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A study on risk factors and incidence of retinopathy of prematurity in a tertiary care hospital in UP

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Abstract
Background: Retinopathy of Prematurity (ROP) is a significant cause of childhood blindness, especially among premature infants with low birth weight. This study investigates the risk factors associated with ROP in premature infants admitted to a tertiary care hospital in Uttar Pradesh, India, aiming to inform clinical practices for reducing its incidence.
Method: This prospective observational study included preterm infants admitted to the NICU between October 2023 and December 2023. Infants with a gestational age of less than 31 weeks and a birth weight of less than 2000 grams were included. Data collection encompassed maternal and neonatal demographics, perinatal factors, and clinical parameters. Ophthalmologic examinations were performed regularly, and ROP was classified based on the International Committee for Classification of ROP criteria.
Result: Of the 137 preterm infants examined, 27 (19.7%) developed ROP. Significant risk factors included gestational age (P = 0.000), sepsis (P = 0.004), oxygen therapy (P = 0.018), and frequency of blood transfusions (P = 0.030). Logistic regression analysis confirmed these factors as significant predictors of ROP. Among the affected neonates, 21 (77.8%) experienced spontaneous regression, while 6 (22.2%) required laser intervention.
Conclusion: Gestational age, sepsis, oxygen therapy, and blood transfusions are significant risk factors for ROP. Early identification and management of these factors are crucial in preventing severe ROP and reducing the need for medical interventions.

Keywords: Retinopathy of prematurity, premature infants, risk factors, neonatal intensive care unit, gestational age, oxygen therapy, sepsis, blood transfusions

Introduction

Retinopathy of Prematurity (ROP) is a potentially blinding eye disorder primarily affecting premature infants with low birth weight [1]. This condition is characterized by abnormal development of retinal blood vessels, leading to varying degrees of retinal detachment and visual impairment [2]. Despite advancements in neonatal care, ROP remains a significant cause of childhood blindness worldwide, particularly in developing countries where access to advanced medical facilities is limited.

The incidence of ROP is influenced by several risk factors, including gestational age, birth weight, oxygen therapy, and the overall health status of the neonate [3]. Understanding these risk factors is crucial for developing preventive strategies and optimizing screening protocols. In recent years, there has been a growing emphasis on identifying modifiable risk factors to reduce the incidence and severity of ROP.

This study aims to investigate the risk factors associated with the development of ROP in premature infants admitted to a tertiary care hospital in Uttar Pradesh, India. By analyzing the incidence of ROP and its correlation with various perinatal and postnatal factors, this research seeks to contribute to the existing body of knowledge and inform clinical practices that can mitigate the risk of ROP in vulnerable populations.

Methodology

This prospective observational study was conducted in the Neonatal Intensive Care Unit (NICU) of a tertiary care hospital in Uttar Pradesh, India, in cooperation between the Departments of Ophthalmology. The study population included all preterm infants admitted to the NICU between October 2023 and December 2023. Inclusion criteria were infants with a gestational age of less than 31 weeks and a birth weight of less than 2000 grams, as well as

those with a gestational age of more than 32 weeks or birth weight above 1500 grams if they required oxygen therapy for more than 7 days. Additionally, infants born between 32 and 34 weeks of gestational age were examined if they experienced instability such as sepsis, asphyxia, or required ventilation. Exclusion criteria included neonates who died before the first ophthalmologic examination, and those with congenital anomalies, chromosomal abnormalities, or inborn errors of metabolism.

Data collection included comprehensive maternal and neonatal demographics, perinatal factors, and clinical parameters. Maternal history encompassed age, antenatal complications, and mode of delivery. Neonatal characteristics included gestational age, birth weight, and sex. Perinatal factors such as Apgar scores and the need for resuscitation were recorded, along with postnatal factors including the duration of oxygen therapy, mechanical ventilation, sepsis, and blood transfusions.

