Section: Ophthalmology

Original Research Article

EPIDEMIOLOGY AND RISK DETERMINANTS OF RETINOPATHY OF PREMATURITY IN A TERTIARY NEONATAL COHORT

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Received *: 05/07/2025*
Received in revised form *: 23/08/2025*
Accepted *: 11/09/2025*

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DOI: 10.70034/ijmedph.2025.3.566

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (3); 3085-3089

ABSTRACT

Background: Retinopathy of prematurity (ROP) has emerged as a significant cause of avoidable childhood blindness worldwide, particularly in middle-income countries where neonatal survival has improved. Early identification of high-risk neonates is essential to initiate timely interventions and prevent irreversible visual disability. This study evaluated the incidence and clinical profile of ROP among premature neonates in a tertiary care hospital setting.

Materials and Methods: This prospective observational study was carried out in the Department of Ophthalmology from July 2024 to June 2025. Infants with gestational age <37 weeks or birth weight ≤2000 g admitted to the neonatal intensive care unit (NICU) were enrolled. Fundus screening was initiated at 4 weeks of postnatal age using indirect ophthalmoscopy and findings were staged according to the International Classification of ROP (ICROP-3). Demographic details, perinatal factors, and ROP severity were documented. Statistical analysis was performed with SPSS version 26.0.

Results: A total of 312 premature infants were screened, of whom 79 (25.3%) developed ROP. The average gestational age among affected infants was 31.2 ± 2.3 weeks, and mean birth weight was 1310 ± 190 g. Stage I disease was the most frequent (41 infants, 51.9%), followed by Stage II (21 infants, 26.6%) and Stage III or higher (17 infants, 21.5%). Severe ROP requiring treatment was noted in 18 infants (22.8% of affected cases). Statistically significant associations were found with gestational age ≤32 weeks ($p<0.001$), birth weight ≤1500 g ($p=0.003$), oxygen supplementation beyond 7 days ($p=0.014$), and sepsis ($p=0.028$).

Conclusion: The incidence of ROP in this neonatal cohort was 25.3%, with nearly one-quarter progressing to severe forms requiring intervention. These findings highlight the critical importance of early screening and stringent neonatal care protocols in reducing the burden of preventable blindness.

Keywords: Retinopathy of prematurity, prematurity, neonatal intensive care, incidence, screening, risk factors.

INTRODUCTION

Retinopathy of prematurity (ROP) is a vasoproliferative disorder of the immature retina that primarily affects preterm and low birth weight infants. It remains a leading cause of preventable childhood blindness worldwide and has been increasingly recognized as a significant public health challenge in developing countries.[1] Improvements in neonatal intensive care services have led to increased survival of premature infants, particularly those born at earlier gestational ages and with lower birth weights, but this has paradoxically contributed to a rising incidence of ROP.[2]

The pathophysiology of ROP is multifactorial and involves abnormal retinal vascular development

triggered by fluctuating oxygen levels, oxidative stress, and systemic morbidity in premature infants.[3] In the normal fetus, retinal vascularization is completed near term. However, preterm birth interrupts this process, and subsequent exposure to supplemental oxygen, infections, or poor postnatal weight gain can initiate aberrant angiogenesis, leading to fibrovascular proliferation, retinal detachment, and blindness if untreated.[4]

Globally, the burden of ROP has been described in terms of three epidemiological "waves." The first wave was reported in high-income countries in the 1940s and 1950s, where unmonitored oxygen therapy caused epidemic blindness. The second wave occurred in the 1970s and 1980s as advanced neonatal care enabled survival of extremely preterm infants. Currently, a "third epidemic" of ROP is unfolding in low- and middle-income countries (LMICs), particularly in South Asia and Latin America, where neonatal care facilities have improved but systematic screening programs are not uniformly established.[5,6]

India accounts for a significant proportion of the global burden of ROP, with estimates suggesting that up to 40% of blindness in preterm children is attributable to this condition.[7] The incidence varies widely across centers, ranging from 20% to 50%, depending on neonatal practices, availability of trained ophthalmologists, and screening protocols.[8] The Indian scenario is particularly concerning because larger and more mature infants, who would not traditionally be considered at risk in high-income countries, also develop severe ROP.[9]

