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Study of Retinopathy of Prematurity in Neonates With Unstable Clinical Course

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ABSTRACT

Background: Retinopathy of Prematurity (ROP) is a major contributor to blindness in children, especially affecting infants born prematurely. Timely identification and treatment are essential to avert permanent vision impairment. Although neonatal care has improved, ROP continues to pose a worldwide health challenge, highlighting the need for screening and awareness of risk factors.

Aim & Objectives: The objective of this study is to identify the risk factors and clinical characteristics of ROP in preterm infants at a tertiary care facility. Specific objectives include assessing the severity of ROP and its progression through follow-up evaluations.

Material and Methods: This prospective, hospital-based research was carried out over a period of 18 months and involved 100 preterm infants, each with a gestational age of less than 37 weeks and a birth weight under 2 kg. Ophthalmic examinations were performed using binocular indirect ophthalmoscopy, and data were analyzed statistically to assess associations with risk factors.

Results: Most infants were examined between 2 to 6 weeks of age, predominantly low birth weights, between 1 and 1.5 kg, born between 32 and 36 weeks gestation with risk factors such as respiratory distress and sepsis. At initial screening, 85% showed normal retinas, while 10% had Stage 1 ROP, 4% had Stage 2-3, and 1% had Stage 3+ with retinal detachment. After four weeks, 93% had normal retina, with no infants at Stage 1; two infants progressed to Stage 2. Statistical analysis showed no significant associations between most risk factors and severity.

Conclusion: Early screening is vital in managing ROP, especially in high-risk preterm infants. The multifactorial nature of ROP underscores the need for vigilant monitoring and further research to optimize prevention and treatment strategies.

Keywords: *Retinopathy of Prematurity, Neonatal Screening, Risk Factors, Preterm Infants.*

1. INTRODUCTION

Retinalopathy of prematurity (ROP), which used to be called retrolental fibroplasia, was found by seeing a complete retinal detachment (RD) behind the lens. It was originally found in premature neonates in the late 1940s. Adding more oxygen to closed incubators prompted the first rise in ROP, which raised the danger of blindness while also raising the survival rate of premature babies. [1] Low oxygen levels have been linked to higher death rates. ROP is still a problem in even the richest countries, even though the management of oxygen supplies has gotten better and other medical facilities around the world have made progress. [2] ROP is frequently divided into phases based on how bad the disease is. The most frequent way to group ROP is the International Classification of ROP (ICROP). Table 1.1 illustrates the five main stages into which ROP is separated. The classification assists in identifying the most effective treatment and care plan for neonates with ROP. To successfully diagnose and treat ROP in premature neonates, routine eye exams are required. [3]

Table 1.1: Stages of ROP

Stage	Changes seen on the Retina
1	"Demarcation line – A line demarcating normal and abnormal blood vessel growth appears"
2	"Ridge – Growth of abnormal blood vessels into the retina"
3	"Extraretinal Neovascular Proliferation"
4a	"Partial retinal detachment with foveoa sparing"
4b	"Partial retinal detachment with involvement of fovea"
5a	"Total retinal detachment in which the optic disc is visible by ophthalmoscopy"
5b	"Total retinal detachment in which the optic disc is not visible"
5c	"Total retinal detachment in which the optic disc is not visible and anterior segment abnormalities"

There are numerous established risk factors for ROP, including genetics, food, medical interventions, maternal, prenatal, and perinatal factors, and demography. The most well-known are low birth weight (BW), low GA, and fluctuating oxygen levels at birth and during the neonatal period due to oxygen supplementation. As BW and GA decline, so does the chance of severe ROP. [4]

The ROP screening requirements should be followed for two reasons. The initial efforts are to identify infants who are at risk for ROP and to constantly monitor their retinal development after birth. Finding infants that are extremely ill and in need of medical care is the second step. The primary goal of ophthalmologic screening for ROP is to detect the restoration of retinal vascular development, often known as the stage I to stage II transition. [5] While early detection is important, not all cases of ROP will need to be treated. The Early Treatment for Retinopathy of Prematurity research (ET-ROP) found that the type of ROP determines whether treatment is necessary. Type I ROP is defined as any stage of zone I ROP with plus disease, zone I stage 3 with or without plus disease, and zone II stage 2 or 3 with plus disease. All of these stages merit treatment. Zone I stage 1 or 2 without plus sickness or zone II stage 3 without addition illness are examples of Type II ROP for which observation is advised. [13] A poor visual prognosis is tightly linked to retinal detachment, the most common unfavorable consequence of ROP. [6, 7]

The current study aims to determine the prevalence, risk factors, and prognosis of babies with Retinopathy of Prematurity in our hospital. Furthermore, this study will help clinicians monitor premature children after screening to ascertain the final outcome and analyze the clinical profile of premature infants with ROP.