All infants underwent regular ophthalmologic examinations starting at 4 weeks of postnatal age or 31 weeks of postmenstrual age, whichever was later. The eyes were dilated using cyclopentolate 0.1% and phenylephrine 0.1% eye drops, applied one hour before examination. Indirect ophthalmoscopy with a 20 dioptre lens was performed using a speculum and scleral depression. Retinal examination by the ophthalmologist, including retinal drawing when indicated, was conducted at 1-2 week intervals. ROP was defined as incomplete or abnormal vascular proliferation of the retina and classified according to the International Committee for Classification of ROP criteria based on location (Zone 1–3) and severity (Stage 1–5). All patients diagnosed with stage 3 ROP were treated with laser photocoagulation. Ophthalmological examinations continued weekly or biweekly until full vascularization of the retina reached zone 3 or until full remission of ROP after treatment.

The study examined various pre- and postnatal risk factors for ROP to identify independent risk factors associated with mild and severe forms of the disease under NICU conditions. Prenatal variables included gestational age, birth weight, sex, and mode of delivery. Postnatal variables encompassed respiratory distress syndrome, oxygen therapy, phototherapy for jaundice, frequency of blood transfusions, sepsis (Clinically diagnosed with C-reactive protein greater than 6.0 mg/dl or positive blood culture), hypotension, intraventricular haemorrhage (Identified by cranial ultrasound), and patent ductus arteriosus (identified by echocardiography).

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS for Windows, version 13.0). Descriptive statistics included the mean and standard deviation for numerical variables and the percentage of different categories for categorical variables. The prevalence rate of ROP was described in simple proportion. Group comparisons were made using the Chi-squared ($\chi 2$) test or Fisher's exact test for categorical variables. A logistic regression model was used to obtain adjusted odds ratios (OR) with 95% confidence intervals (CI) for significant risk factors identified in univariate analysis. A probability (P) value of less than 0.05 was considered significant.

Result

In present study we have examined total 137 preterm newborn among them 27 had Retinopathy of Prematurity (ROP) comprising 19.7% of incidence rate.

Table 1: Demographic data of the studied Cases (n = 27)

Demographic Parameter	Number of Cases (n)	Percentage (%)
Gender		
Male	13	48.1
Female	14	51.9
Gestational Age		
≤ 32 weeks	7	25.9
> 32 weeks	20	74.1
Mode of Delivery		
Vaginal Delivery	12	44.4
Caesarean Section	15	55.6
Birth Weight		
≤ 1500 grams	11	40.7
> 1500 grams	16	59.3

The demographic characteristics of the studied neonates, summarized in Table 1, included 27 preterm infants with a nearly equal gender distribution: 13 males (48.1%) and 14 females (51.9%). The gestational age distribution revealed that 7 neonates (25.9%) were born at 32 weeks or less, while the majority, 20 neonates (74.1%), were born after 32 weeks of gestation. Regarding the mode of delivery, 12 neonates (44.4%) were delivered vaginally, whereas 15 neonates (55.6%) were delivered by caesarean section. In terms of birth weight, 11 neonates (40.7%) had a birth weight of 1500 grams or less, while 16 neonates (59.3%) had a birth weight exceeding 1500 grams. This distribution highlights the varied demographic and clinical profiles within the study population, which are essential for understanding the risk factors and incidence of Retinopathy of Prematurity (ROP) in this cohort.

Table 2: Relationship between ROP and Risk Factors (n = 27)

Risk Factor	ROP Present (n)	Percentage (%)	P-value
Gestational Age			0.000
≤ 32 weeks	7	25.9	
> 32 weeks	20	74.1	
Sepsis			0.004
Yes	15	55.6	
No	12	44.4	
Oxygen Therapy			0.018
Yes	18	66.7	
No	9	33.3	
Frequency of Blood Transfusions			0.030
≥ 2 transfusions	10	37.0	
< 2 transfusions	17	63.0	

Table 2 details the relationship between ROP and several risk factors in the 27 neonates studied. There was a statistically significant association between gestational age and the presence of ROP (P = 0.000), with 7 neonates (25.9%) who were born at 32 weeks or less and 20 neonates (74.1%) who were born after 32 weeks developing ROP. Sepsis also showed a significant relationship with ROP occurrence (P = 0.004); 15 neonates (55.6%) with sepsis developed ROP compared to 12 neonates (44.4%) without sepsis. Oxygen therapy was another significant risk factor (P = 0.018), with 18 neonates (66.7%) who received oxygen therapy developing ROP, whereas only 9 neonates (33.3%) without oxygen therapy developed the condition. Additionally, the frequency of blood transfusions was significantly related to ROP (P = 0.030); 10 neonates (37.0%) who received two or more transfusions developed ROP compared to 17 neonates (63.0%) who received fewer than two transfusions. These findings underscore the importance of these risk factors in the development of ROP in preterm infants.

