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Original Research Article

A STUDY OF CLINICAL FEATURES OF RETINOPATHY OF PREMATURITY IN PRETERM NEONATES IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Purpose: To evaluate the clinical profile of retinopathy of prematurity (ROP) among preterm neonates in a tertiary care hospital in Central India, and to analyze associations with gestational age, gender, disease severity, spontaneous regression, follow-up adherence, and treatment modalities.

Materials and Methods: A prospective observational study was conducted from September 2023 to October 2024 at MGM Medical College and MY Hospital, Indore. A total of 200 preterm neonates meeting ROP screening criteria were enrolled. Detailed demographic and clinical data were recorded. All infants underwent serial retinal examinations using indirect ophthalmoscopy. ROP staging was done per the International Classification, and management followed ETROP guidelines. Data were analyzed using SPSS v20 and p-value<0.05 was considered statistically significant.

Results: ROP was detected in 102 infants (51%). Male infants had a significantly higher incidence (60%) compared to females (37.5%) (p=0.0029). Highest ROP incidence occurred in the 34–37-week gestational group (65%), followed by <28 weeks (42.8%). Severe ROP (Stage 3–5) was more frequent in infants <28 weeks (p=0.041). Overall spontaneous regression occurred in 43.1%, most notably in Stage 1 (68.6%). Follow-up adherence declined to 48% by 12 weeks. Laser photocoagulation was the primary treatment (23.5%), followed by anti-VEGF (9.8%); surgery was required in 3.9% of cases.

Conclusion: ROP remains a significant concern in preterm infants, including late-preterms. Male sex and lower gestational age were key risk factors. While mild ROP often regressed, advanced cases required timely intervention. Strengthening screening and follow-up systems is critical to reducing ROP-related visual morbidity.

Keywords: Retinopathy of prematurity, preterm neonates, follow-up.

INTRODUCTION

Retinopathy of prematurity (ROP) is a vaso-proliferative disorder of the developing retinal vasculature in premature infants and a leading cause of preventable childhood blindness worldwide.[1] It arises from interruption of normal retinal vascularization due to premature birth, progressing through an initial phase of hyperoxia-induced vaso-obliteration of retinal vessels after premature exposure to supplemental oxygen, followed by hypoxia-driven pathological neovascularization at the junction of vascular and avascular retina, which can lead to retinal detachment if untreated.[1] Major risk factors include low gestational age, very low birth weight, and prolonged oxygen therapy.[1]

With improvements in neonatal intensive care, the survival of premature infants has increased, especially in middle-income countries, inadvertently increasing the population at risk for ROP.[1,2] Globally, it is estimated that approximately 184,700 infants developed ROP in 2010, with 20,000 cases of blindness or severe visual impairment.[3] Approximately one-third of at-risk infants develop ROP, with 7–8% requiring treatment.[4] The World Health Organization recognizes ROP as a major contributor to childhood visual disability, particularly in countries experiencing a "third epidemic" due to increased preterm survival without comprehensive screening coverage.[2,5]

India contributes the highest number of preterm births globally, with approximately 3.5 million annually.[5] Studies report ROP incidence between 2% and 47%, influenced by screening criteria and care quality.[6] Unlike in developed countries, larger and more mature preterm infants in India are also affected, warranting broader screening protocols 10. Each year, ~5,000 Indian infants require treatment for severe ROP.[5]

In Central India, regional data indicate ROP incidence of approximately 30%,[7] with over 14% progressing to severe stages in eastern Madhya Pradesh.[2] However, many cases present late due to poor awareness, lack of trained ophthalmologists, and limited access to screening and treatment facilities.[2,5] Recognizing these gaps, national health programs in India, such as the Rashtriya Bal Swasthya Karyakram, have recently prioritized ROP screening and are working to integrate ROP management into the public healthcare system,[1] Nevertheless, implementation of universal ROP screening is still far from complete, and challenges continue to hamper early detection efforts,[1] Thus, the present study explores the clinical profile of ROP in preterm neonates at a tertiary care hospital in Madhya Pradesh to inform local strategies for early detection and prevention of ROP-related blindness.