Several risk factors for ROP have been consistently reported, including low gestational age, low birth weight, prolonged oxygen therapy, sepsis, blood transfusions, and poor postnatal growth.[10] Identifying these factors in a regional context is essential for designing effective prevention and intervention strategies. Timely screening and treatment, particularly with laser photocoagulation or intravitreal anti-VEGF therapy, can prevent disease progression and preserve vision in the majority of cases.[11]

Despite the availability of guidelines, adherence to ROP screening protocols remains suboptimal in many Indian neonatal units. This underscores the need for hospital-based epidemiological data to guide policy and practice. Against this background, the present study was undertaken to determine the incidence and clinical profile of ROP among premature neonates admitted to a tertiary care hospital.

The findings aim to strengthen the evidence base for systematic screening and contribute to the prevention of avoidable childhood blindness in India.

MATERIALS AND METHODS

Study Design and Setting: This was a prospective observational study conducted in the Department of Ophthalmology, in collaboration with the Neonatal Intensive Care Unit (NICU) of XXXXX college. The study was carried out over a one-year period, from July 2024 to June 2025. The primary objective was to determine the incidence and clinical profile of retinopathy of prematurity (ROP) among premature neonates admitted during the study period.

Study Population: All preterm neonates with a gestational age less than 37 completed weeks and/or a birth weight ≤2000 g were eligible for inclusion. Infants with congenital ocular anomalies (e.g., coloboma, congenital cataract, microphthalmia) or those deemed unfit for ocular examination due to systemic instability were excluded. Written informed consent was obtained from parents or guardians prior to enrollment.

Screening Protocol: Ocular screening was initiated at 4 weeks of chronological age or at 31 weeks of postmenstrual age, whichever was later, in accordance with national guidelines. Indirect ophthalmoscopy was performed using a +28D condensing lens and a pediatric lid speculum under topical anesthesia with 0.5% proparacaine eye drops. The retina was examined in all quadrants, with special attention to the posterior pole and peripheral zones. Pupillary dilation was achieved using tropicamide (0.5%) and phenylephrine (2.5%) instilled 30 minutes prior to the examination.

ROP staging and zone classification were documented according to the International Classification of Retinopathy of Prematurity, third edition (ICROP-3). The presence of plus disease, pre-plus changes, or aggressive posterior ROP was specifically recorded. Each infant underwent repeat examinations at 1–2 week intervals until complete vascularization of the retina or regression of disease was noted. Infants requiring treatment were managed with laser photocoagulation or intravitreal anti-VEGF injection as per standard guidelines.

Data Collection: Detailed perinatal and neonatal information was collected, including gestational age, birth weight, gender, mode of delivery, Apgar scores, duration of oxygen therapy, need for mechanical ventilation, sepsis, intraventricular hemorrhage, and blood transfusions. Maternal factors such as antenatal steroid use, multiple gestations, and pregnancy-induced hypertension were also recorded. All data were compiled using a structured proforma and entered into Microsoft Excel 2019 for analysis.

Statistical Analysis: Data analysis was performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables such as gestational age and birth weight were expressed as mean ± standard deviation. Categorical variables were summarized as frequencies and percentages. The incidence of ROP was calculated as the proportion of affected infants among the total screened cohort. Group comparisons between ROP and non-ROP infants were carried out using the chi-square test or Fisher's exact test for categorical variables, and independent-sample t-test for continuous variables. Logistic regression analysis

was applied to identify independent predictors of ROP. A p-value of <0.05 was considered statistically significant.

Ethical Considerations: The study protocol was reviewed and approved by the Institutional Ethics Committee prior to initiation. Written informed consent was obtained from the parents or legal guardians of all enrolled neonates, ensuring confidentiality and the right to withdraw at any stage without compromise in clinical care.

