Retinopathy of Prematurity, A Hospital based Study

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ABSTRACT

Introduction: Retinopathy of prematurity is a vasoproliferative disorder of the retina among premature infants. It is an important cause of preventable blindness in children. Recent advances in neonatal care in the last decade have improved the survival rates of premature infants, consequently the incidence of retinopathy of prematurity has increased in parallel. The objective of the present study was to identify the risk factors associated with development of ROP in preterm neonates.

Material and Methods: This was a prospective observational study conducted on all preterm neonates admitted in the neonatology section of Government Medical College Srinagar who fulfilled the criteria for ROP screening.

Results: A total of 150 preterm neonates were screened, out of which 32 had ROP of different stages. 7 babies were detected with stage 3 ROP and needed laser therapy. Risk factors associated with ROP were studied

Conclusion: Our study revealed 21.3% incidence of ROP. Prematurity, low birth weight and oxygen therapy were found to be strong predictors of ROP. Sepsis, blood transfusion and apnea were found to be statistically significant factors associated with ROP.

Keywords: Retinopathy, Prematurity, Newborn

INTRODUCTION

Retinopathy of prematurity is a vasoproliferative disorder of the retina among premature infants. It is an important cause of preventable blindness in children. Recent advances in neonatal care in the last decade, have improved the survival rates for premature infants. Consequently, the incidence of retinopathy of prematurity has increased in parallel. Retinopathy of prematurity is under constant epidemiological study around the world.[1]

Early identification of retinal damage and the institution of appropriate treatment prevent blindness and offer the child better overall development.[2] Retinopathy of prematurity is characterized by abnormal neovascular development in the retina of premature infants. These abnormal blood vessels are fragile and can leak or bleed, scarring the retina and pulling it out of position. This causes a tractional retinal detachment, which is the main cause of visual impairment and blindness in retinopathy of prematurity.[3] Retinopathy of prematurity begins to develop between 32 and 34 wks after conception and has 2 distinct phases.[4] During the acute first phase the normal vasculogenesis of retina is disturbed by the relative hyperoxia of the extra-uterine environment. This causes the vaso-obliteration and non – vascularisation of some areas of the anterior retina.[5] The subsequent hypoxia causes a second chronic phase characterized by proliferation of vascular and glial cells, arterio-venous shunt formation, occasionally leading to involution or permanent cicatricial changes and visual impairment.[6,7]

In 1942, Terry[8] first described retrolental fibroplasia with implication of oxygen therapy as the causative agent. However, reports have found retinopathy of prematurity in cases without oxygen therapy and even after oxygen therapy, not all premature infants develop retinopathy of prematurity.[9] Three factors have shown consistent and significant association with retinopathy of prematurity, low gestational age, birth weight and prolonged exposure to supplementary oxygen following delivery.[10]

Other putative risk factors include mechanical ventilation[11], sepsis[12], intraventricular hemorrhage[10], surfactant therapy[13], anemia[14], frequent blood transfusions[14], and apnea.[11] The precise roles of these factors individually in the progression of the disease have not yet been determined.[15]

Studies from India reporting incidence of retinopathy of prematurity provide interesting insights. Overall incidence of retinopathy of prematurity varies from 20% -52% with more recent studies reporting lower rates of retinopathy of prematurity ranging from 20%-30%.[16-23]

Based on current incidence and risk factors reported in Indian literature following group of neonates should be screened.

- babies with weight <1500gm and gestational age <32wks,
- selected preterm neonates with a birth weight between 1500 and 2000 or gestational age of >32 wks with sickness like cardiorespiratory support, prolonged oxygen therapy, apnea of prematurity, anemia needing blood transfusion, neonatal sepsis, intraventricular hemorrhage, surfactant therapy or believed by their attending pediatrician or neonatologist to be at high risk. This 'third criterion' is important as it brings in many neonates in screening guidelines without raising the screening parameters.[24,25]

This study aimed to record the profile of retinopathy of

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prematurity in preterm infants admitted in Neonatal Unit of Goverment Medical College Srinagar, to identify the risk factors associated with development of ROP in these preterm neonates

MATERIAL AND METHODS

The present study, carried for one and a half year, was a prospective study conducted in Postgraduate Department of Paediatrics, G. B. Pant Hospital Srinagar which has a level III Neonatal ICU, an associated hospital of Govt. Medical College Srinagar.

Inclusion criteria

- Gestational age <32 wks and birth weight <1500gm.
- Gestational age >32wks, birth weight between 1500 to 2000gm plus risk factors like need of cardio respiratory support, prolonged oxygen therapy, apnea of prematurity, anemia needing blood transfusion and neonatal sepsis, intraventricular hemorrhage, surfactant therapy or believed by the attending neonatologist to be at high risk.

The initial examination of these infants were performed at 31 wks of gestation or 4 wks postnatally, whichever was later.