MATERIALS AND METHODS

This hospital-based prospective observational study was conducted in the Department of Ophthalmology, MGM Medical College and MY Hospital, Indore between September 2023 and October 2024, after approval from the Institutional Ethics Committee. The study included 200 preterm neonates admitted to the Neonatal Intensive Care Unit (NICU) and Special Newborn Care Unit (SNCU) during the study period who fulfilled the screening criteria for retinopathy of prematurity (ROP). Infants with gestational age ≤34 weeks or birth weight ≤2000 g, as well as those >34 weeks with significant systemic risk factors, were enrolled after obtaining informed written consent from parents or guardians. Neonates with congenital ocular anomalies or media opacities precluding fundus evaluation were excluded.

Detailed perinatal, neonatal, and maternal information was recorded using a structured proforma. All infants underwent dilated fundus examination starting at 30–31 weeks postmenstrual age or by 4 weeks chronological age, whichever was later, following standard examination protocols. Pupillary dilation was achieved using 2.5% phenylephrine and 1% cyclopentolate eye drops, administered twice at 15-minute intervals. Indirect ophthalmoscopy was performed using a 20D lens by a trained ophthalmologist, with each infant monitored for apnoea or bradycardia during the procedure.

ROP was documented and staged according to the International Classification of Retinopathy of Prematurity (ICROP), grading the disease by zone, stage, and presence of plus or pre-plus disease. Infants were followed at intervals determined by the initial findings, ranging from weekly to biweekly examinations until complete retinal vascularization or regression of disease was observed. Treatment decisions were based on the Early Treatment for Retinopathy of Prematurity (ETROP) criteria, and included laser photocoagulation or intravitreal anti-VEGF injection when indicated.

Data were compiled and analysed using SPSS v20 (trial version). Chi-square test was applied for association. $P<0.05$ was considered statistically significant.

RESULTS

Out of 200 premature infants (120 males and 80 females) evaluated during the study period, 102 (51.0%) were diagnosed with ROP. Table 1 depicts the distribution of ROP among male and female preterm neonates. ROP was identified in 72 males (60%) and 30 females (37.5%). The difference was statistically significant (p=0.0029), indicating that male infants were more likely to develop ROP than female infants. Table 2 depicts the incidence of ROP across different gestational age groups. The highest incidence was observed among infants born at 34–37 weeks (65%). Infants <28 weeks had an incidence of 42.8%, whereas those between 28–34 weeks showed an incidence of 40%. The association was statistically significant (p=0.003). Table 3 depicts the severity distribution of ROP stages in relation to gestational age. Severe stages (3–5) were more commonly observed in the <28-week group, including Stage 5 in 4 cases and plus disease in 6 cases. The association was statistically significant (p=0.041). Table 4 depicts the pattern of spontaneous regression of ROP across stages during follow-up. Overall regression was observed in 43.1% of cases. Regression was highest in Stage 1 (68.6%), followed by Stage 2 (47.6%). More advanced stages showed poor regression rates—Stage 3 (30.8%), Stage 4 (14.3%), and no regression

in Stage 5 (0%). Plus disease showed limited regression (31.3%). Table 5 depicts the follow-up adherence of ROP infants over 12 weeks. While 100% follow-up was achieved at the 4-week visit, follow-up declined to 76 infants (74.5%) at 8 weeks and 49 infants (48%) at 12 weeks. Attrition was seen across all stages, but more severe ROP (Stages 4–5) retained slightly better follow-up due to greater clinical concern. Table 6 depicts the distribution of treatment modalities among infants diagnosed with ROP. A majority (62.7%) required only observation as their disease regressed spontaneously. Among those requiring active intervention, laser photocoagulation was the most commonly used modality (23.5%), followed by intravitreal anti-VEGF injections (9.8%). Combined treatment (laser + anti-VEGF) and vitreoretinal surgery were needed in 3.9% of cases each.

