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Study of Incidence and Risk Factors of Retinopathy of Prematurity in a Tertiary Care Hospital in Central India

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Abstract
Retinopathy of Prematurity is a leading cause of preventable childhood blindness, particularly in developing countries like India, where neonatal survival rates are improving. This study aimed to determine the incidence and risk factors for ROP in a tertiary care hospital in Central India. Methods: A two-year prospective observational study was conducted in which 158 preterm infants who met the inclusion criteria, i.e. gestational age ≤34 weeks, birth weight ≤2000 grams, or associated risk factors, were enrolled. Infants were screened as per the Rashtriya Bal Swasth Karyakram guidelines, India, and Retinopathy of Prematurity was diagnosed and graded according to the International Classification of Retinopathy of Prematurity .Data analysis was performed using Epi Info™ software. Results: The overall incidence was 27.2%, with 7% of cases presenting with aggressive posterior Retinopathy of Prematurity.Risk factors that are significantly related are preterm, low birth weight, babies receiving oxygen, having respiratory distress syndrome, neonatal sepsis, blood transfusion, anaemia and hypoglycaemia. Conclusions: The results highlight the need for early screening, strict oxygen monitoring, and timely intervention to reduce the burden of Retinopathy of Prematurity -related blindness. This study is consistent with global trends showing that the incidence in developing countries differs from that in high-income countries due to differences in the quality of neonatal care. Strengthening screening programs, increasing awareness among healthcare providers, and improving neonatal care practices are crucial to reducing the impact of Retinopathy of Prematurity in India.
Keywords: *ROP, low birth weight, gestational age, oxygen, respiratory distress.*

Introduction

Background of ROP

Retinopathy of Prematurity (ROP) is a disorder affecting premature infants, characterized by abnormal retinal vascular development, often leading to blindness. Initially described as retrolental fibroplasia (RLF) in the 1940s, it was associated with unmonitored oxygen therapy in premature infants. It was characterized by the formation of fibrous tissue behind the lens, leading to blindness and severe visual impairment.(1) Advances in neonatal care have

improved survival rates but also increased the incidence of ROP globally, making it a significant cause of childhood blindness. The condition has a broad spectrum ranging from mild transient changes to severe vasoproliferation and retinal detachment. Severe ROP contributes up to 40% of childhood blindness in affected regions.[2]

ROP remains a leading cause of preventable blindness worldwide, with higher incidence and severity in low-resource settings like India. Unlike developed countries, where ROP predominantly affects very low birth weight infants, in India, even heavier infants are susceptible.[3] Early identification of risk factors and timely intervention are critical to preventing blindness and ensuring better developmental outcomes for premature infants.

Objective of Study

1. Primary Objective: To find the incidence of retinopathy of prematurity in a tertiary eye care hospital in central India population
2. Secondary Objective: To find the risk factors for retinopathy of prematurity in a tertiary eye care hospital in central India population.

Materials and Methods

This was a prospective observational study that involved the screening and monitoring of preterm infants in the neonatal intensive care unit (NICU) of a tertiary teaching hospital in Central India over a period of two years, for the development of ROP. A minimum sample size of 65 was calculated based on prior studies (10) , using a 95% confidence interval and 10% precision. However, 158 infants were ultimately included in the study.

Inclusion Criteria

Only inborn neonatal intensive care unit (NICU) infants were included in the study that fulfilled either of the following

- All infants born at 34 weeks or less gestational age
- All infants weighing 2000 grams or less at birth
- All infants born at more than 34 weeks gestational age with associated risk factors (oxygen therapy given via mechanical ventilator/continuous positive airway pressure/ high flow nasal canula /nasal prongs/ hood for any duration, respiratory distress syndrome, multiple blood transfusions, sepsis, interventricular haemorrhage, anaemia, ductus arteriosus, hypoglycaemia)

Exclusion Criteria

Infants lost (death, lost to follow up) before complete vascularization of retina

- Infants with incomplete data on gestational age and birth weight
- Infants with ocular disorders which hinder with fundus examination
- Infants with hereditary retinal abnormalities

This Study was conducted after getting approval from institutional ethics committee and as per the guidelines of declaration of Helsinki. Data was recorded in a pre-designed proforma including baseline maternal and neonatal details (e.g., gestational age, birth weight, risk factors).Data was entered into Microsoft Excel 2019 and analysed using Epi Info™ 7.2.6.0. Associations were analysed using Pearson's chi-square and Fisher's exact tests (significance: $p<0.05$).