Procedure

All infants were examined with indirect ophthalmoscope, 20D and 28D lens under topical anaesthesia. Pupils were dilated with tropicamide and phenylephrine drops at 15 minutes interval (3 times), 30 minutes before consultation. The examination was done by a Paediatric ophthalmologist. Retinopathy of prematurity was graded into stages and zones as per the ICROP classification. Infants with normal vascularisation were not examined again. Those with retinopathy of prematurity were examined till regression had occurred or till they reached the threshold for treatment. An analysis of the risk factors and profile of retinopathy of prematurity were performed.

STATISTICAL ANALYSIS

Statistical software SPSS (version 20.0) was used to carry out the statistical analysis of data. Data was presented by means of descriptive statistics viz. means, standard deviations and percentage and presented by bar diagrams. Student's independent t-test was employed for parametric data, Chi square or Fisher's exact test, whichever appropriate, was used. P-value less than 0.05 was considered statistically significant.

RESULTS

In our study, total patients were 150. Out of it, 32 infants had ROP of different stages and 118 were normal. Incidence came out to be 21.3%. ROP was present in 22.4% of males and 20.3% of females. Most of the patients who developed

Gestational Age	ROP Present		ROP Absent		P-value
	Numb	%age	Numb	%age	
≤28	18	56.3	11	9.3	<0.001*
29-31	8	25.0	35	29.7	
32-34	5	15.6	32	27.1	
<37	1	3.1	40	33.9	
Mean±SD	29.0±2.52		32.7±3.08		

Table-1: Showing gestational age of studied patients

Gestational Age	ROP Present		ROP Absent		P-value
	Numb	%age	Numb	%age	
< 1.5 kg	24	75	60	50.8	<0.001*
1.5-2 kg	8	25	58	49.2	
Mean±SD	1.36±0.255		1.67±0.227		

*Statistically Significant Difference (P-value<0.05)

Table-2: Showing birth weight (kgs) of studied patients

Risk Factor		ROP Present		ROP Absent		P-value
		Numb	%age	Numb	%age	
Sepsis	Yes	26	81.3	70	59.3	0.022*
	No	6	18.8	48	40.7	
Blood Transfusion	Yes	9	28.1	13	11.0	0.023*
	No	23	71.9	105	89.0	
Apnea	Yes	11	34.4	10	8.5	<0.001*
	No	21	65.6	108	91.5	
DVET	Yes	5	15.6	11	9.3	0.335#
	No	27	84.4	107	90.7	
Pressor Support	Yes	10	31.3	26	22.0	0.279#
	No	22	68.8	92	78.0	

*Statistically Significant Difference (P-value<0.05); # statistically non significant

Table 3: Risk factors associated with ROP patients

Risk Factors	Odds Ratio	95% CI	P-value
Gestational Age	3.13	1.21-5.43	0.032*
Birth Weight	6.26	4.87-8.51	0.005*
Sepsis	7.53	5.64-9.52	0.016*
Oxygen therapy	4.19	2.89-6.08	0.039*
Blood Transfusion	1.27	0.68-1.95	0.748
Apnea	0.57	0.19-0.92	0.388
*Statistically Significant Difference (P-value<0.05); #Statistically Non-significant Difference (P-value>0.05)			
Table-4: Logistic regression analysis			

ROP had gestational age ≤32 weeks. Mean age of patients who developed ROP was 29.0± 2.52. Mean age in whom ROP was absent was 32.7 ± 3.08. This shows lower the gestational age, more are the chances of ROP development. The difference was statistically significant.

Table 1 shows the gestational age distribution of studied patients. 4 groups were formed. Our study shows most of the patients who developed ROP had gestational age ≤32 weeks. Mean age of patients who developed ROP was 29.0± 2.52 weeks. Mean age in whom ROP was absent was 32.7 ± 3.08 weeks.

Mean weight of studied patients who developed ROP was 1.36 ± 0.255 kg and mean weight in whom ROP was absent 1.67 ±0.227 kg. It shows lower the birth weight, more are the chances of development of ROP. The difference was statistically significant.

Table-2 shows birth weight distribution of studied patients. Two groups were formed. Mean weight of studied patients who developed ROP was 1.36 ± 0.255 and mean weight in whom ROP was absent 1.67 ±0.227. It shows lower the birth weight, more are the chances of development of ROP. The difference was statistically significant.

71.9% of patients received oxygen who developed ROP while it was absent in 28.1%. The difference was statistically significant. 34.4% patients received invasive ventilation who developed ROP while it was absent in 65.5% patients. The difference was not statistically significant.

Table-3 shows association of risk factors with ROP among studied patients. Our study showed that sepsis, apnea and blood transfusion were significant risk factors associated with ROP. DVET and pressor support were found statistically insignificant.

59.4% babies had stage I ROP, 18.8 stage II ROP and 21.9% showed stage III ROP. All patients in stage III ROP received laser treatment.

