimposition, elongation and shortening of images as compared with other modalities and there is feature of measurement of very small changes in the density.<sup>30,31</sup> CT has several advantages, such as images segmentation – an important source of information in cases which involves the evaluation of internal points. Another advantage is easy images manipulation, improved imaging quality with excellent color scale and transparency as well as information regarding measurement of volume and area as well as both angular and linear measurements. With the help of antemortem CT image the post mortem image can be created using the added advantage considering that craniometric points can be precisely located and measurements can be accurately performed. Besides, the film provide information regarding with the positioning of the patient, angulation, slice thickness, kV, exposure time, size of the visual field, etc. There are other details about the patient such as name, age and sex of the patient on the film. The CT film has also information like that name of the assisting physician, hospital, and other relevant information.

## CBCT IN AGE ESTIMATION

There are number of methods for age estimation using the teeth. The most accurate method is analysis of dentin apposition. This apposition is a continuous, age-associated process, which alters the size of the pulp chamber. It can be affected by the pathological conditions like caries. There has been use of several methods in order to assess the volume of pulp chamber giving information about the secondary dentin apposition. These methods include cross sections of the teeth as well as taking radiographs. Both panoramic and periapical radiographs have been used to assess the pulp/tooth area ratio of maxillary canines. The major disadvantage of radiographs is that they are two-dimensional projections and do not give information regarding volume which is three dimensional entity. Therefore, the buccolingual analysis should be carried along with the mesiodistal measurements. Cone beam Computed tomography (CBCT) is one of the most reliable method for this purpose.

## CBCT IN FACIAL RECONSTRUCTION

The soft tissue details can be obtained from the skeletal remains of the dead body. This method of regenerating the face of the dead person from the skeletal remains is known as the

facial reconstruction. The concept of the facial reconstruction belong to the branch of anthropology. Moreover this concept is quite useful in forensic identification. The concept of facial reconstruction is as old as ancient history in Europe where the clay artists used to reconstruct the face of the dead person by putting clay according to the facial contours on the skeleton. In order to achieve accurate details several methods have been introduced to digitize the method of facial reconstruction. CBCT is one of the most reliable method in this regard. The initial technology which was used to digitize the details of the skull was Laser technology. The details provided by the CBCT images of the skull of the dead person are very fine details in all three planes. With the help of such fine details and computer software premortem face of the person can be recreated. Cone-beam computed tomography commonly used in dentistry that can produce higher resolution in digitization of the skull while producing lower levels of radiation. Several studies are being carried out to further increase the utilization of CBCT in this field.

## CONCLUSION

Over the last decade, the importance and valaability of forensic science has taken a giant leap. This can be attributed to the introduction of maxillofacial imaging in forensics. The newer modality of CT and MRI introduction and their effective utilization in these condition. MR is the favored imaging modality for non-forensic post-mortem imaging and is mainly used to analyze non-traumatic findings. The primary focus in forensic imaging is on traumatic findings, with extra importance on the analysis regarding gunshot injuries. There are very few studies oriented towards imaging findings of drug abuse and intoxication, despite of their considerable contribution to the case load of forensic investigations. The recent research indicates that radiology is becoming an invaluable tool in post-mortem investigations, whether they are performed in the course of forensic investigation, or during hospital-based morbidity / mortality review. Research efforts in this field are conducted worldwide and forensic radiology may indeed emerge as a distinct subspecialty of forensic medicine and radiology.

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# Profile of Primary Angle Closure Glaucoma in Patients having Diabetes at Tertiary Hospital of Kumaon Region, Uttarakhand

Shanti Pandey<sup>1</sup>, Vivekanand Satyawali<sup>2</sup>, Kalpana<sup>3</sup>, Pankaj Kumar<sup>4</sup>

## ABSTRACT

**Introduction:** Glaucoma is important cause of blindness world wide. Primary angle closure glaucoma is more prevalent in south east asian countries, because of anatomical reason in asian peoples. This study was carried out to study the profile of primary angle glaucoma and to study the profile of subtypes of Primary Angle Closure Glaucoma in patients having diabetes at Tertiary hospital of Kumaon.