Study Procedures

- **Screening Schedule:**
  The first screening examination for infants was done after four weeks of birth. The main outcome was the occurrence of any ROP which was recorded according to the international classification of ROP (ICROP). In the absence of ROP the infants were followed up every week till retina maturation was complete. Infants with normal vascularization up to

periphery were not examined again. The classification of ROP was based on ROP status of the worse eye. In cases of symmetrically affected eyes, status of right eye was used. Laser photocoagulation was advised within 72 hours of diagnosis to the infants that fulfilled the criteria according to ETROP study. For examination pupillary dilation was achieved using 2.5% phenylephrine and 0.4% tropicamide and binocular indirect ophthalmoscope with a +20D lens, aided by a paediatric speculum and scleral depressor was used to evaluate the fundus. Topical antibiotic eye drops (tobramycin 0.3%) were prescribed for 7 days, post screening.

Results

Out of 158 infants **72.8% (n=115)** Developed mature retina and **27.2% (n=43)** Developed Retinopathy of Prematurity (ROP). Among the 43 infants with ROP 10.1% (n=16), were in stage 1, 7.6% (n=12) in stage 2, 2.6% (n=4) in stage 3 and 7% (n=11) **Aggressive ROP (AP-ROP)**. The earliest screening was done at 30 weeks and the last infants screened was at 40 weeks with median of 31±3.23 weeks. Maximum study subjects were screened between 35-39 weeks (43.6%, n=69) followed by 30-34 weeks (41.8%, n=66) and 14.6 % (n=23) were screened at 40 weeks. Out of the total 158 infants, male infants were 52.5% (n=83) whereas remaining 47.5% (n=75) were female. Among the 43 ROP infants there were 21 (48.8%) females and 22 (51.2%) males. With a p value >0.05, the sex has no significant association with final outcome of retina. Among the total infants screened there was almost equal distribution in the infants being born to primigravida 50.6% (n= 80) and multigravida 49.4% (n=78) mothers. Among the 43 infants that developed ROP 25 (58.1%) were outcome of a multipara pregnancy and 18 (41.9%) were outcome of primigravida pregnancy. With a p value >0.05, the type of pregnancy has no significant association with final outcome of retina.

Table 1: Distribution of infants according to Final Outcome

Final Outcome	Number of infants (n=)	Percent (%)
Mature Retina	115	72.8
ROP	43	27.2
Total	158	100.0

Table 2 : Distribution of infants according to their diagnosis

Diagnosis	Number of infants (n=)	Percent (%)
MATURE RETINA	115	72.7
STAGE 1 ROP	16	10.1
STAGE 2 ROP	12	7.6
STAGE 3 ROP	4	2.6
AGGRESSIVE - ROP	11	7.0
Total	158	100.0

Table 3: Distribution of infants according to time of screening

Time of Screening	Number of infants (n=)	Percent (%)
30-34 weeks	66	41.8
35-39 weeks	69	43.6
≥40 weeks	23	14.6
Total	158	100.0

Table 4 Distribution and association between sex of infants and final outcome

		Final Outcome		
		Mature Retina (n=115)	Retinopathy of Prematurity (n=43)	
Sex	Female infants	54	21	P value 0.833
	Male infants	61	22	
Total		115	43	

Table 5: Distribution and Association between type of pregnancy of mother and final outcome

		Final Outcome		
		Mature Retina (n=115)	Retinopathy of Prematurity (n=43)	
Type of pregnancy	Multigravida	53	25	p value 0.177
	Primigravida	62	18	
Total		115	43	

