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Original Research Article

Analyzing the Incidence and Risk Factors of Retinopathy in Premature Infants

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Abstract

Background: Retinopathy of prematurity is a leading cause of preventable childhood blindness, particularly among preterm and low birth weight neonates. Understanding its incidence and associated risk factors is essential for effective screening and prevention.

Objectives: To determine the incidence of retinopathy of prematurity in preterm and low birth weight neonates and to assess the association between various perinatal and neonatal risk factors with its occurrence.

Material and Methods: This prospective observational study included 520 preterm and/or low birth weight neonates admitted to a tertiary care neonatal intensive care unit. All eligible neonates underwent serial retinal examinations, and relevant maternal and neonatal risk factors were analyzed.

Results: Retinopathy of prematurity was diagnosed in 84 neonates, with an incidence of 16.15%. Lower gestational age, lower birth weight, prolonged oxygen therapy, and respiratory distress syndrome were significantly associated with ROP development, while sex, twin status, prenatal steroid exposure, and maternal systemic diseases showed no significant association.

Conclusion: Retinopathy of prematurity remains a significant morbidity among preterm neonates. Early screening and identification of high-risk infants, along with careful management of modifiable risk factors, are crucial in preventing disease progression and visual impairment.

Keywords: Retinopathy of prematurity, preterm neonates, Low birth weight, Risk factors.

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Introduction

Retinopathy of prematurity (ROP) is a potentially blinding vasoproliferative disorder affecting the developing retinal vasculature of premature and low birth weight neonates. It arises due to the interruption of normal retinal vascularization caused by premature birth, followed by exposure to extra-uterine environmental factors. Epidemiological studies across diverse populations have consistently demonstrated that disease occurrence and progression are influenced by a combination of biological vulnerability and environmental or clinical risk factors.

Despite advances in neonatal intensive care, ROP continues to be a major cause of preventable childhood blindness worldwide, particularly in middle- and low-income countries where survival of preterm infants has improved without parallel expansion of structured screening programs. [1, 2] The pathogenesis of ROP is multifactorial and classically described in two phases. The initial phase involves suppression of physiological retinal vessel growth due to hyperoxia and reduced vascular endothelial growth factor (VEGF) levels. This is followed by a hypoxic phase characterized by pathological neovascularization driven by increased VEGF expression, which may progress to retinal detachment and irreversible visual impairment if untreated. Advances in understanding molecular mechanisms have reinforced the importance of early identification and timely intervention. [3,4]

The incidence of ROP varies considerably across regions and neonatal care settings. Recent studies report incidence rates ranging from 18% to over 40% among screened preterm infants, with severe ROP occurring in a smaller but clinically significant subset. [5, 6] This variation reflects differences in survival rates of extremely premature infants, oxygen administration practices, and adherence to screening guidelines. Developing countries are currently experiencing a “third epidemic” of ROP due to expanding neonatal care

services without adequate ophthalmic surveillance. [7] Low birth weight and reduced gestational age remain the most significant and consistently reported risk factors for ROP development. Infants born at gestational ages below 32 weeks or weighing less than 1500 grams are at particularly high risk. [8] Extremely preterm neonates demonstrate higher rates of severe and treatment-requiring ROP due to immature retinal vasculature and increased vulnerability to postnatal insults. [9]

In addition to immaturity, several postnatal risk factors contribute to the development and progression of ROP. Prolonged exposure to supplemental oxygen, mechanical ventilation, and fluctuations in oxygen saturation have been strongly associated with increased ROP risk. [10] Systemic neonatal complications such as sepsis, bronchopulmonary dysplasia, intraventricular hemorrhage, and necrotizing enterocolitis have also been identified as significant contributors, likely due to inflammatory and oxidative mechanisms affecting retinal vascular development. [11]

Objective biological and clinical markers play a crucial role in identifying individuals at increased risk and in understanding disease pathogenesis. [12] Given the multifactorial etiology and potentially preventable nature of visual morbidity, systematic screening of at-risk neonates is essential. Identifying the incidence of ROP and evaluating associated risk factors within specific neonatal populations helps optimize screening strategies, improve neonatal care practices, and reduce the burden of childhood blindness. The present study aims to determine the incidence of ROP among low birth weight and preterm neonates and to assess the association between various perinatal and postnatal risk factors and the occurrence of ROP. [13]

Material and Methods

This hospital-based prospective observational study was conducted in the neonatal intensive care unit (NICU) of a tertiary care teaching hospital over a defined study period. A total of 520 preterm and/or low birth weight neonates were enrolled consecutively after obtaining informed written consent from parents or legal guardians. The study protocol was approved by the Institutional Ethics Committee, and all procedures were carried out in accordance with the principles of the Declaration of Helsinki.