**Material and methods:** This study was conducted in out patient department (OPD) of ophthalmology at Sushila Tiwari hospital, Haldwani from November 2012 to November 2014. Total 225 patients were included in this study on the basis of inclusion and exclusion criteria. A complete ophthalmological and systemic examination was done-

**Results:** In present study primary angle closure glaucoma was the commonest type of glaucoma 95 (42.2%), followed by primary open angle glaucoma 72 (32%). Most the patients in primary angle closure glaucoma(PACG) were females(59.4%) in this study. Majority(41.6) were in older age group of 56-65 years. This study also shows that PACG subgroup was most common(68.8%) among all three categories, followed by PAC(17.9%) and PACS were diagnosed in 10.5% cases. Ocular pain was the commonest presenting symptom of PACG subgroup(47.1%), with highest mean IOP recorded in PACG group (23.04).

**Conclusion:** PACG was the most common angle closure subtype followed by PAC and PACS in Kumaon region. Increasing age and females were more associated with primary angle closure glaucoma. In our study female gender, diminution of vision, presence of ocular pain, were diagnosed in PACG stage of primary angle closure glaucoma.

**Keywords:** Primary angle closure glaucoma, primary angle closure, primary angle closure suspect, kumaon, gonioscopy.

## INTRODUCTION

Glaucoma is the second most common cause of preventable blindness in the world. Approximately 60.5 million people throughout the world affected by open angle glaucoma and angle closure glaucoma, and this number will be increasing to 79.6 million by the year 2020.<sup>1</sup> Unfortunately large number of people remain undiagnosed, because of nonspecific symptomatology of this disease, various population based studies have also endorsed this fact. Primary angle closure glaucoma (PACG) has been reported to be more prevalent in South East Asian countries than the rest of the world.<sup>2</sup> In a study in a North Indian hospital<sup>3</sup> PAC and glaucoma constituted 45.9% of all primary adult glaucoma seen. This is attributed to the fact that Asians usually have smaller eyes, associated with shorter axial length as compared to others. And also in hilly areas as in Kumaon region of Uttarakhand, peoples still have eye structure more prone for angle closure.

Various studies have been done in different regions of India to study the profile of primary angle closure glaucoma but

yet no such study has been performed in Kumaon region of Uttarakhand.

This is a cross sectional study to analyze the demographic and clinical profile of primary angle closure glaucoma in a tertiary hospital of Kumaon region.

## MATERIAL AND METHODS

This study was conducted in Out Patient Department (OPD) of Ophthalmology, Dr. Susheela Tiwari Government Hospital, attached to the Government Medical College, Haldwani, District Nainital, Uttarakhand. The period of study was 1.5 years i.e. from November 2014 to April 2016. All the 95 Patients who visited the OPD and were diagnosed as primary angle closure glaucoma and were classified in their subtypes, based on their presenting complaints, best Corrected Visual Acuity (BCVA) using Snellen's chart, Intra ocular pressure (IOP-by Goldmann applanation tonometer), gonioscopy (using single mirror goniolens), optic nerve head evaluation with 90 D biomicroscopic lens and Humphrey threshold 24-2 visual field analysis using Swedish interactive threshold algorithm (SITA) strategy were included in the study.

Patients with primary open angle glaucoma, Congenital glaucoma, Juvenile glaucoma, Secondary glaucoma and those who were < 35 years of age were excluded from the study.

Those who were found to have angle closure were further classified using International Society of Geographical and Epidemiological Ophthalmology (ISGEO) Classification.<sup>2</sup>

ISGEO classification:

### Primary Angle Closure Suspect (PACS)

Posterior irido trabecular contact (ITC)  $\geq 270^\circ$   
Normal IOP, optic disc and visual field

### Primary Angle Closure (PAC)

Posterior irido trabecular contact (ITC)  $\geq 270^\circ$   
Raised IOP and/or Peripheral Anterior synechiae  
Normal optic disc  
No field defects

### Primary Angle Closure Glaucoma (PACG)

PAC with optic disc changes/ Visual field defects

<sup>1</sup>Associate Professor, <sup>4</sup>Post Graduate, Department of Ophthalmology,

<sup>2</sup>Associate Professor, Department of Medicine, Government Medical College Haldwani, <sup>3</sup>Consultant, Department of Ophthalmology, Charitable Organisation, Haridwar, India

**Corresponding author:** Dr Shanti Pandey, Type-4, k-2, Medical College Campus, Haldwani, Nainital Uttarakhand, India

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Systemic examination was done by physician (cardiovascular examination, blood pressure, and relevant investigation regarding blood sugar fasting and postprandial and HbA<sub>1</sub>C). For this diabetic and hypertensive patients were followed up in diabetic clinic at our hospital. All patients were examined for diabetes.