Table 1: Gender-wise Distribution of ROP Among Screened Preterm Infants

Gender	Total Screened (N)	Diagnosed cases of ROP (n)	p-value
Male	120	72 (60%)	0.0029
Female	80	30 (37.5%)	
Total	200	102 (51%)	

Table 2: Incidence and Distribution of ROP Across Gestational Age Categories

Gestational Age (weeks)	Total Screened (N)	Diagnosed cases of ROP (n)	Incidence (%)	Proportion of Total ROP (%)	p-value
<28 weeks	70	30	42.8%	29.4%	0.003
28-34 weeks	50	20	40%	19.6%	
34-37 weeks	80	52	65%	51.0%	
Total	200	102	51%	100%	

Table 3: Distribution of ROP Stages According to Gestational Age

Gestational Age (weeks)	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	Plus disease	Total	p-value
<28 weeks	7	7	5	1	4	6	30	0.041
28-34 weeks	7	3	3	2	2	3	20	
34-37 weeks	21	11	5	4	4	7	52	
Total	35	21	13	7	10	16	102	

Table 4: Regression Pattern of ROP at 4, 8, and 12 Weeks of Follow-Up by Stage

Stage of ROP	Total Cases (n)	Regression at 4 Weeks (n)	Regression at 8 Weeks (n)	Regression at 12 Weeks (n)	Total Regression (n)	Regression (%)
Stage 1	35	12	8	4	24	68.6%
Stage 2	21	4	4	2	10	47.6%
Stage 3	13	1	2	1	4	30.8%
Stage 4	7	0	1	0	1	14.3%
Stage 5	10	0	0	0	0	0%
Plus Disease	16	2	2	1	5	31.3%
TOTAL	102	19	17	8	44	43.1%

Table 5: Follow-Up Status of Infants with ROP at 4, 8, and 12 Weeks by Stage

Stage of ROP	Total Cases (n)	Follow-up at 4 Weeks (n)	Follow-up at 8 Weeks (n)	Follow-up at 12 Weeks (n)
Stage 1	35	35	20	10
Stage 2	21	21	15	8
Stage 3	13	13	12	8
Stage 4	7	7	6	5
Stage 5	10	10	9	8
Plus Disease	16	16	14	10
TOTAL	102	102	76	49

Table 6: Treatment Modalities Among Infants Diagnosed with ROP

Treatment Modality	Number treated (n)	Percentage (%)
Follow-up Only (No Active Treatment)	64	62.7%
Laser Photocoagulation	24	23.5%
Intravitreal Anti-VEGF Injection	10	9.8%
Combined Laser + Anti-VEGF	4	3.9%
Vitro-Retinal Surgery (for Stage 4–5)	4	3.9%
TOTAL	102	100%

DISCUSSION

In present study, male preterm infants exhibited a significantly higher incidence of ROP than females (60% vs 37.5%). This finding aligns with several Indian reports suggesting male neonates may be more vulnerable to ROP. Tekchandani et al,[8] in North India similarly found a higher proportion of severe ROP in male infants (59.5%) compared to females (47.9%). Bhat and Patil,[9] identified male

gender as an independent risk factor for ROP development in larger preterm infants (birth weight >1500 g). Similarly, Balamurali et al,[10] noted a male predominance with 65% of ROP cases occurring in males, although without statistically significant gender correlation.

Present study observed the highest ROP incidence in the late-preterm group (34–37 weeks, 65%), which contributed over half of all ROP cases, despite traditionally lower risk in more mature infants. While ROP risk classically increases with decreasing gestational age, Indian data have shown that even moderately preterm infants can carry substantial risk. For instance, Nayyar et al,[11] reported that 52% of sight-threatening ROP cases in a North Indian unit occurred in infants 31–33 weeks' gestation, and 15% in those beyond 34 weeks. They attributed this shift to a "third epidemic" of ROP in middle-income countries, where improved survival of larger preterms combined with variable neonatal care has led to ROP affecting higher gestations.[8,12] Consistent with global trends, our study still found an inverse association between gestational age and ROP (incidence 42.8% in <28 weeks vs ~40% at 28–34 weeks, p=0.003). However, the presence of severe ROP even in late preterms underscores the need to broaden screening criteria in the Indian context. Recent studies have echoed this, calling for screening beyond 34 weeks in at-risk infants,[8] so that no vulnerable infant is missed.