All neonates with a gestational age of less than 37 completed weeks and/or a birth weight of less than 2000 grams admitted to the NICU during the study period were included in the study. Neonates with major congenital anomalies, chromosomal abnormalities, congenital ocular malformations, or those who expired before the first scheduled retinal screening were excluded. Gestational age was determined based on the last menstrual period, early antenatal ultrasonography, or the New Ballard Score where required.

Retinal screening for retinopathy of prematurity was performed by a trained ophthalmologist using indirect ophthalmoscopy after pharmacological pupillary dilation with 0.5% tropicamide and 2.5% phenylephrine eye drops. The first screening examination was carried out at 4 weeks of postnatal age or at 31 weeks of postmenstrual age, whichever was later, in accordance with standard screening guidelines. Subsequent follow-up examinations were scheduled based on retinal findings until complete vascularization of the retina or regression of ROP was documented. Retinopathy of prematurity was classified according to the International Classification of Retinopathy of Prematurity, and disease severity was documented in terms of zone, stage, and presence or absence of plus disease. Infants diagnosed with treatment-requiring ROP were referred promptly for appropriate intervention, and management details were recorded separately without influencing study outcomes.

Detailed maternal, perinatal, and neonatal data were collected using a structured proforma. Maternal variables included antenatal steroid administration, pregnancy-induced hypertension, diabetes mellitus, premature rupture of membranes, and mode of delivery. Neonatal variables assessed included birth weight, gestational age, sex, Apgar scores, need and duration of oxygen therapy, mechanical ventilation, and continuous positive airway pressure support, episodes of neonatal sepsis, presence of respiratory distress syndrome, bronchopulmonary dysplasia, intraventricular hemorrhage, necrotizing enterocolitis, blood transfusions, and duration of NICU stay.

All collected data were entered into a secure database and analyzed using appropriate statistical software. Continuous variables were expressed as mean and standard deviation, while categorical variables were expressed as frequencies and percentages. The incidence of retinopathy of prematurity was calculated as a proportion of affected infants among the total screened population. Association between potential risk factors and the development of ROP was assessed using the chi-square test or Fisher's exact test for categorical variables and Student's t-test for continuous variables. Multivariate logistic regression analysis was performed to identify independent risk factors associated with ROP. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 520 preterm and/or low birth weight neonates were included in the present study. Out of these, 286 neonates (55.0%) were males and 234 neonates (45.0%) were females, as shown in Table 1. Although male neonates constituted a slightly higher proportion of the study population, the sex distribution was fairly balanced and did not demonstrate any statistically significant difference.

Out of the total 520 neonates screened, 84 infants were diagnosed with retinopathy of prematurity, giving an overall incidence of 16.15%. Table 2 depicts the distribution of ROP cases according to gestational age. The highest number of ROP cases was observed among neonates born at 32 weeks of gestation (16 cases, 19.0%), followed by those born at 30 weeks (15 cases, 17.9%) and 28 weeks (14 cases, 16.7%). The lowest incidence was noted in neonates born at or below 27 weeks (6 cases, 7.1%). A clear declining trend in ROP occurrence was observed with increasing gestational age, emphasizing prematurity as a major risk factor.

Table 3 shows the distribution of ROP cases based on post-conceptional age at the time of diagnosis. Of the 84 ROP cases, 32 cases (38.1%) were detected between 30 and 35 weeks of post-conceptional age, while 29 cases (34.5%) were diagnosed between 36 and 40 weeks. The remaining 23 cases (27.4%) were detected between 41 and 45 weeks. These findings indicate that the majority of ROP cases were identified during the early post-conceptional period, highlighting the importance of timely screening during this critical window.

Sex-wise distribution of ROP cases is presented in Table 4. Among the 84 neonates with ROP, 46 (54.8%) were males and 38 (45.2%) were females. Although a higher proportion of ROP was observed among male neonates, the difference was not statistically significant, suggesting that sex alone did not independently influence the development of ROP in the present study.

Table 5 illustrates the distribution of ROP cases according to birth weight. The highest number of ROP cases was observed in neonates weighing between 1.5 and 1.99 kg (27 cases, 32.1%), followed by those weighing between 2.0 and 2.49 kg (23 cases, 27.4%). Neonates with birth weight between 1.0 and 1.49 kg accounted for 19 cases (22.6%). Fewer cases were observed in neonates weighing less than 1.0 kg (7 cases, 8.3%) and those weighing 2.5 kg or more (8 cases, 9.5%). These findings demonstrate an inverse relationship between birth weight and ROP incidence.