## STATISTICAL ANALYSIS

The data collected was coded and entered into Microsoft Excel. Analysis was done using SPSS version 16 and descriptive interpretation of data was done in the form of percentages.

## RESULTS

Overall 225 glaucoma patients were selected on the basis of inclusion criteria from outpatient department.

PACG was the commonest type of glaucoma accounting for 42.2% of cases, followed by primary open angle glaucoma (32%). Primary angle closure subtypes PACG was the most common subtype, observed in (71.6%) patients followed by PAC (17.9%) while PACS were observed in (10.5%) patients (Table-1).

Patients of glaucoma progressively increased as the age advanced, and was highest (42.10%) in the age group of 56-65 years but beyond 65 years of age group number of glaucoma

patients were only 17.89%. In our study 59% patients were female and 41% were males (Table-2)

Most of the patients(54.73%) were having visual acuity in the range of 6/6-6/18, and only 4.21% patients were presented with no light perception. Patients in PACS and PAC subtypes the diminution of vision was less when compared with PACG subtype, where it was severely diminished (Table-3).

Ocular pain was the commonest presenting symptom of PACG group(47.1%), while 23.5% of patients of PAC group also complained of ocular pain. The second commonest symptoms in PACG group was decreased vision (41.1%).

The 90% patients in PACS and 52.9% patients in PAC group were not having any symptoms of glaucoma. In present study highest mean IOP was recorded in PACG group (23.04), and lowest in PACS (16.72) (Table-4).

## DISCUSSION

Worldwide open angle glaucoma is more common but among Asians prevalence of angle closure glaucoma is more.<sup>1,3</sup> Possible explanation of increased prevalence of angle closure glaucoma is because of inherent structural factors in Asian eyes like small hyperopic eyes<sup>4,5</sup> and short axial length.<sup>6</sup>

In this study PACG was the most common angle closure subtype; observed in (68.8%) patients followed by PAC

	Types of Glaucoma				Subtypes of primary angle closure glaucoma		
	POAG	NTG	GS	PACG	PACS	PAC	PACG
No. of Patients (%)	72(32%)	22(9.7%)	36(16%)	95(42.2%)	10 (10.5%)	17 (17.9%)	68 (71.6%)

Table-1: Showing types of Glaucoma and subtypes of Primary angle closure glaucoma

Age group	N. of patients(%)
35-45	14(14.73)
46-55	24(25.26)
56-65	40(42.10)
>65	17(17.89)
Total	95(100)

Table-2: Age wise distribution of patients with primary angle closure

Visual acuity (BCVA)	Subtypes of angle closure glaucoma			
	PACS (n.)	PAC(n.)	PACG (n.)	Total n.(%)
6/6-6/18	9	10	33	52(54.73)
<6/18-6/60	1	7	26	34(35.78)
<6/60-3/60	0	0	3	3(3.15)
<3/60-Perception of light	0	0	2	2(2.10)
No light Perception	0	0	4	4(4.21)
Total	10	17	68	95(100)

Table-3: Visual acuity at presentation among the patients with primary angle closure

Symptoms	Subtypes of angle closure glaucoma			
	PACS(%) (n-10)	PAC(%) (n-17)	PACG(%) n-68	Total(%) n-95
Asymptomatic	9(90)	9(52.9)	0	18(18.94)
Decreased vision	1(10)	3(17.6)	28(41.1)	32(33.68)
Heaviness	0	1(5.9)	4(5.9)	5(5.26)
Headache	0	1(5.9)	15(22.1)	16(16.84)
Colored haloes	0	0	5(7.4)	5(5.26)
Ocular pain	0	4(23.5)	32(47.1)	36(37.89)
Mean IOP(mmHg)	16.72	18.32	23.04	

