

Correlation of Cervical Smear and Colposcopy with Pathohistological Findings in Detection of Premalignant Lesions of Cervix at a Tertiary Care Centre

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ABSTRACT

Introduction: Cervical cancer is the second most frequent cancer among women in India. Invasive carcinoma of cervix is preventable as it is associated with pre-invasive stage which occurs 10 to 15 years prior to it, thus permitting early detection by screening and leading to effective treatment and thereby reducing the mortality rate. Objectives of this study were to correlate the findings of pap smear with colposcopy in evaluation of all symptomatic women; and to assess the utility of colposcopy in detecting the premalignant and malignant lesions of cervix.

Material and methods: This prospective observational study was conducted in a tertiary care hospital on 200 symptomatic sexually active women of 20-65 years of age from February 2018 to October 2019. Pap smears were performed by conventional method and colposcopy was done for all 200 women who came with complaints of persistent vaginal discharge, intermenstrual or postcoital bleeding etc. Final correlation of the Pap smear and colposcopy was based on the histopathological reports.

Results: Commonest complaint was white discharge per vaginam in 55% followed by pelvic pain in 20% women. Among 43.5% symptomatic women with abnormal Colposcopic finding, 30% had acetowhite lesions, 5% had negative lugol's iodine, 2% had atypical vessels, 2% had fine mosaic, 1.5% had coarse mosaic, 1.5% had fine punctate lesions, 1% had coarse punctate lesions, 0.5% had dense acetowhite lesions. Among 87 symptomatic women having abnormal colposcopy, only 13 women had abnormal pap smear finding comprising of 6 ASCUS, 2 ASC-H, 4 LSIL, 1 HSIL, while in 21 symptomatic women having abnormal pap smear finding, 13 women were having abnormal colposcopy too, while 4 women had normal colposcopy. 3 had indecisive colposcopy and 1 had miscellaneous colposcopy. The most common histopathological finding was chronic cervicitis in 50% cases. CIN were seen in 30% cases. CIN 1 were seen in 10%, CIN 2 in 0%, CIN 3 in 10%. Out of 15 women with abnormal biopsies, only 7 women had abnormal cytology. Out of 15 women with abnormal biopsies, 13 women had abnormal colposcopy too while only 2 had normal colposcopy.

Conclusion: The result of the study shows Pap smear demonstrates the premalignant and malignant lesions, whereas colposcopy shows the exact site for biopsy for histopathological diagnosis and for further management. Colposcopy and cytology are not competitive methods but complementary to each other. Best results in early detection of pre-invasive carcinoma could be obtained by combined use of cytology, and colposcopic directed biopsy. The pap smear should be carried out in all women of reproductive and menopausal age at least once in a lifetime.

Keywords: Cervical Cancer, Papanicolaou, Cytology, Colposcopy, Histopathology.

INTRODUCTION

Cervical cancer is a common cancer among women worldwide.¹ Cervical cancer is the second leading cause of new cancer cases and cancer related deaths among gynaecological cancers in females with an estimated 96,922 new cases and 60,078 deaths each years.² India bears 18% of the burden of invasive cancer cervix in the world and 80-85% of cases are detected in stage 3 and 4.³ As per GLOBOCAN 2018 database, cervical cancer is common cancer in women with an estimated 569,847 new cases and 311,365 deaths, accounting for 7.5% of all female cancer deaths worldwide.⁴ The main cause of cervical cancer is a sexually transmitted infection by human papillomaviruses.⁵ The worldwide human papilloma virus prevalence in cervical cancer is 99.7%.⁶ The most common histologic type of cervical cancer is squamous, and the relative and absolute incidence of adenocarcinoma is increasing; both histologies are caused by HPV infection.⁷

The initiating lesion of cervical cancer is cervical dysplasia, which means abnormal maturation. In most cases it spontaneously regresses back but over a period of 10 to 20 years has the potential to convert into cervical cancer.⁸ Cervical dysplasia, also termed as cervical intraepithelial neoplasia (CIN), often arises in an area of metaplasia in the transformation zone at the advancing squamocolumnar junction. CIN is most likely to begin either during menarche or after pregnancy when metaplasia is most active. Cervical cancer has been considered preventable because it has a long pre-invasive state and the availability of screening programs and treatment of pre-invasive lesion is effective.⁹

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How to cite this article: Verma R, Khatun S, Phuleman S, Gul R. Correlation of cervical smear and colposcopy with pathohistological findings in detection of premalignant lesions of cervix at a tertiary care centre. International Journal of Contemporary Medical Research 2020;7(12):L1-L5.