2. MATERIAL AND METHODS

In order to assess retinopathy of prematurity (ROP) in 100 premature newborns at risk, a prospective, hospital-based study was conducted at Muzaffarnagar Medical College over the course of 18 months. Neonatals with a gestational age of less than 37 weeks and a birth weight of less than 2 kg were the focus of the inclusion criteria, which included both inborn and outborn newborns. Prior to examination, informed parental consent was obtained, and standard ophthalmic procedures were followed. Pupils were dilated using tropicamide and phenylephrine, and topical anaesthesia was administered. The posterior pole and peripheral retina were inspected for indications of ROP, including plus disease and severity staging, using binocular indirect ophthalmoscopy with scleral depression. Descriptive statistics and chi-square tests were used to assess correlations between variables in the methodical recording and analysis of data using SPSS version 21. P-values below 0.05 were regarded as statistically significant. The institutional ethics committee granted ethical approval. In order to provide information for early detection and care, the study sought to determine the incidence, severity, and risk factors related with ROP in this high-risk neonatal population.

3. RESULTS

In present study, most infants were examined between 2 to 6 weeks of age, with the majority (74.3%) in the 2-4 weeks age group. The gender distribution shows a slight male predominance at 59%. Regarding birth weight, over half of the infants (57%) weighed between 1 and 1.5 kg, with smaller proportions weighing less (0.5-1 kg) or more (1.5-2 kg). Most babies were born between 32 and 36 weeks of gestation, indicating a predominantly moderate prematurity group. A significant majority (85%) were delivered via cesarean section, likely reflecting obstetric preferences or medical indications, while 15% were delivered vaginally. Overall, this profile helps contextualize the participants' demographic background, which is essential for understanding risk factors and interpreting the study findings regarding ROP prevalence. **(Table 1)**

Table 1: Socio-demographic profile of participants:

Variables	Number	Percentage
Age group		
0-2 weeks (inborn)	09	25.7%
2-4 weeks(inborn)	26	74.3%
Total inborn	35	100%
4-6 weeks (outborn)	38	58.5%
6-8 weeks (outborn)	14	21.5%
8-10 weeks (outborn)	13	20%
Total outborn	65	100%
Gender		
Male	59	59%
Female	41	41%
Birth weight (in kg)	**No. of cases**	**Percentage (%)**
0.5-1 kg	22	22%
1-1.5 kg	57	57%
1.5-2 kg	21	21%
Gestational age	**No. of cases**	**Percentage (%)**
24-28 weeks	11	11%
28-32 weeks	16	16%
32-36 weeks	73	73%
Mode of delivery	**No. of cases**	**Percentage (%)**
LSCS	85	85%
NVD	15	15%

Table 2 shows the distribution of participants based on their ROP severity at initial screening and after a 4-week follow-up. At the time of screening, the majority (85%) had normal retinas without ROP. A small portion had mild ROP (Stage 1 at 10%), while fewer had more severe stages (Stage 2-3 in 4%, Stage 3+ with retinal detachment in 1%). After 4 weeks, the number of infants with normal retinas increased to 93%, indicating spontaneous improvement or resolution in some cases. No infants remained at Stage 1, but 2 cases were referred for ROP at Stage 2 or higher, and 5 were referred altogether, likely due to progression or suspicion of advanced disease. This suggests that some infants' ROP either regressed or progressed, emphasizing the importance of follow-up for monitoring and timely intervention.

Table 2: Distribution of participants according to ROP grading at the time of screening and at follow up after 4 weeks:

ROP grade at the time of screening	No. of cases (n)	Percentage (%)
Normal	85	85%
Stage 1	10	10%
Stage 2-3	04	4%
Stage 3+ RD	01	1%

ROP grade at follow up after 4 weeks		
Normal	93	93%
Stage 1	00	0%
Stage 2- Refer	02	2%
Refer	05	5%

The bar graph in **Figure 1** illustrates the prevalence of various risk factors among the study participants. Each bar's length corresponds to the percentage of infants affected by that risk factor. The highest percentages are seen with a history of respiratory distress (100%) and sepsis (100%), indicating all infants had either of these conditions. A significant proportion also had a history of mechanical ventilation (66%) and phototherapy (75%). Transfusion history was noted in 32%, while congenital heart disease was less common at 16%. Use of surfactant was the least common risk factor, affecting only 7% of infants. Thrombocytopenia was present in 46%. This visual emphasizes that respiratory distress and sepsis were the most prevalent risk factors in this cohort, potentially highlighting their importance in the development or progression of ROP in these premature infants.