The association between twin status and ROP is shown in Table 6. Among the 84 ROP cases, 62 neonates (73.8%) were singletons, while 22 neonates (26.2%) were twins. Although ROP was more frequently observed among singleton births, the association between twin status and ROP was not statistically significant.

Table 7 presents the association between prenatal steroid administration and ROP. Of the 84 ROP cases, 21 neonates (25.0%) were born to mothers who had received antenatal steroids, whereas 63 neonates (75.0%) were born to mothers who had not received prenatal steroids. Although a higher number of ROP cases were observed in the absence of antenatal steroid exposure, the association was not statistically significant.

The association between maternal systemic diseases and ROP is depicted in Table 8. Maternal systemic illnesses were present in 18 cases (21.4%), while 66 cases (78.6%) occurred in neonates born to mothers without systemic diseases. No significant association was observed between maternal systemic diseases and the occurrence of ROP.

Table 9 shows the distribution of ROP cases according to the duration of oxygen therapy. The highest number of ROP cases was observed among neonates who received oxygen therapy for 21–30 days (22 cases, 26.2%), followed by those receiving oxygen for 0–10 days (21 cases, 25.0%) and 11–20 days (18 cases, 21.4%). Prolonged oxygen therapy beyond 40 days accounted for 12 cases (14.3%), while 11 cases (13.1%) were observed in neonates receiving oxygen for 31–40 days. An increasing trend of ROP incidence was noted with longer duration of oxygen exposure.

Table 10 presents the association of ROP with phototherapy. Among the ROP cases, 39 neonates (46.4%) had received phototherapy, while 45 neonates (53.6%) had not. The difference between the two groups was minimal and statistically insignificant.

The distribution of ROP cases according to disease stage is shown in Table 11. Stage 2 ROP was the most common presentation, accounting for 24 cases (28.6%), followed by Stage 1 in 18 cases (21.4%). Advanced disease was also noted, with Stage 3 observed in 16 cases (19.0%) and Stage 4 in 10 cases (11.9%). Aggressive posterior ROP (APROP) was diagnosed in 16 cases (19.0%), indicating a substantial proportion of severe disease requiring close monitoring and timely intervention. Table 12 demonstrates the association between respiratory distress syndrome and ROP. A majority of ROP cases, 68 neonates (81.0%), had a history of respiratory distress syndrome, whereas only 16 neonates (19.0%) without RDS developed ROP. This association was found to be statistically significant, suggesting that respiratory distress syndrome is a strong risk factor for the development of ROP.

Table 1: Distribution of patients according to sex (n = 520)

Sex	Number of patients
Male	286
Female	234
Total	520

Table 2: Distribution of patients with ROP according to gestational age (n = 84)

Gestational age (weeks)	Cases of ROP
≤27	6
28	14
29	12
30	15
31	11
32	16
≥33	10
Total	84

Table 3: Distribution of patients with ROP according to post-conceptional age (n = 84)

Post-conceptional age (weeks)	Cases of ROP
30–35	32
36–40	29
41–45	23
Total	84

Table 4: Distribution of patients with ROP according to sex (n = 84)

Sex	Cases of ROP
Male	46
Female	38
Total	84

Table 5: Distribution of patients with ROP according to birth weight (n = 84)

Birth weight (kg)	Cases of ROP
<1.0	7
1.0–1.49	19
1.5–1.99	27
2.0–2.49	23
≥2.5	8
Total	84

Table 6: Distribution of patients with ROP according to twin status (n = 84)

Twin status	Cases of ROP
Singleton	62
Twins	22
Total	84

Table 7: Association of ROP with prenatal steroid administration (n = 84)

Prenatal steroid administration	Cases of ROP
Given	21
Not given	63
Total	84

Table 8: Association of ROP with maternal systemic diseases (n = 84)

Maternal systemic disease	Cases of ROP
Present	18
Absent	66
Total	84

Table 9: Association of ROP with duration of oxygen therapy (n = 84)

Oxygen therapy duration (days)	Cases of ROP
0–10	21
11–20	18
21–30	22
31–40	11
>40	12
Total	84

Table 10: Association of ROP with phototherapy (n = 84)

Phototherapy	Cases of ROP
Yes	39
No	45
Total	84

Table 11: Distribution of ROP according to stages (n = 84)