Birth weight was measured in kilograms, minimum being 0.9 kg maximum being 2.3 kg with a mean value of 1.44±0.36 kg. The minimum week at delivery was 26 weeks, maximum was 40 weeks with a median of 31±3.22 weeks. With a p value of <0.001 birth weight, gestational age at birth , use of supplemental oxygen via mechanical ventilator/continuous positive airway pressure/ high flow nasal canula /nasal prongs/ hood for any duration, respiratory distress syndrome , multiple blood transfusions , sepsis , and aneamia were all were found to be a statistically significant risk factor for development of retinopathy of prematurity. Numerically higher value of ROP infants among the non-hypoglycaemic infants could possibly be due to various other significant associated risk factors among them. With a p value of < 0.05 this association was also found to be a statistically significant risk factor for development of retinopathy of prematurity. Intraventricular haemorrhage and ductus arteriosus on the other hand were not found to be statistically significant risk factors for development of retinopathy of prematurity.

Table 6: Various risk factors and their association with ROP

Parameters	Final Outcome		
	Mature Retina (n=115)	Retinopathy of Prematurity (n=43)	
Birth Weight			
ELBW (extremely low birth weight)	1	6	Chi sq. = 32.7 P value <0.001
VLBW (very low birth weight)	52	33	
LBW (low birth weight)	62	4	
Gestational age at birth			
<30 weeks	16	24	ChiSq = 32.04 P value <0.001
31-32 weeks	40	10	
33-34 weeks	19	6	
>34 weeks	40	3	
Oxygen			
Yes	55	43	Fisher's exact P value < 0.001
No	60	0	
Respiratory Distress Syndrome			
Yes	40	35	ChiSq = 27.27 P value <0.001
No	75	8	
Neonatal Sepsis			
Yes	13	24	ChiSq = 34.57 P value <0.001
No	102	19	
Blood transfusion			
Yes	18	18	ChiSq= 12.21 P value <0.001
No	97	25	
Anaemia			
Yes	19	21	ChiSq= 17.28 P value <0.001
No	96	22	
Hypoglycemia			
Yes	57	10	ChiSq = 8.87 P value <0.05
No	58	33	
Intraventricular Haemorrhage			
Yes	25	7	ChiSq = 0.57 P value = 0.5
No	90	36	
Ductus Arteriosus			
Yes	9	2	ChiSq = 0.48 P value = 0.48
No	106	41	

Discussion

In the present study, there was no significant difference among the gender of the infants under study with male being only slightly more than females. the study conducted by Mamta C et al. [4], in North India, Yadav R et al.[5], Nepalese[6] study ,from West Bengal by Mukherjee S et al.[7] and other studies from South India[8], also reported male babies being marginally more than females in their study.

the infants under study being born were almost equally divided between primigravida and multi gravida mother. The study done by Yadav R[5], also reported similar results

The current study recorded the median gestational age at birth as 31±3.22 weeks. This result was replicated by many other previously done studies including one done by Rao et al in South India[10]. In the study done by Mamta C et al.[4], more than half neonates screened for ROP were delivered at 33-34 weeks followed by 30-32 weeks. In another Indian study by Deb D et al.[11], the mean gestational age for study group was 30.8 ± 2.3 weeks.