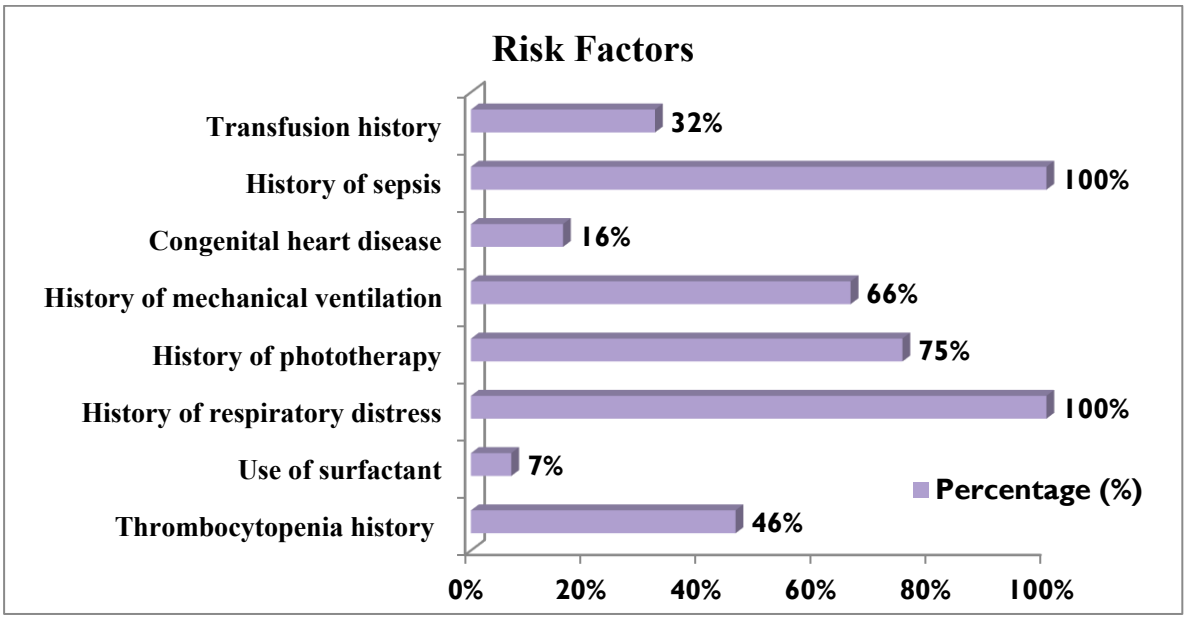

Figure 1: Distribution of participants according to presence of risk factors for ROP

Table 3 examines how various risk factors are associated with differing ROP severity stages at screening. For each factor, the distribution of infants across ROP grades (normal, Stage 1, Stage 2-3, and Stage 3+ with retinal detachment) is presented, along with p-values indicating statistical significance. None of the associations reach significance (all p-values > 0.05), suggesting no strong link between these factors and ROP severity in this study. For example, infants with a history of thrombocytopenia showed a somewhat higher proportion at higher ROP stages, but the difference wasn't statistically significant (p=0.52). Similarly, factors like surfactant use, phototherapy, mechanical ventilation, congenital heart disease, and transfusions showed no significant correlation with ROP grading. Despite observed trends, these results imply that these risk factors alone may not predict ROP severity in this cohort, emphasizing the multifactorial nature of ROP development.

Table 3: Association of risk factors with the grading of ROP at the time of screening:

RISK FACTORS	Normal	Stage 1	Stage 2-3	Stage 3+ RD
Thrombocytopenia history				
Yes	40	03	02	01
No	45	07	02	00
p value= 0.52				

Use of surfactant				
Yes	04	02	01	00
No	81	08	03	01
p value= 0.15				
History of phototherapy				
Yes	61	10	03	01
No	24	00	01	00
p value= 0.25				
History of mechanical ventilation				
Yes	54	07	04	01
No	31	03	00	00
p value= 0.41				
Congenital heart disease				
Yes	14	01	00	01
No	71	09	04	00
p value= 0.09				
Transfusion history				
Yes	23	06	02	01
No	62	04	02	00
p value= 0.06				

4. DISCUSSION

Our study compared the age of screening of inborn and out born patients. Inborn patients (n=35) were mainly screened at 2-4 weeks (74.3%), with a mean age of 2.74 weeks, indicating they were screened earlier. A study by **Kim SJ et al** highlighted that lower gestational age was a significant risk factor for ROP, with infants born before 30 weeks at higher risk. [8] The results in present study indicated that 59% of the participants were male, while 41% were female. This distribution showed a higher representation of males in the study population, with males outnumbering females by a margin of 18%. Some studies had reported a higher prevalence in male infants, while others found no significant gender differences. According to a study by **Kim SJ et al.,** there are a number of studies that suggest male gender may be a risk factor for the development of ROP. [8] Gender and the date of ROP development were not shown to be significantly correlated in a study by **Tapak L. et al**. The majority of the babies were first-born (81.4%) and male (55.3%). [9]