Table-4: Showing symptoms and mean IOP in primary angle closure subtypes

(19.4%) and PACS (11.6%) patients. In similar study by Paul *et al* from Kolkata India, PACG was most common entity.<sup>7</sup> Similar finding was observed by Ichhpujani P *et al*<sup>8</sup> in a hospital based study in North India. Prevalence of glaucoma was found to be increasing with increase in age and similar observations were seen in various other studies.<sup>9-11</sup> In this study most of the patients were in the age group of 56-65% years, followed by in the age group of 46-55 years. In various other studies<sup>9-11</sup> the mean age of patients with glaucoma was comparable to this study. In our study PACG was more common in females (59%) than in males. Das J *et al*<sup>3</sup> studied that female preponderance was seen for acute or intermittent ACG glaucoma. Similar remark was made by Ramakrishnan R *et al*<sup>12</sup> Arvind Comprehensive Eye Survey in Southern India. Chennai Glaucoma Study (CGS) also reported that PAC and PACG was more common in women.<sup>13</sup> In our study most common presenting symptom in PACG group was ocular pain followed by decreased vision. In contrast to this Sihota *et al*.<sup>14</sup> also documented ocular pain to be most common in the acute and subacute angle closure glaucoma, 62.1% and 45.5% respectively.

Patients in PACS and PAC subtypes the diminution of vision was less when compared with PACG subtype, where it was severely diminished. As the PACS, PAC and PACG are the spectrum of the same disease, so as the disease advances it is expected that visual acuity will also worsen and it is also obvious from our study that number of patients having poor visual acuity are in the group of advance stage of disease that is in PACG subtype. Mean IOP was greater in PACG group as compared with PACS and PAC, this is due the fact that with advancing course of disease mean IOP used to increase. It correlated with study done by Paul *et al*<sup>15</sup> who also documents that mean IOP increases with stage of disease.

## CONCLUSION

In Kumaon region it was observed that primary angle closure glaucoma was commonest among primary glaucoma cases. PACG was the most common angle closure subtype followed by PAC and PACS. Increasing age and females are significantly associated with primary angle closure glaucoma. On the basis of study it seems unlikely that screening for diabetes among patients with closed angle glaucoma will uncover many undiagnosed diabetics.

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# Role of Platelet Rich Plasma Therapy in Alopecia Areata- A Prospective Study

Asim Kumar<sup>1</sup>, R.P. Sharma<sup>2</sup>, Suraj Bali<sup>3</sup>, Priyanka Arya<sup>4</sup>

## ABSTRACT

**Introduction:** Alopecia Areata is an autoimmune, reversible, patchy hair loss most commonly involving scalp, although other regions of body may be affected. Platelet rich plasma is an autologous concentration of platelets with a greater count in a small volume of plasma. Study aimed to evaluate the effect of PRP therapy in Alopecia Areata.

**Material and Methods:** In this prospective study 30 patients of AA were recruited and injected with 2-3 ml of autologous PRP made by double spin method into the lesional area over the scalp by insulin syringe once a month for 3 months. Outcome was assessed at the end of study by clinical photographs as regrowth of hair, SALT Score and Itching and Burning score.

**Results:** Administration of autologous PRP has led to observable hair regrowth in 70% of patients with mean decrease in SALT Score ( $36.41 \pm 16.41$  to  $25.59 \pm 20.54$ ,  $P < 0.001$ ) and Itching and burning score ( $1.67 \pm 0.80$  to  $0.27 \pm 0.45$ ,  $P < 0.001$ ) respectively.

**Conclusions:** Our study suggests that PRP injections may have a positive therapeutic effect in Alopecia Areata. It is easy to perform and shows effective results without any remarkable adverse effects.