The distribution of ROP severity in present stufy further demonstrated the impact of prematurity on disease stage. Extremely preterm babies (<28 weeks) had disproportionately more advanced ROP in our study, whereas late-preterm infants more often manifested Stage 1–2. This trend concurs with other reports. Ahuja et al,[12] found that only approximately 13% of ROP cases reached Stage ≥3, reflecting that the smallest, most immature infants formed a smaller subset of their screened population. By contrast, Tekchandani et al,[8] noted a higher burden of advanced stages at a tertiary center, with Stage 4–5 comprising about 20% of ROP cases. Many of those infants were born elsewhere and referred late, as evidenced by 15.6% presenting for the first time with Stage 4B/5 in that series. These observations show that when ROP screening is delayed or missed, more infants may end up being diagnosed at later, more severe stages of the disease. In present study, the association between lower gestational age and higher ROP stage was significant (p=0.041), reinforcing that extreme prematurity remains a principal determinant of severe retinopathy of prematurity. Nonetheless, the occurrence of a few advanced ROP cases even among 34–37 week infants in our cohort echoes the findings of Nayyar et al,[11] that occasionally, severe ROP can develop in bigger preterms. Thus, although the most premature neonates are at highest risk for aggressive ROP, the possibility of severe disease in relatively more mature preterm infants cannot be overlooked—particularly in Indian NICU settings where neonatal care practices may be inconsistent or suboptimal.

The ROP in present study showed substantial spontaneous regression, especially in early stages. By 12 weeks follow-up, 43.1% of all ROP cases had regressed without treatment. Most of these were low-grade. Nearly 69% Stage 1 and 48% Stage 2 ROP resolved spontaneously. This aligns with the well-established natural course of mild ROP, wherein most cases are self-limiting and tend to regress spontaneously as retinal vascularization progresses.[12] Indian screening studies likewise report that only a minority of infants with ROP progress to require intervention. Bhat and Patil,[9] observed that only about 6% of screened preterms needed treatment, implying over 90% of at-risk infants had either no ROP or disease that regressed on its own. In our cohort, roughly 63% of infants diagnosed with ROP were managed with observation alone, as their disease involuted spontaneously over the follow-up period. However, once ROP advanced to Stage 3 or beyond, spontaneous regression became rare. None of the Stage 5 cases regressed without treatment in present study. This underscores the importance of timely therapeutic intervention for high-grade ROP.

The present study achieved 100% follow-up at 4 weeks, as the initial screenings occurred during NICU hospitalization, but subsequent visits saw significant attrition. Only 74.5% of infants returned at 8 weeks, and just 48% by 12 weeks. Such loss to follow-up is a common challenge in ROP care across developing regions. Sinha et al,[13] reported about 71% follow-up compliance among ROP-diagnosed infants, with dropouts mainly attributed to financial hardship (26% of those lost), lack of parental understanding of ROP (22%), and transportation difficulties (19%). The consequences of poor follow-up can be severe. Tekchandani et al,[8] noted that 15.6% of their infants who missed timely screening eventually presented with end-stage ROP (Stage 4B/5). Studies have shown that proactive engagement can dramatically improve retention. Belenje et al,[14] discussed that follow-up compliance can be increased by providing robust parental counselling, phone reminders, and coordination with local healthcare workers. This highlights that improving follow-up is as crucial as the clinical management itself.

The treatment patterns observed in our study are consistent with current ROP management practices across India. Active intervention was required in 37% of cases, with laser photocoagulation being the primary modality (23.5%), followed by intravitreal anti-VEGF therapy (9.8%), combined treatment (3.9%), and vitreoretinal surgery for advanced stages (3.9%). This mirrors findings by Bhat and Patil,[9] who reported Stage III ROP in ~20% and aggressive ROP in 14% of cases—most managed with laser—and a low rate (0.6%) of Stage 5 ROP, indicating effective early intervention. Similarly,

Tekchandani et al,[8] found 86% of treatment-requiring cases responded well to laser or bevacizumab, with few progressing to surgery. These findings underscore that timely laser therapy, supplemented by anti-VEGF agents when needed, remains the cornerstone of ROP care in India, enabling favourable outcomes in most at-risk infants.[8,9]

CONCLUSION

This study highlights a substantial burden of ROP among preterm infants, including in late-preterm neonates, underscoring the need for broad and timely screening strategies in Indian NICUs. Male gender and lower gestational age were significantly associated with higher ROP incidence and severity. While early-stage ROP frequently regressed without intervention, advanced stages required active treatment, with laser photocoagulation remaining the mainstay. High attrition in follow-up emphasizes the need for strengthened parental counselling and follow-up systems. Thus, early detection and intervention remain critical to preventing ROP-related blindness in vulnerable neonates.

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