RESULTS

A total of 312 premature infants meeting the inclusion criteria were screened during the study period. The overall incidence of ROP was 25.3% (79/312). The mean gestational age of the cohort was 32.4 ± 2.6 weeks, and the mean birth weight was 1480 ± 280 g. Among infants who developed ROP, both gestational age and birth weight were significantly lower compared to those without ROP (p<0.001).

Table 1: Baseline Demographic Characteristics of Study Population

Variable	Total (N=312)	ROP (n=79)	No ROP (n=233)	p-value
Mean gestational age (weeks)	32.4 ± 2.6	31.2 ± 2.3	32.8 ± 2.5	<0.001
Mean birth weight (g)	1480 ± 280	1310 ± 190	1535 ± 270	<0.001
Male gender (%)	178 (57.0)	46 (58.2)	132 (56.6)	0.81
Cesarean delivery (%)	162 (51.9)	41 (51.9)	121 (52.0)	0.98

Table 2: Incidence and Severity of ROP (n=79)

Stage of ROP	Number of Infants	Percentage (%)
Stage I	41	51.9
Stage II	21	26.6
Stage III or higher	17	21.5
Total	**79**	**100**

Table 3: Neonatal Risk Factors Associated with ROP

Risk Factor	ROP (n=79)	No ROP (n=233)	p-value
Oxygen therapy >7 days (%)	42 (53.2)	65 (27.9)	0.014
Mechanical ventilation (%)	18 (22.8)	24 (10.3)	0.012
Sepsis (%)	27 (34.2)	39 (16.7)	0.028
Blood transfusion (%)	21 (26.6)	32 (13.7)	0.021

Table 4: Logistic Regression Analysis of Independent Predictors of ROP

Variable	Adjusted Odds Ratio (OR)	95% CI	p-value
Gestational age ≤32 wks	2.91	1.62–5.21	<0.001
Birth weight ≤1500 g	2.47	1.31–4.15	0.003
Oxygen therapy >7 days	1.98	1.12–3.22	0.014
Sepsis	1.76	1.05–3.01	0.028

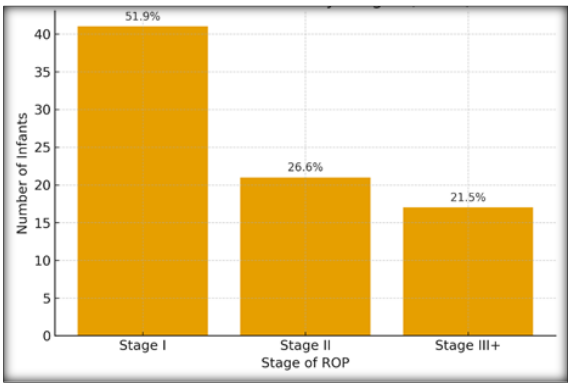

Figure 1: Distribution of ROP by Stages (n=79)

Of the 312 premature infants screened, 79 (25.3%) developed ROP. The mean gestational age among ROP infants was 31.2 ± 2.3 weeks, significantly lower than the non-ROP group (32.8 ± 2.5 weeks, p<0.001). Similarly, the mean birth weight of affected infants was 1310 ± 190 g, compared to 1535 ± 270 g in those without ROP (p<0.001).

Among infants with ROP, Stage I disease was the most common, affecting 41 infants (51.9%), followed by Stage II in 21 infants (26.6%), and Stage III or higher in 17 infants (21.5%). Severe ROP requiring treatment was observed in nearly one-quarter of affected neonates.

Analysis of neonatal risk factors revealed that prolonged oxygen therapy (>7 days) was present in 53.2% of ROP infants, compared to 27.9% of non-ROP infants (p=0.014). Mechanical ventilation was also more frequent among affected infants (22.8% vs 10.3%, p=0.012). Additionally, 34.2% of ROP infants had sepsis, compared to 16.7% in non-ROP infants (p=0.028). The need for blood transfusions was similarly higher in the ROP group (26.6% vs 13.7%, p=0.021).