**Keywords:** Alopecia Areata, PRP, SALT Score, Growth factors

## INTRODUCTION

Alopecia Areata (AA) is a non-scarring, autoimmune, inflammatory hair loss on the scalp, and/or body. The pathogenesis of AA is still not fully understood and clinical phenotype and disease course is variable. Recently, the pathomechanism of AA has been thought to be a tissue-specific autoimmune disease and it has been speculated that melanogenesis-related protein, such as tyrosinase, acts as autoantigen.<sup>1</sup>

It is the most common condition to cause inflammation induced hair loss.<sup>2</sup> It usually presents with well differentiated patches of hair loss, which can progress to complete loss of hair from the scalp, Alopecia Totalis (AT) or from the whole body in severe cases Alopecia Universalis (AU).<sup>3</sup>

Histopathology is characterized by typical inflammatory lymphocytic infiltrates in the peribulbar region and increased number of hair follicles in a resting phase, catagen and telogen hairs.<sup>4</sup>

As most patients are relatively young and disease burden is commonly substantial so it may lead to development of psychological stress and can be associated with loss of self-esteem and depression.<sup>5</sup>

Platelet-rich plasma is defined as autologous blood with a concentration of platelets 4-7 times above baseline values.<sup>6</sup>

Platelet-rich plasma has been used since the 1990s; its use in medicine is growing due to its potential to enhance healing and soft tissue repair.<sup>7</sup>

PRP is known to contain more than 20 different growth factors, various studies suggest that the main mechanism of action is

recruitment of reparative cells by growth factors released from platelets.<sup>8</sup>

Recently, it has been found to be useful in acne scarring, wound healing, fat transplantation and also in survival and growth of hair, both in vitro and in vivo.<sup>9</sup>

But still the exact mechanisms by which PRP exerts its effects on hair follicles are not known. A recent study has shown in vitro that PRP stimulates the proliferative phase and transdifferentiation of hair stem cells and hereby produce new follicular units.<sup>10</sup>

Aim of our study was to evaluate the efficacy and safety of PRP therapy in Alopecia Areata.

## MATERIAL AND METHODS

From May 2014 to April 2015 at the department of Dermatology and STD L.L.R.M. Medical college, Meerut. 30 Patients (24 men, 6 women) of Alopecia Areata were enrolled on the basis of inclusion exclusion criteria of age 18 years and above with written informed consent who had not taken any form of treatment for it in the past 6 month. Study was approved by our institutional ethical committee.

Diagnosis was based mainly on clinical observation and inclusion criteria were -patients willing for procedure and of age group 18 years and above. Exclusion criteria were- Patients with history of bleeding disorder, on anticoagulant medications (aspirin, warfarin, heparin) with active infection at local site having keloidal tendency or psoriasis or lichen planus because of risk of koebner phenomenon with low pain threshold and having Alopecia Totalis or Alopecia Universalis.

All the patients of Alopecia Areata were subjected to the detailed history including- Demographic, disease, treatment, family, past medical and surgical history.

Systemic examination was done to exclude any associated systemic disease. Cutaneous examination was done to diagnose AA lesions with a special emphasis on number and symmetry and to exclude any scalp or hair disorders.

Following investigations were carried out in each patient- Complete Blood count, bleeding time, clotting time, Blood Sugar, Thyroid Profile.

PRP was prepared from patient's own blood, drawn at the time of treatment. 20cc venous blood drawn will yield 2-3cc of PRP. PRP was prepared by a process known as differential

<sup>1</sup>JR3, <sup>2</sup>Professor, <sup>3</sup>Assistant Professor, <sup>4</sup>JR2, L.L.R.M. Medical College, Meerut U.P., India

**Corresponding author:** Dr Asim Kumar, R.N. G-10, PG Boys Hostel L.L.R.M. Medical College, Meerut, U.P., India

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centrifugation. In it acceleration force is adjusted to sediment certain cellular constituents based on different specific gravity.<sup>11</sup> Patients should not be on any medication, including aspirin and other non-steroidal anti-inflammatory drugs, during the 2 weeks before this study.

PRP was prepared by using a double-spin method. The equipment's we used were- Digital Bench Top Centrifugation machine, Tarson Pasteur Pipette, Tarson 14ml conical test tubes, 10 ml syringe, Insuline syringe, sodium citrate solution 3.8% w/v, 10% calcium chloride solution.

All steps were done under complete aseptic sterile condition.