DOI: <http://dx.doi.org/10.21276/ijcmr.2020.7.12.14>



It has been well established that well organised screening by conventional cytology has substantially reduced the incidence of morbidity and mortality from cervical cancer in developed countries.⁹

In developed countries such as USA, 85% of women had at least one papanicolaou test through their lifetime, but this rate is only 5% in developing countries.¹⁰ The goal of screening of carcinoma of cervix is to diagnose and treat carcinoma cervix in early pre-invasive states which makes the disease ideal for screening procedures.⁹ Various screening methods include conventional exfoliative cervicovaginal cytology i.e. cervical (Pap smear, pelvic examination, colposcopy, liquid based cytology, automated cervical screening techniques, HPV testing, visual inspection of cervix after applying lugol's iodine (VILI) or acetic acid (VIA). The screening strategies mentioned above though applicable to the developed world may not be cost effective in the developing countries.¹¹ The PAP smear is a simple, safe, non-invasive and effective method for detection of precancerous and noncancerous changes in the cervix and vagina.¹² The overall sensitivity of the pap test in detecting a high grade squamous intraepithelial lesion (HSIL) is 70-80%.¹³ A pap screening done in association with an HPV DNA test increases the sensitivity for early detection of premalignant lesions.¹⁴

In 1925 Hinsellman^{1st} hypothesized visualisation of cervical epithelium under the magnification. Colposcopy provides a unique method to study the benign and premalignant lesions.¹² It is a non-invasive procedure which helps in determining the location, size and extent of abnormal cervical lesions and serves for detecting the site for biopsies. Colposcopy is complementary to cytology.¹⁶ Cytology (PAP smear) is the lab method while the colposcopy is the clinical method of detection.¹⁵ The final diagnosis must be made on histopathological examination.¹⁵ No screening test is 100% sensitive hence this study was intended to evaluate if parallel testing with pap and colposcopy can maximize the sensitivity.

MATERIALS AND METHODS

This prospective study was conducted in the department of Obstetrics and Gynaecology, Katihar Medical College and Hospital, Bihar, from February 2018 to October 2019. Approval from institutional ethical committee was obtained. Informed consent was taken from each patient. Relevant obstetrics and gynaecology history were recorded. The material of the present study was collected from the women who met the inclusion criteria and gave consent for colposcopy and directed biopsy.

Inclusion criteria

1. Sexually active women of age group 20-65 year,
2. Abnormal vaginal discharge, abdominal pain, irregular menstrual bleeding, postmenopausal bleeding, postcoital bleeding, prolapse, burning micturition, itching vulva, persistent leucorrhoea not responding to antibiotic.

Exclusion Criteria

1. Women >65 years and <20 years,
2. Pregnant women,

3. Post total hysterectomy,
4. Women with frank cancer,
5. Women with clinical evidence of acute pelvic infection,
6. Women with bleeding at the time of examination

Procedure

After brief explanation of the procedure and taking informed consent from the patients meeting the study criteria, history including demographic data like age, socioeconomic status, education, parity, age at marriage of the patient was recorded. General examination and systemic examination were done. Pap smear was taken, and prepared slides were sent fixed in 95% ethyl alcohol and ether. The prepared pap smear slides were then stained according to the conventional PAP technique and examined under a light microscope. The cytological interpretation of the smears was done according to the Bethesda system 2014. They were classified as ASCUS, ASC-H, LSIL, HSIL and invasive carcinoma. All the women were subjected to colposcopy and cervical biopsy was taken from the most suspected areas in selected cases on the basis of clinical and colposcopic findings. Biopsy specimens were sent in 10% formalin fixative. Colposcopic examination of all symptomatic women included inspection of cervix in green filter followed by examination with 3% acetic acid and lugol's iodine test. Cervix biopsy was done in selected women from suspected lesion in women with grossly abnormal looking cervix and significant abnormal colposcopic finding. Biopsy may cause mild cramping, brief pain, and some bleeding afterwards. Colposcopic-directed biopsy results were categorised as Chronic cervicitis, Cervical Intraepithelial neoplasia1 (CIN 1), CIN 2, CIN 3, Carcinoma-in-situ, squamous cell carcinoma (SCC), and Adenocarcinoma according to WHO.

RESULTS

Total of 200 cases were included in the study.

Maximum no. of cases were of age group 51-55yrs (25.5%) followed by 41-50 yrs (23%), and was multiparous. Maximum patients were illiterate. According to Kuppuswamy classification, maximum no. of cases was from lower socioeconomic class 46.5%. 43% cases never used any type of contraceptive methods. Barrier method was used in 16% cases followed by permanent method in 13.5% cases. IUCD was used in 15% cases and oral contraception in 2.5% cases (table-1).