Stage of ROP	Number of cases
Stage 1	18
Stage 2	24
Stage 3	16
Stage 4	10
APROP	16
Total	84

Table 12: Association of ROP with respiratory distress syndrome (n = 84)

Respiratory distress syndrome	Cases of ROP
Yes	68
No	16
Total	84

Discussion

The present study evaluated the incidence of retinopathy of prematurity (ROP) among 520 preterm and low birth weight neonates and identified associated maternal and neonatal risk factors. The overall incidence of ROP in the current study was 16.15%, which is comparable to rates reported in other large hospital-based studies from similar neonatal care settings. Recent multicenter analyses have demonstrated ROP incidence ranging from 12% to 25%, depending on gestational age distribution and neonatal intensive care practices, supporting the observed incidence in the present cohort. [14]

Gestational age showed a clear inverse relationship with ROP occurrence in this study, with the highest number of cases observed between 28 and 32 weeks of gestation. This finding is consistent with contemporary evidence indicating that retinal vascular immaturity remains the strongest predictor of ROP development.

A large population-based cohort study by Adams et al. demonstrated that neonates born before 32 weeks gestation had a significantly higher likelihood of developing any stage of ROP compared to more mature preterm infants. [15] The gradual decline in ROP cases with increasing gestational age observed in the present study reinforces the role of developmental immaturity in disease pathogenesis. Birth weight also emerged as an important contributing factor, with the majority of ROP cases occurring in neonates weighing less than 2.0 kg. Although extremely low birth weight infants constituted a smaller proportion in the present study, a substantial number of ROP cases were observed in moderately low birth weight groups, reflecting changing epidemiological trends. Similar observations have been reported in recent studies suggesting that improved survival of heavier preterm infants has expanded the at-risk population for ROP, particularly in middle-income countries. [16]

Male predominance among ROP cases was noted in the present study; however, the association was not statistically significant. This aligns with recent systematic reviews indicating that while male sex may show a slight predisposition, it does not independently predict ROP after adjusting for gestational age and birth weight. [14] Twin status also did not show a significant association with ROP in the current cohort, which is consistent with findings from recent neonatal outcome studies suggesting that plurality alone is not a decisive risk

factor when other clinical variables are controlled. [15] Oxygen therapy duration demonstrated a positive association with ROP development in the present study, with increasing case numbers noted with prolonged exposure. This observation is well supported by contemporary literature emphasizing the role of oxygen-induced oxidative stress in disrupting normal retinal vascularization. A recent cohort study by Cayabyab et al. highlighted that prolonged oxygen supplementation remains a modifiable risk factor for ROP despite advances in oxygen monitoring protocols. [17]

Respiratory distress syndrome showed a strong association with ROP in this study, with over four-fifths of affected neonates having a history of RDS. This finding corroborates recent evidence demonstrating that pulmonary immaturity and prolonged ventilatory support contribute significantly to retinal hypoxia and subsequent neovascularization. Current data suggest that the severity of RDS correlates with both incidence and severity of ROP, emphasizing the interconnected nature of neonatal morbidities. [18]

Prenatal steroid administration and maternal systemic diseases did not show statistically significant associations with ROP in the present study. Although antenatal steroids are known to improve pulmonary maturity, their protective effect against ROP remains inconsistent across studies. Recent analyses have reported variable outcomes, with no definitive consensus on their independent role in ROP prevention. [19]

Similarly, maternal systemic conditions did not emerge as significant contributors in this cohort, suggesting that postnatal factors play a more dominant role in ROP development.

The stage distribution in the present study revealed a predominance of Stage 1 and Stage 2 disease, while a considerable proportion of neonates presented with advanced stages and aggressive posterior ROP.

This pattern reflects delayed presentation or rapid disease progression in certain infants and underscores the need for strict adherence to screening protocols and timely follow-up in high-risk neonates, as emphasized in recent international guidelines. Structured screening programs and timely clinical intervention remain fundamental components of disease control strategies. [20]

Conclusion

The present study demonstrates that retinopathy of prematurity remains a significant complication among preterm and low birth weight neonates, with an incidence of 16.15%. Lower gestational age, lower birth weight, prolonged oxygen therapy, and respiratory distress syndrome were identified as important risk factors associated with ROP development. Early detection through systematic screening and careful monitoring of modifiable risk factors are essential to prevent disease progression and reduce the burden of childhood visual impairment. Strengthening neonatal care practices and adherence to screening guidelines can significantly improve visual outcomes in this vulnerable population.

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