1. 9cc of whole blood was withdrawn in two 10 ml syringes containing 1 c.c. 3.8% Sodium Citrate solution as an anticoagulant with ratio 1:9 (anticoagulant : blood) from the patient undergoing PRP treatment. Then it was divided into 4 test tubes each containing 4.5 ml of blood.
2. The citrated blood was centrifuged at 1500 rpm for 5 minutes in 4 test tubes known as soft spin.
3. At the end of centrifugation the whole blood was divided into 3 parts: the bottom layer consists mostly of RBCs, an upper layer that contains some platelets and WBC and in between them third part, buffy coat that is rich in platelets and WBC.
4. The upper layer and superficial buffy coat were transferred by micropipette into two sterile test tubes.
5. Then centrifuged again at 3000 rpm for another 5 minutes known as hard spin to aid in formation of soft pellets at the bottom of tube.
6. The upper portion of volume, that is 2/3<sup>rd</sup> composed mainly of platelet poor plasma (PPP) was collected and was used for massage after PRP injection.
7. PRP which is lower 1/3<sup>rd</sup> part after homogenization taken into two insulin syringes containing .2ml/ml calcium chloride as activator.
8. Then PRP was immediately injected into the area of AA over the scalp in amount of .1ml/cm<sup>2</sup> by insulin syringe.

Since life of Platelet is very short, therefore all necessary operations are consecutive.

Platelet counts were checked frequently. PRP injections were given once every month for 3 months.

All Patients were evaluated at every visit and assessment was done at the end of study (3<sup>rd</sup> month) by-

1. SALT Score- Which represent hair regrowth as percentage of change from baseline by independent observer evaluation of clinical photographs taken at each visit.
2. Subjective assessment of burning/itching sensation was also performed on a 4-point scale: 3- strong, 2-moderate, 1-mild, 0-no burning/itching sensation.

## STATISTICAL ANALYSIS

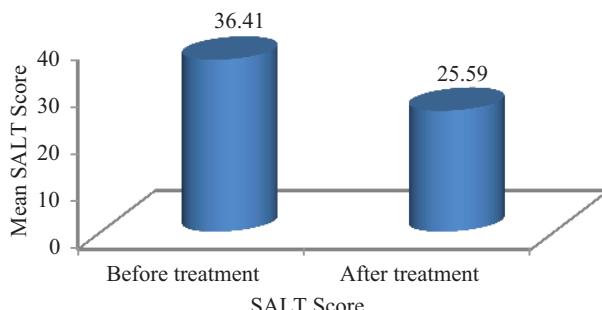
For statistical analysis SPSS software for windows, version 17.0 was used. Chi-square test was used For non-continuous data. Analysis of variance test was used to measure the mean and standard deviation of various treatment groups. Paired t-test was used for intra-group comparison. Value of 'P' <0.05 was indicative of significant difference.

## RESULTS

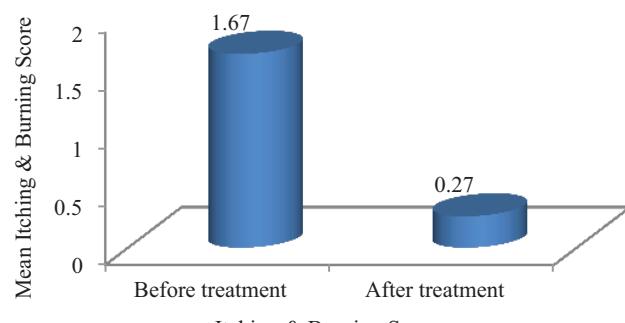
30 patients were enrolled with single to multiple (1-5 and mean

2.4±1.02) distributed AA scalp patches with age ranging from 20-36 years (27.3±5.33 years). There were twenty four males (80%) and six females (20%) patients. All patients had normal blood investigations (Complete Blood count, bleeding time, clotting time, Blood Sugar, Thyroid Profile).

All patients 30 (100%) reported sudden onset with 09 patients (30%) having progressive course and 21 patients (70%) having



**Figure-1:** Comparison of SALT Score before and after PRP treatment



**Figure-2:** Comparison of Itching and Burning Score before and after PRP treatment



**Figure-3:** Result in a 24 year male of Alopecia Areata Before and After 3 sittings of PRP treatment



**Figure-4:** Result in a 26 year male of Alopecia Areata Before and After 3 sittings of PRP treatment

stationary course. The mean of disease duration was  $3.3 \pm 1.8$  months.