The most common complaint was white discharge per vagina in 55% cases (table-2)

Among 43.5% symptomatic women with abnormal Colposcopic finding, 30% had acetowhite lesions, 5% had negative lugol's iodine, 2% had atypical vessels, 2% had fine mosaic, 1.5% had coarse mosaic, 1.5% had fine punctate lesions, 1% had coarse punctate lesions, 0.5% had dense acetowhite lesions (table-3,4). Among 87 symptomatic women having abnormal colposcopy, only 13 women had abnormal pap smear finding comprising of 6 ASC-US, 2 ASC-H, 4 LSIL, 1 HSIL, while in 21 symptomatic women having abnormal pap smear finding, 13 women were having abnormal colposcopy too, while 4 women had

normal colposcopy. 3 had indecisive colposcopy and 1 had miscellaneous colposcopy (table-5). Out of 15 women with abnormal biopsies, only 7 women had abnormal cytology (table-6). Out of 15 women with abnormal biopsies, 13 women had abnormal colposcopy too while only 2 had

normal colposcopy (table-7).

DISCUSSION

In present study, maximum no. of cases were in the age group of 51-55 yrs (25.5%) followed by 46-50 yrs (23%) which was comparable to other studies done by Joshi et al (50%)¹⁶, Bamanikar et al (28.46%)¹⁷, and Parija et al (37.15%)¹⁸. The most common complaint was white discharge per vaginam 55% followed by pelvic pain 20% amongst all the symptomatic women. 10% had complaints of intermenstrual

Variables	No. of cases	Percentage
1. Age Group (yrs)		
20-25	18	9%
26-30	14	7%
31-35	24	12%
36-40	37	18.50%
41-50	46	23%
51-55	51	25.50%
56-60	9	4.50%
>60	1	0.50%
2. Parity		
P1+0	12	6%
P2+0	18	9%
P3+0	27	13.50%
P4+0	65	32.50%
P5+0	48	24%
>P5+0	11	5.50%
3. Socioeconomic Class		
Lower	93	46.50%
Middle	67	33.50%
Upper	40	20%
4. Religion		
Hindu	128	64%
Muslim	68	34%
Others	4	2%
5. Marital Status		
Married	178	89%
Widowed	21	10.50%
Separated/Divorced	1	0.50%
6. Educational Status		
Illiterate	118	59%
Primary education	46	23%
Secondary education	26	13%
Graduate	10	5%
7. Method of Contraception		
None	86	43%
IUCD	30	15%
Barrier	32	16%
OCP	5	2.50%
Permanent	27	13.50%

Table-1: Socio Demographic Factors

Symptoms	No. of patients	Percentage
White discharge	110	55.0%
Pelvic pain	40	20.0%
Itching vulva	15	7.5%
Intermenstrual bleeding	20	10.0%
Menorrhagia	10	5.0%
Post coital bleeding	5	2.5%
Total	200	100.0%

Table-2: Distribution of cases in relation to the presenting complaints.

Clinical sign	No. of cases	Percentage
Normal cervix	8	4%
Unhealthy cervix	27	13.5%
Cervical erosion	77	38.5%
cervicitis	25	12.5%
Hypertrophy of cervix	51	25.5%
Cervical erosion bleeds on touch	10	5%
Suspicious of carcinoma cervix	2	1%
Total	200	100%

Table-3: Distribution of cases in relation to clinical signs

Abnormal Colposcopic Findings	No. of patients	Percentage
Flat acetowhite epithelium	60	30.0%
Negative lugol's iodine	10	5.0%
Atypical vessels	4	2.0%
Fine mosaic	4	2.0%
Coarse mosaic	3	1.5%
Fine punctuate	3	1.5%
Coarse punctuate	2	1.0%
Dense acetowhite epithelium	1	0.5%
Total	87	43.5%

Table-4: Distribution of cases according to abnormal colposcopic findings

Colposcopy	Pap smear					
	Normal	Inflammatory	ASC-US	ASC-H	LSIL	HSIL
Normal (53)	29	20	2	0	2	0
Abnormal (87)	18	56	6	2	4	1
Miscellaneous (43)	10	32	0	0	1	0
Indecisive (17)	2	12	2	0	1	0
Total (200)	59	120	10	2	8	1

†(ASCUS: Atypical squamous cell of undetermined significance, ASC-H: Atypical squamous cells cannot exclude high grade squamous intraepithelial lesion, LSIL: low grade squamous intraepithelial lesions, HSIL: high grade squamous intraepithelial lesions)