The present study reported almost half of study participants having very low birth weight followed by low birth weight with a mean of 1440±360 grams and minimum being only 900 grams. In the study from South India by Deb D et al.[11], 1425 ± 437.9 grams was the mean birth weight seen in their study group that was similar to our study. Another study from South India by Rao et al, the mean birth weight was 1353 ± 278 grams.(10) A study in Nepal by Bastola P et al.[12], also reported a comparative mean birth weight of 1340.66±355.10 grams. In a study conducted in North India by Tekchandani U et al.[13], the birth weight was found to be comparable to our study with mean birth weight of 1451 ± 405 grams. In the present study, study participants were screened for retinopathy of prematurity, earliest at 30 weeks, maximum between 35-39 weeks and the latest was done at 40 weeks. When the study participants in current study had their final evaluation, the final outcome saw almost 2/3rd study participants having a mature retina and the remaining quarter developing Retinopathy of Prematurity. The study conducted by Sherief S et al.[14], reported more infants having retinopathy of prematurity as compared to our present study results. Rao et al in South India reported 21.6% of study population developing any ROP and 6.7% having severe ROP.[10]. In the study done in North India by Mamta C et al.[4], the percentage of retinopathy of prematurity that developed in neonates was less as compared to our study. The study conducted by Mukherjee S et al. in West Bengal[7], 38.5% developed ROP which is more than that reported in our present study. The study by Ahuja A et al.[8], reported 32.6% eyes being affected by retinopathy of prematurity. The study conducted by Bastola P et al.[12] in Nepal reported more than half study subjects having retinopathy of prematurity in at least one eye. In the current study, Maximum had stage 1 ROP followed by Stage 2 ROP and Aggressive ROP. The North Indian study done by Mamta C et al.[4], reported more than half neonates having stage 1 ROP followed by stage 2 which was similar to the results of our present study. The study done by Tekchandani U et al.[13], reported higher percentage of incidence of ROP at 32.3% with maximum being in stage 2 at time of screening followed by aggressive posterior ROP in 20.1% cases. The study by Rao et al.[10] also reported most infants in stage 2 of disease and none progressed to stage 4 or 5. The study by Mukherjee S et al.[7], had 13.2% having severe ROP, 6.2% aggressive posterior ROP with 0.9% who had adverse outcomes. The present study tried to find out association between period of gestation and the final outcome of retina and it was seen that pre- term babies are significantly more associated with retinopathy of prematurity. The study by Tekhandani U et al.[13], and study by Ahuja A et al.[8], also had similar results. Birth weight and outcome the present study showed that the final outcome of retina is significantly associated with the birth weight of baby. Lower the birth weight, higher the chances of developing

Retinopathy of Prematurity. In the study from North India by Tekchandani U et al.[13], it was similarly observed that lower birth weight was significantly associated with development of retinopathy of prematurity. The current study reported that factors like gestational age at birth, oxygen supply at time of birth, respiratory distress syndrome, neonatal sepsis, blood transfusion, anaemia and hypoglycaemia had a significant association with the retinal outcome whereas intraventricular haemorrhage and presence of ductus arteriosus had no significant association. The study conducted by Bastola P et al.[12] reported supplemental oxygen, low birth weight, twin pregnancy, blood transfusion, sepsis, and birth asphyxia as major risk factors in development of retinopathy of prematurity. Mukherjee S et al.[7], in their study reported oxygen and prematurity as significant risk factors for developing retinopathy of prematurity. Mamta C et al.[4], reported significant association between the occurrence of retinopathy of prematurity and gestational age 1-week of total oxygen supplementation, continuous positive airway pressure (CPAP), mechanical ventilation, blood transfusion and surfactant were also significantly associated with ROP. In the study conducted by Yadav R[5], birth weight, gestational age and time span of oxygen exposure reported a strong association with retinopathy of prematurity. Multivariate analysis done by Ahuja A et al.[8], showed low birth weight to be an independent risk factor for development of retinopathy of prematurity.

Conclusion

Incidence of ROP in central India as found to be 27.2% in our in the present study is similar to those reported in northern and southern parts of India still erring on a higher side. The results of this study provide constructive information for neonatologists and ophthalmologists for clinical practice regarding the prevention of and screening for ROP in preterm infants. It was found that retinopathy of prematurity developed in higher number in infants receiving oxygen, having respiratory distress syndrome, neonatal sepsis, blood transfusion, anaemia and hypoglycaemia. Hence, improving perinatal care to reduce preterm births, optimizing treatment with effective management of sepsis and monitoring supplemental oxygen by ventilation methods are also important strategies that could reduce the incidence of ROP in developing countries like India in the coming years.

The notable short comings of this study were the sample size, single centre and lack of photographic documentation.

Strengths of the study were that only inborn babies were included, so the weight monitoring and risk factor assessment was accurate, Screening was done by a single ophthalmologist, hence ruling out any observer bias.

Author Contribution

Harsha singh: Conceptualization, Methodology, Software Data curation, Writing- Original draft preparation.Visualization, Investigation. **Minal vyawahare** Supervision.**: Piyush madan** Validation , Writing- Reviewing and Editing.

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Conflict of Interest

There are no Conflict of Interest

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