Patients were further subdivided into two groups- responders 21 (70%) and non-responders 09(30%). the mean age among responders was  $27.24 \pm 5.4$  yrs and among non-responder was  $27.44 \pm 7.4$  yrs. Out of 30 patients, (70.83%) males showed response compared to (66.67%) females who responded to treatment. There was no significant difference between the two groups (responders and non-responders) as regards to patient's age, sex.

There was a significant difference of SALT score with better hair regrowth and better SALT score after treatment as the mean decreased, from  $36.41 \pm 16.14$  before treatment to  $25.59 \pm 20.54$  after treatment.

There was a significant difference of Itching and burning score with better Itching and burning score after treatment as the mean decreased from  $1.67 \pm 0.80$  before treatment to  $0.27 \pm 0.45$  after treatment.

## DISCUSSION

Alopecia Areata (AA) is characterized by rapid and complete loss of hair in one or more round to oval patches, usually on the scalp but can involve any part of body.<sup>12</sup>

AA is considered an organ-specific autoimmune disease, stemming from loss of the hair follicle's (HFs) immune privilege.<sup>3</sup>

Mostly the therapies are immunosuppressive and treatment is still challenging. None of the available treatment is completely curative or preventive.<sup>14</sup>

Platelet rich plasma (PRP) is an autologous preparation of platelets in concentrated plasma.<sup>15</sup>

PRP is known to contain more than 20 different growth factors, The growth factors contained in platelets of blood plasma include platelet derived growth factor, transforming growth factor- $\beta$ , vascular endothelial growth factor, epidermal growth factor, and connective tissue growth factor. They are known to activate the proliferative phase and trans differentiation of hair and stem cells and thereby produce new follicular units.<sup>16</sup>

We relied in our observations on the fact that the characteristic of hair regrowth in Alopecia Areata is, the emergence of vellus or indeterminate hair that may give an idea of the potential utility of a new therapeutic agent and promise of responsiveness of a patient to treatment that would be followed by hair pigmentation.<sup>17</sup>

At the end of the study about 21 (70%) patients had a complete regrowth of pigmented hair, while 9 (30%) patients had partial/no regrowth of hair.

Our results showed statistically significant improvement in SALT score and Itching and Burning score with regrowth of hair in PRP treated patches of 70% of our patients.

Our study had shown that the age, gender, disease duration or course had no influence on the effect of PRP in responding patients which further strengthens the potent local effect of PRP. Since AA is characterized by an extensive inflammatory infiltrate, responsible for secretion of a variety of inflammatory cytokines, it is possible that the anti-inflammatory effects of PRP may be of great benefit in this condition.<sup>18</sup>

There was tolerable temporary burning sensation which disappeared shortly after injection but no other side effects were

noticed. All patients had no relapse at the end of the study or after 6 months of follow up.

Other investigators reported some side effects or complications, the main side effect being local infection and pain at the site of PRP injection.

We have achieved our results by using platelet count done on each patient that yielded a mean platelet count value of  $11,600,000/\mu\text{L}$  with a range of 750,000 to  $14,000,000/\mu\text{L}$ . The platelet count must be one of the most important factor to standardize studies investigating the role of PRP therapy in Alopecia Areata.

Beside quantitative value any alterations in the quality of platelets during its preparation may affect the regenerative potential of PRP, but our study is limited to this point.<sup>19</sup>

However, the challenge remains to evaluate the results using objective parameters, such as histopathological and/or dermoscopic evaluation.

Taken together the present study suggests autologous PRP as a potential treatment modality for AA, being a safe and a more efficient alternative for other therapeutic modalities.

## CONCLUSION

PRP has emerged as a new treatment modality. It is easy to perform and shows effective results without any remarkable adverse effect in the treatment of Alopecia Areata and can be regarded as a valuable alternative for treatment of it. However histopathological and dermoscopic studies are needed to detect ultrastructural changes following PRP injection in Alopecia Areata.

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