With 57% of individuals falling into the 1-1.5 kg birth weight range, the data from this study showed a considerable prevalence of low birth weight in the community under investigation. Of the participants, 22% were in the 0.5–1 kg group and 21% were in the 1.5–2 kg group. According to the findings, low birth weight was a known risk factor for ROP. According to a study by **Kim SJ et al**., birth weight less than 1500 g is a significant risk factor for ROP. [8] An earlier onset of ROP was significantly predicted by lower birth weight, according to a study by **Tapak L. et al**. [9]

According to our study's results, 73% of the participants were between the ages of 32 and 36 weeks, 16% of the individuals were in the 28–32 week group, and 11% were in the 24-28 week group. According to a study by **Kim SJ et al.,** babies born before 30 weeks of pregnancy were more likely to have ROP. [8] Lower gestational age was highlighted as a key predictor in the development of ROP in the **Yucel Y et al.** study. 28 ELGA infants with a median GA of 24 (22–25) w and 347 ELBW infants with a median BW of 800 (540–1000) g were present. [10]

In our study, the distribution of ROP grading at the initial screening showed that a significant proportion of preterm infants did not develop ROP at the time of the first screening, but 15% had some degree of ROP, requiring continued monitoring. The findings indicated that a significant majority, 85%, of participants were classified as normal, showing no signs of ROP.

Stage 1 ROP was observed in 10% of participants, while 4% were into the Stage 2-3 category. Only 1% of participants were classified as having Stage 3+ with Retinal Detachment (RD). **Good WV et al** reported an overall ROP incidence of 15–35% in screened preterm neonates, with Stage 1 ROP being most common at initial screening. [11] **Reynolds JD et al** found that 10–20% of neonates screened for ROP show Stage 1 or Stage 2 ROP, similar to this study's findings. [12] The results of our study indicated a positive trend in the participants' eye health at follow up, with 93% classified as normal, showing no signs of ROP. **Good WV et al** reported that Stage 3 ROP requires intervention in 10–15% of cases, comparable to the 10% treatment rate observed in this study. [11]

In our study, 100% of the participants had a history of respiratory distress and history of sepsis, indicating that these conditions are universal among the study group and are significant risk factors for ROP. Additionally, 75% of participants have a history of phototherapy, and 66% have a history of mechanical ventilation. A research by **Kim SJ et al** identified prolonged mechanical ventilation as a significant risk factor for severe ROP. [8] A study by **Tapak L et al** found that the duration of mechanical ventilation was a significant predictor for the time to ROP development. [9] Sepsis, a severe infection, has been identified as a risk factor for ROP due to its association with systemic inflammation and instability. A research by **Kim SJ et al** found that neonatal infections (e.g., sepsis) significantly increase ROP risk. [8] **Tang W et al.** came to the conclusion that high postpartum oxygen levels, low birth weight, and early birth were independent risk factors for ROP. ROP may also be linked to laboratory markers in premature newborns, including platelet count, blood glucose, inflammatory cell, lipid, hemoglobin, and blood transfusion levels. [13]

5. CONCLUSION

Early ROP screening is crucial for preterm newborns, particularly those with low birth weight and gestational age, as this hospital-based study makes clear. Even though sepsis, respiratory distress, and maternal health issues were common risk factors, none of them significantly affected the severity of ROP. The results highlight the complex nature of ROP and support prompt intervention, careful screening, and additional study to identify underlying causes for improved treatment and results.

6. LIMITATIONS OF THE STUDY

As our sample size was only 100, the results may not be as broadly applicable. Its application to other areas with different populations and healthcare resources is further limited by the fact that research was carried out at a single tertiary care hospital. Due to the short follow-up period, late progression or late-onset ROP problems may have gone unnoticed. Also, an important component of comprehensive care, the present study did not assess the affected infants' long-term visual and functional outcomes.

7. RELEVANCE OF THE STUDY

This study is essential because it will help pediatricians to detect, understand, and treat Retinopathy of Prematurity (ROP) early, which is a major cause of childhood blindness that could have been averted. Our study showed that many babies who were born too early had the same risk factors. It is very important to take proper care of babies and have regular eye examination to avoid ROP development. This study also provides useful information for different screening processes that can decrease the number of people who lose their vision because of ROP by giving better care to newborns and getting them aid as soon as possible.

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Conflict of interest: None declared

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