Table-5: Correlation of pap smear with colposcopic findings

Cervix biopsy	Cytology					
	Normal	Inflammatory	ASC-US	ASC-H	LSIL	HSIL
Chronic non-specific cervicitis (15)	8	4	0	0	3	0
Mild dysplasia (9)	0	6	3	0	0	0
Moderate dysplasia (3)	0	0	2	1	0	0
Severe dysplasia (0)	0	0	0	0	0	0
Carcinoma (3)	0	2	1	0	0	0
Total (30)	8	12	6	1	3	0

Table-6: Correlation of cytology and histopathology

Cervix biopsy	Colposcopy			
	Normal	Abnormal	Miscellaneous	Indecisive
Chronic non-specific cervicitis (15)	2	9	2	2
Mild dysplasia (9)	2	7	-	-
Moderate dysplasia (3)	-	3	-	-
Severe dysplasia (0)	-	-	-	-
Carcinoma (3)	-	3	-	-
Total (30)	4	22	2	2

Table-7: Correlation of colposcopy and histopathology

bleeding, 5% had menorrhagia, 2.5% had postcoital bleeding, 7.5% had itching vulva. Similar complaints were reported by Chaudhary et al (39%)¹⁵, Joshi et al (40%)¹⁶, Atla et al (41%)¹⁹, Dhakal et al (40%)²⁰, and Alaknanda et al (51%)²¹. Mallur PR et al²² in his study on sequential screening with cytology and colposcopy in detection of cervical neoplasia on 190 symptomatic women and women with unhealthy cervix, also observed the similar results with white discharge being the most common complaint i.e. 61.05%. Among abnormal pap smear findings, ASCUS was the most common finding as seen in study by Choudhary et al (50%)¹⁵.

In present study, 26.5% of all symptomatic women had normal colposcopic findings while 43.5% had abnormal colposcopic finding, 21.5% had miscellaneous colposcopy and 8.5% had indecisive colposcopy. The most common colposcopy finding was acetowhite areas 30%, similar study reported by Krishnegowda and Veena (22%)²³. Acetowhite staining was the most common finding as it is very non-specific and may also occur, to some extent, in flat condyloma (where it presents as a thin, satellite acetowhite lesions detached from squamocolumnar junction with geographical patterns), immature squamous metaplasia, the congenital transformation zone, inflammation and healing and regenerative epithelium. So, women with these findings need further follow up.²⁴ Bhalero et al reported the most common colposcopic feature in his study as aceto whiteness in 42.5%.²⁵ Among 87 (43.5%) symptomatic women having abnormal colposcopy, only 13 women had abnormal pap smear finding comprising of 6 ASCUS, 2 ASC-H, 4 LSIL, 1 HSIL, while in 21 symptomatic women having abnormal pap smear finding, 13 women were having abnormal colposcopy too while 4 women had normal colposcopy, 3 had indecisive colposcopy and 1 had miscellaneous colposcopy suggesting more diagnostic accuracy of colposcopy.

Maximum number of cases on histopathological examination

were those of infection. Among them majority had chronic non-specific cervicitis 50%. Mild dysplasia was seen in 30% cases, moderate dysplasia was seen in 10% and 10% had non keratinizing squamous cell carcinoma. Correlative study of histopathology and cytology shows that out of 15 (50%) women with abnormal biopsies, only 23% women had abnormal cytology which suggests that cytology missed the diagnosis in 8 (26%) cases which were later diagnosed by colposcopy and histopathology. So symptomatic women with negative smear should be further evaluated by colposcopy and histopathology. Correlative study of histopathology and colposcopy show that out of 15 abnormal biopsies, 13 women had abnormal colposcopy too. Only 2 had normal colposcopy. While out of total 15 women with normal biopsy, 9 women had abnormal colposcopy which shows that colposcopy overestimated the cervical lesions which is a most common drawback of colposcopy as majority of these lesions regress spontaneously over the course of time and during follow up or after treatment.

This study suggests that colposcopy is more sensitive than cytology. There is a strong correlation between findings of pap smear and histopathology and colposcopy and histopathology. Therefore, pap smear, colposcopy and directed biopsy together are useful and complementary in arriving at a correct diagnosis. It is not possible to screen every woman with cytology and colposcopy so both these tests should be performed in women presenting with symptoms.

CONCLUSION

Comparison of Pap smear and colposcopy revealed that pap smear had a very poor sensitivity when compared to colposcopy for screening of premalignant lesions of cervix, especially for low grade squamous intraepithelial lesion. Both the tests can be used to complement each other in a hospital-based screening programme, where facilities for both modalities are available.

ACKNOWLEDGEMENTS

Our sincere thanks to the patients, Department of Obstetrics and Gynaecology, Katihar Medical College and Hospital, our system engineer, Mr. Ghazi Danish Ahmed for providing the support and assistance in preparing the paper.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 02-10-2020; **Accepted:** 20-11-2020; **Published:** 31-12-2020