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Original Research Article

INCIDENCE OF RETINOPATHY OF PREMATURITY AND ITS ASSOCIATION WITH MATERNAL AND NEONATAL RISK FACTORS AMONG PRETERM NEONATES - A HOSPITAL BASED OBSERVATIONAL STUDY

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ABSTRACT

Background: Retinopathy of Prematurity (ROP) is a vaso-proliferative disorder of the retina that primarily affects premature and low birth weight infants. It is a significant cause of preventable childhood blindness, especially in developing countries. Early identification of neonates at risk and prompt intervention is crucial in preventing disease progression and permanent visual impairment. The aim is to determine the incidence of ROP and assess its association with maternal and neonatal risk factors among preterm neonates admitted to the NICU.

Materials and Methods: This was a prospective observational study conducted over one year in the Neonatal ICU of Jorhat Medical College and Hospital. A total of 70 inborn preterm neonates with birth weight <2000 grams or gestational age <34 weeks, and 34–36 weeks with clinical risk factors were screened for ROP. Ophthalmological evaluation followed the International Classification of ROP guidelines. Data on maternal and neonatal risk factors were collected and analysed using descriptive statistics and Chi-square tests. A p-value <0.05 was considered statistically significant.

Results: Out of 70 neonates screened, ROP was diagnosed in 18 cases, accounting for an incidence of 25.7%. Significant associations were observed with gestational age <32 weeks ($p = 0.0039$), birth weight <1.5 kg ($p = 0.0000028$), respiratory distress syndrome ($p = 0.019$), mechanical ventilation ($p = 0.0012$), birth asphyxia ($p = 0.0001$), neonatal sepsis ($p = 0.019$), and apnoea ($p = 0.0136$). Use of antenatal corticosteroids was found to be protective ($p = 0.029$). Maternal factors like gestational hypertension, GDM, and PPROM showed no statistically significant association.

Conclusion: Lower gestational age, low birth weight, and certain neonatal complications are major risk factors for ROP. Structured screening, timely interventions, and preventive neonatal and antenatal care are key to reducing ROP incidence and severity.

Keywords: Retinopathy of prematurity, Preterm neonates, Risk factors, Antenatal steroids, Neonatal outcomes.

INTRODUCTION

Vision is a vital sensory modality that plays a critical role in early childhood development, influencing cognitive, motor, and social skill acquisition. Proper development of the visual system requires a clear, focused image to be transmitted from the eyes to the brain. Any disruption in this process during the early stages of life can lead to irreversible visual impairment or blindness. In India, the prevalence of childhood blindness is estimated at 6.5 per 10,000 children, with retinal conditions accounting for approximately 19.3% to 22% of these cases.[1]

Retinopathy of Prematurity (ROP) is a vaso-proliferative disorder of the immature retina that predominantly affects preterm and low birth weight infants, particularly those born before 34 weeks of gestation or weighing less than 2000 grams.2 It arises due to incomplete retinal vascularization, which becomes vulnerable to aberrant angiogenesis when exposed to postnatal risk factors, particularly supplemental oxygen. Hypoxia in the peripheral retina induces overexpression of vascular endothelial growth factor (VEGF), leading to the formation of fragile, disorganized blood vessels that may result in haemorrhage, fibrosis, retinal detachment, and ultimately blindness.[2,3]

Several neonatal risk factors are strongly associated with the development of ROP. These include extreme prematurity (≤32 weeks), low birth weight (≤1750 grams), prolonged oxygen therapy, mechanical ventilation, sepsis, and blood transfusions. Fluctuating oxygen levels caused by mechanical ventilation further exacerbate abnormal retinal vascular development.[4,5]

In addition, maternal risk factors such as preeclampsia, gestational diabetes, intrauterine growth restriction (IUGR), multiple gestations, and antenatal exposure to tobacco, alcohol, or other substances are implicated in the aetiology of preterm birth and may indirectly contribute to the development of ROP.[5,6]