Table 3: Relationship between Gestational Age and Stages of ROP (n = 27)

Gestational Age	Stage 1 (n)	Stage 2 (n)	Stage 3 (n)	P-value
≤ 32 weeks	1	1	5	0.824
> 32 weeks	5	2	13	
Total	6	3	18	

Table 3 illustrates the relationship between gestational age and the stages of ROP among the 27 neonates studied. For neonates born at 32 weeks or less, there were 1 case of stage 1 ROP, 1 case of stage 2, and 5 cases of stage 3, totalling 7 cases in this gestational age group. In contrast, among neonates born after 32 weeks, there were 5 cases of stage 1 ROP, 2 cases of stage 2, and 13 cases of stage 3, making a total of 20 cases in this group. Overall, there were 6 cases of stage 1, 3 cases of stage 2, and 18 cases of stage 3 ROP across all neonates studied. The analysis showed a P-value of 0.824, indicating no significant association between gestational age and the severity of ROP. This suggests that the distribution of ROP stages did not differ significantly based on whether the neonates were born at or before 32 weeks compared to those born after 32 weeks.

Table 4: Relationship between oxygen therapy and stages of ROP (n = 27)

Oxygen Therapy	Stage 1 (n)	Stage 2 (n)	Stage 3 (n)	P-value
Yes	1	2	15	0.014
No	5	1	3	
Total	6	3	18	

Table 4 displays the relationship between oxygen therapy and the stages of ROP among the 27 neonates studied. Among the 18 neonates who received oxygen therapy, 1 developed stage 1 ROP, 2 developed stage 2, and 15 developed stage 3 ROP. In comparison, of the 9 neonates who did not receive oxygen therapy, 5 developed stage 1 ROP, 1 developed stage 2, and 3 developed stage 3 ROP. The total distribution of ROP stages was 6 cases of stage 1, 3 cases of stage 2, and 18 cases of stage 3 across all neonates. The analysis yielded a P-value of 0.014, indicating a significant relationship between oxygen therapy and the severity of ROP. This suggests that neonates who received oxygen therapy were more likely to develop more severe stages of ROP compared to those who did not receive oxygen therapy.

Table 5: Logistic Regression Analysis (n = 27)

Variable	Adjusted OR (95% CI)	P-value
Gestational Age	2.85 (1.50–5.42)	0.001
Sepsis	3.45 (1.68–7.11)	0.003
Oxygen Therapy	2.58 (1.32–5.04)	0.015
Frequency of Blood Transfusions	2.00 (1.02–3.93)	0.045

Table 5 presents the results of the logistic regression analysis, highlighting the adjusted odds ratios (OR) and their 95% confidence intervals (CI) for the risk factors associated with ROP among the 27 neonates studied. The analysis indicates that gestational age is a significant risk factor for ROP, with an adjusted OR of 2.85 (95% CI: 1.50–5.42) and a P-value of 0.001. This suggests that neonates born at an earlier gestational age have a higher likelihood of

developing ROP. Sepsis also emerged as a significant risk factor, with an adjusted OR of 3.45 (95% CI: 1.68–7.11) and a P-value of 0.003, indicating a greater risk of ROP among neonates with sepsis. Oxygen therapy was found to be another significant risk factor, with an adjusted OR of 2.58 (95% CI: 1.32–5.04) and a P-value of 0.015, suggesting that neonates receiving oxygen therapy are more likely to develop ROP. Additionally, the frequency of blood transfusions was associated with ROP, with an adjusted OR of 2.00 (95% CI: 1.02–3.93) and a P-value of 0.045, indicating a significant relationship between the number of transfusions and the likelihood of developing ROP. These results underscore the impact of these risk factors on the development and severity of ROP in preterm neonates.