Table-4 shows the logistic regression analysis of significant factors. Our study showed that low gestational age, low birth weight, sepsis, oxygen therapy were found to be independent risk factors for ROP.

DISCUSSION

Retinopathy of prematurity is a disorder of retinal vascular development in preterm infants. It continues to be a significant complication in preterm neonates despite advances in neonatal care and remains a major cause of childhood blindness worldwide.

Our study was a prospective cohort hospital based study. We studied 150 patients. Out of it, 76 were males and 74 were females. All babies with birth weight <1500g and gestation <32 weeks were screened. Babies with birth weight 1.5- 2 kg and gestational age >32 weeks were included if they were associated with risk factors like need of cardiorespiratory support, prolonged oxygen therapy, apnea of prematurity, anemia needing blood transfusion and neonatal sepsis, intraventricular hemorrhage, surfactant therapy or believed by the attending neonatologist to be at high risk. These criterias were included in view of various studies conducted on ROP screening that had shown ROP in bigger and much mature infants as compared to criteria given by West. There are varying screening criteria described by different authors Hakeem AHA Abdel[26], et al. have suggested the same screening criteria. Chaudhari S et al.[16] also screened all babies with birth weight <1500g and ≤32 weeks and babies with birth weight between 1.5-2 kg and >32 weeks were screened if they had some associated risk factors. Vinekar[27], et al.[26] suggested that scenario in developing countries is quite different. Larger and gestationally older infants are more likely to develop ROP compared to their counterparts in western countries. Hence, the application of western screening guidelines for developing countries has been questioned by Jalali, et al.[28]

Incidence

The incidence of ROP in our study was 21.3% which was lower than 29.2% in Singapore.[11] This can be explained by the fact that this study involved only very low birth weight infants. However, it is higher than the study done in Beijing[29] which involved infants with higher gestational age and birth weight (up to 2 kg and/ or 34 weeks gestational age) and reported an incidence of 10.8%.

Risk factors

ROP is a multifactorial disease. In our study, low gestational age, low birth weight, sepsis, oxygen therapy and frequent blood transfusions were found to be risk factors for development of ROP independently.

As regard the effect of low gestational age on occurrence of ROP, we found it the most important risk factor in ROP. This was in agreement with the results of studies done by Shah et al.[11] In our study, mean gestational age in weeks of ROP patients was 29.0±2.52 vs 32.7± 3.08 of those without ROP. It shows lower the gestational age, more are the chances of development of ROP.

As regard the effect of birth weight on the occurrence of ROP. In our study, mean birth weight in kg of ROP patients

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was 1.36±0.255 vs 1.67± 0.227 of those without ROP. It was found to be significant factor associated with ROP. It was in agreement with Shah et al.[11] Babies with birth weight <1.5 kg showed that 28.57% of this group had ROP, while 12.12% of patients with birth weight between 1.5-2 kg had ROP. It shows lower the birth weight, more are the chances of development of ROP.

We found that sepsis was significantly associated with development of ROP. This was in agreement with Shah et al.[11]

Oxygen therapy was found to be independent risk factor for development of ROP. This was in agreement with studies done by Murthy KR et al[29], Weinberger B et al.[30] In our study, no correlation was found between duration of oxygen therapy and development of ROP.

We found that mechanical ventilation and CPAP were non-significant risk factors for ROP and this agreed with Murthy et al.[29] Blood transfusion was found to be significant risk factor for development of ROP and this agreed with Chawla et al.[9]

In our study, apnea was also found to be significant risk factor for development of ROP. This was in agreement with Aggarwal et al.[19]

Our study revealed non-significant relationship between sex and development of ROP. This was in disagreement with Darlow et al[31], who found that male sex is a significant risk factor.

Other risk factors including phototherapy, DVET, pressor support, respiratory distress syndrome showed non-significant relationship with the occurrence of ROP.

In multivariate analysis after logistic regression analysis, it was confirmed that low gestational age, low birth weight, sepsis and oxygen therapy were independent risk factors for development of ROP.

In our study, 19 (59.4%) babies developed stage I ROP, 6 (18.8%) developed stage II, 7 (21.9%) developed stage III ROP. 7 babies who developed stage III ROP required laser intervention. These cases improved with laser and ROP regressed with regular follow up. All babies with stage I and II showed regression of ROP on follow up.

CONCLUSION

Retinopathy of prematurity is an important preventable cause of blindness in preterm infants. In our study the incidence of ROP came out to be 21.3%. Prematurity, low birth weight and oxygen therapy were found to be strong predictors of ROP. Sepsis, blood transfusion, apnea were found to be statistically significant factors associated with ROP.

No correlation was found between duration of oxygen therapy and association of ROP. Spontaneous regression was seen in patients with stage 1 and stage 2 ROP. Patients with stage 3 ROP were treated with laser.

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