Early identification through timely ophthalmologic screening is essential to prevent irreversible visual loss. According to national and international guidelines, infants born at <34 weeks gestation or with a birth weight <2000 grams should undergo the first retinal examination at 4 weeks of age or earlier if the gestational age is <28 weeks or birth weight is <1200 grams.[7,8] The International Classification of Retinopathy of Prematurity (ICROP) is used to classify the disease by stage, zone, and extent. Interventions such as laser photocoagulation and anti-VEGF therapy (e.g., intravitreal bevacizumab) have significantly improved outcomes in severe and aggressive forms of ROP.[9,10]

Recognizing the growing burden of ROP in India, the Ministry of Health and Family Welfare under the National Health Mission launched the Rashtriya Bal SwasthyaKaryakram (RBSK) in 2013. This initiative promotes systematic screening of preterm infants for ROP to enable timely treatment and reduce the risk of childhood blindness and developmental delays.

Given the preventable nature of ROP, this study aims to determine the incidence of ROP among preterm neonates and explore its association with various maternal and neonatal risk factors in a tertiary care hospital setting, thereby contributing to improved screening strategies and neonatal outcomes.

MATERIALS AND METHODS

This prospective observational study was conducted over a period of one year in the Neonatal Intensive Care Unit (NICU) of the Departments of Paediatrics and Ophthalmology at Jorhat Medical College and Hospital. The study population included inborn preterm neonates admitted to the NICU who met the inclusion criteria. Neonates with a birth weight <2000 grams or gestational age <34 weeks were enrolled, along with those between 34–36 weeks gestation having specific risk factors such as respiratory distress syndrome, oxygen therapy >6 hours, sepsis, apnoea, birth asphyxia, blood/exchange transfusion, and maternal conditions like gestational hypertension or diabetes. Neonates who died or were lost to follow-up before complete screening, or those with congenital ocular abnormalities were excluded. The final sample size was 70, selected using a consecutive sampling technique.

Screening for Retinopathy of Prematurity (ROP) was performed as per the Rashtriya Bal SwasthyaKaryakram (RBSK) guidelines. After obtaining informed consent, detailed maternal and neonatal data were recorded using structured proformas. Initial ROP screening was carried out at 4 weeks of age (or earlier in high-risk neonates) using indirect ophthalmoscopy under pharmacological pupil dilation. Screening was conducted by trained ophthalmologists following the International Classification of ROP (ICROP) criteria. Follow-up examinations were scheduled based on retinal findings. Infants requiring treatment for Type 1 ROP or advanced stages were referred to higher centres for laser or surgical intervention.

Data were collected through direct observation and medical record review. The incidence of ROP and associations with maternal and neonatal risk factors were analysed using Microsoft Excel. Descriptive statistics summarized demographic data, while Chi-square tests were used for univariate analysis. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 162 preterm neonates were admitted to the neonatal intensive care unit during the study period.

Of those, 70 neonates met the inclusion criteria and were enrolled in the study (n = 70).

Out of 70 preterm neonates enrolled in the study, 18 infants were diagnosed with Retinopathy of Prematurity (ROP), indicating an overall incidence of 25.7%. This finding reflects the significant burden of ROP among at-risk preterm neonates admitted to the NICU and underscores the need for systematic screening and follow-up.

Distribution of ROP POSITIVE CASES according to GESTATIONAL AGE

The incidence of ROP showed a strong inverse relationship with gestational age. Infants born at <30 weeks had the highest incidence (7/14: 50%), closely followed by those born at 30–31 weeks (7/15; 46.6%). The incidence sharply declined in infants born at 32–33 weeks (3/26; 11.5%) and 34–36 weeks (1/15; 6.7%). Statistical analysis revealed a significant association between gestational age and ROP (Chi-square = 13.35, p = 0.0039), confirming that lower gestational age is a major risk factor for the development of ROP. [Figure 1]