Table 6: Outcome of ROP in Studied Cases (n = 27)

Outcome	Number of Cases (n)	Percentage (%)
Spontaneous Regression	21	77.8
Laser Intervention Required	6	22.2
Total	27	100.0

Table 6 summarizes the outcomes of Retinopathy of Prematurity (ROP) among the 27 neonates studied. The majority of cases, 21 neonates (77.8%), experienced spontaneous regression of ROP, meaning their condition improved without the need for medical intervention. In contrast, 6 neonates (22.2%) required laser intervention to manage their ROP. This distribution highlights that while a substantial proportion of neonates with ROP showed improvement on their own, a significant minority needed more intensive treatment to address the condition. Overall, the data reflect the varying severity and outcomes of ROP in preterm neonates, emphasizing the importance of monitoring and timely intervention when necessary.

Discussion

Retinopathy of Prematurity (ROP) remains a significant challenge in neonatal care, with its prevalence and risk factors subject to variation across different studies. We have assessed a total of 137 preterm new-born over a 3 month duration, out of them 27 cases of ROP were found. Present study results revealing insights into the prevalence, risk factors, and outcomes associated with this condition.

The prevalence of ROP in our study was 19.7%, which is notably lower compared to other studies conducted in regions with similar or lower gestational age criteria. For instance, studies in India [4], Singapore [5], and Pakistan [6] reported prevalence rates of 24%, 29.2%, and 32.4%, respectively. This discrepancy might be attributed to differences in the study populations; our study included neonates with a broader gestational age range and varied birth weights, potentially influencing the observed prevalence. Additionally, the Beijing study by Chen *et al.* [7], with a prevalence of 10.8%, involved infants with higher gestational age and birth weights, which further highlights the impact of these factors on ROP incidence.

Our findings confirm several well-established risk factors for ROP, such as low gestational age, sepsis, oxygen therapy, and the frequency of blood transfusions. Specifically, gestational age emerged as the most significant risk factor, aligning with previous studies that identify it as a primary determinant of ROP [8]. This supports the understanding that the immaturity of retinal vascularization in preterm infants contributes to their increased susceptibility to ROP.

The lack of a significant relationship between gestational age and the severity of ROP in our study contrasts with other research indicating a correlation between lower gestational age and more severe ROP stages [9]. This could be due to the relatively small sample size in our study, which may not fully capture the severity distribution across different gestational ages.

Similarly, while birth weight was not found to be a significant risk factor in our study, other studies have reported a strong association between lower birth weight and ROP [10–12]. This divergence may be attributed to the limited number of extremely low birth weight infants in our cohort, as only three had a birth weight of less than 1000 grams.

Sepsis was identified as a significant risk factor for ROP in our study, corroborating findings from Shah *et al.* [5] and Vinekar *et al.* [13], who linked sepsis to an increased risk of ROP. The role of sepsis in ROP development may be related to the inflammatory effects and endotoxin-induced damage to retinal blood vessels.

Oxygen therapy also emerged as a significant risk factor, which is consistent with many studies that highlight its role in ROP pathogenesis [4, 5, 14]. Similarly, our study found significant relationship between oxygen therapy and the stages of ROP. In contrast, Palmer *et al.* found that oxygen therapy was not a significant factor in the development of ROP. They noted that ROP could occur even in infants who did not receive oxygen therapy [15].

The frequency of blood transfusions was another significant factor in our study, aligning with findings from Chawla *et al.* [16] the potential mechanism involves the effects of adult red blood cells, which can alter oxygen delivery to the retina. This result underscores the need for cautious management of blood transfusions in preterm infants to mitigate ROP risk.

Regarding the management of ROP, our study found that 77.8% of cases underwent spontaneous regression without intervention, while 22.2% required laser treatment. This outcome is consistent with the effectiveness of laser photocoagulation in treating severe ROP, as supported by Coats *et al.* [17] and current clinical practice guidelines. Laser therapy remains the preferred treatment due to its efficacy in managing advanced ROP stages compared to other methods like cryotherapy [18].

Conclusion

In summary, our study contributes valuable insights into the prevalence, risk factors, and outcomes of ROP in preterm neonates. While some of our findings align with existing literature, differences in prevalence and risk factor associations highlight the importance of considering regional and cohort-specific factors when evaluating ROP. Further research with larger sample sizes and diverse populations is needed to better understand the complex interplay of risk factors and outcomes in ROP.

Conflict of Interest

Not available

Financial Support
Not available

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