Multivariate logistic regression identified four independent predictors of ROP: gestational age ≤32 weeks (OR 2.91, 95% CI: 1.62–5.21, p<0.001), birth weight ≤1500 g (OR 2.47, 95% CI: 1.31–4.15, p=0.003), oxygen therapy beyond 7 days (OR 1.98, 95% CI: 1.12–3.22, p=0.014), and sepsis (OR 1.76, 95% CI: 1.05–3.01, p=0.028).

These findings demonstrate that lower gestational age, low birth weight, prolonged oxygen exposure, and systemic infections significantly increase the risk of ROP in this population. The overall incidence of

25.3% reflects the continuing burden of ROP in tertiary care neonatal units, underscoring the need for rigorous screening protocols.

DISCUSSION

Retinopathy of prematurity (ROP) continues to be one of the most important avoidable causes of childhood blindness, particularly in countries with improving neonatal survival rates. The present study, conducted at a tertiary care hospital in South India, sought to estimate the incidence of ROP and identify key risk determinants in premature infants.

The rationale for this investigation stemmed from the growing recognition of a "third epidemic" of ROP in low- and middle-income countries, where increased availability of neonatal intensive care has not always been accompanied by robust screening protocols.[12] This imbalance results in survival of vulnerable preterm neonates at high risk of vision-threatening ROP. Our study adds valuable evidence from a regional cohort, demonstrating an incidence of 25.3%, with nearly one-quarter of affected infants requiring treatment.

The incidence observed here aligns with previous Indian studies reporting rates between 20% and 50%.[13,14] While our findings are comparable to those from urban NICU-based cohorts, they are lower than some reports from smaller centers where ROP incidence is considerably higher, likely due to variations in oxygen monitoring and neonatal care practices.[15] The predominance of early-stage disease in our series, with Stage I accounting for 51.9% of cases, is consistent with other prospective studies where the majority of infants present with milder disease that regresses spontaneously.[16] However, the proportion progressing to severe ROP (21.5%) underscores the ongoing need for vigilant follow-up.

Risk factor analysis revealed that low gestational age and birth weight were the strongest predictors of ROP, findings that have been consistently corroborated in international literature.[17] Prolonged oxygen exposure emerged as another significant factor, echoing historical and contemporary evidence that unregulated oxygen supplementation is a central driver of ROP pathogenesis.[18] Sepsis and blood transfusion were also associated with increased risk, supporting prior reports that systemic instability and oxidative stress augment susceptibility.[19]

From a clinical perspective, these results reinforce the critical role of timely screening in at-risk neonates, particularly those ≤32 weeks gestation or ≤1500 g at birth. The identification of modifiable factors such as oxygen therapy and infection control highlights opportunities for preventive interventions at the NICU level. Adherence to established screening guidelines, coupled with availability of treatment modalities such as laser photocoagulation and anti-VEGF injections, can substantially reduce the burden of ROP-related blindness [20].

This study has certain limitations. Being a single-center study, the findings may not fully reflect population-level trends. The relatively small sample size of affected infants may have limited the power to detect weaker associations. Additionally, follow-up beyond the neonatal period was not within the study scope, preventing assessment of long-term visual outcomes.

CONCLUSION

This prospective study demonstrated that the incidence of retinopathy of prematurity in our tertiary care neonatal cohort was 25.3%, with nearly one-quarter of affected infants requiring treatment. Lower gestational age, low birth weight, prolonged oxygen therapy, and neonatal sepsis emerged as significant independent predictors. The majority of cases presented in early stages; however, a substantial proportion progressed to severe disease, highlighting the necessity of strict surveillance.

Our findings underscore the critical importance of rigorous ROP screening protocols tailored to the Indian context, where more mature and heavier infants are also at risk. Preventive strategies such as careful oxygen monitoring and infection control can substantially reduce disease burden. Strengthening neonatal screening services, enhancing parental awareness, and ensuring timely availability of treatment modalities are essential to reducing preventable blindness from ROP. Future multicenter studies are warranted to provide national-level data and guide policy formulation.

Acknowledgements

The authors thank the departmental staff for their assistance during examinations, and the parents who consented to participate in the study.

Conflicts of Interest

The authors declare there are no conflicts of interest related to this study.

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