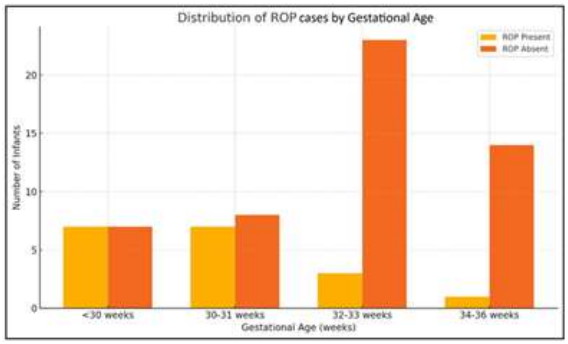

Figure 1: Distribution of ROP POSITIVE CASES according to GESTATIONAL AGE

A similar trend was observed with birth weight. All infants with birth weight <1 kg developed ROP (4/4; 100%), while 60% (9/15) of those in the 1.1–1.5 kg group were affected. The incidence decreased substantially in infants weighing 1.6–1.9 kg (3/23; 13%) and >2 kg (2/28; 7.1%). This trend was statistically significant (Chi-square = 21.93, p = 0.0000028), indicating that lower birth weight is a strong and significant predictor of ROP. [Table 1]

The male preponderance was noted among infants with ROP. Out of the 18 ROP-positive cases, 61.1% were males, and 38.9% were females.

In this study, most ROP cases were detected in the early stages, with Stage I accounting for 50% and Stage II for 27.7%, while no cases progressed to Stage V, indicating timely detection and potential for effective intervention. [Figure 2] Regarding disease location, Zone II was most commonly affected (44.4%), followed by Zone III (33.3%) and Zone I (22.2%), emphasizing the need for comprehensive retinal screening to identify ROP across both central and peripheral retinal zones.

Table 1: Distribution of ROP CASES according to BIRTH WEIGHT

Birth weight (kg)	Infants screened	ROP present	ROP absent
≤ 1.0 kg	4	4	0
1.1 – 1.5 kg	15	9	6
1.6 – 1.9 kg	23	3	20
≥ 2.0 kg	28	2	26
Total	70	18	52

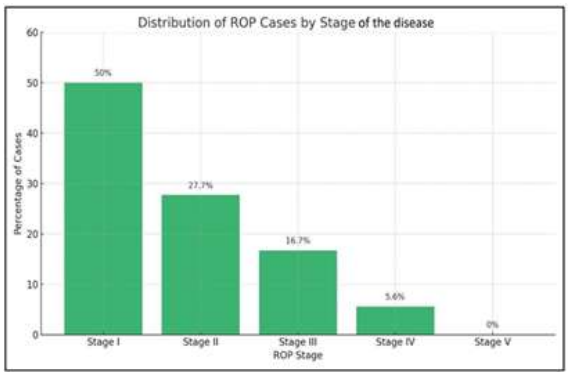

Figure 2: Distribution of ROP CASES according to STAGE

Out of the ROP cases, 61.2% had no plus disease, while 22.2% had pre-plus, and 16.6% had plus disease, indicating active vascular changes. Though most cases were mild, nearly 39% exhibited signs of disease progression, necessitating close monitoring and timely intervention.

In the present study, neither gestational hypertension nor gestational diabetes mellitus (GDM) showed a statistically significant association with the development of Retinopathy of Prematurity (ROP). Among 22 mothers with gestational hypertension, 6 neonates developed ROP, while 12 cases were observed among 48 neonates without such history (Chi-square = 0, p = 1; RR = 1.09). Similarly, out of 20 neonates born to mothers with GDM, 5 developed ROP compared to 13 cases among 50 neonates without GDM (Chi-square = 0, p = 1; RR = 0.96). These findings suggest that maternal conditions like gestational hypertension and GDM

did not significantly influence ROP incidence in this cohort.

In the univariate analysis, several neonatal and antenatal risk factors showed significant associations with the development of Retinopathy of Prematurity (ROP). Notably, use of antenatal steroids was found to have a protective effect, with only 4 out of 33 neonates exposed to antenatal steroids developing ROP, compared to 14 out of 37 in those without steroid exposure. This association was statistically significant (Chi-square = 4.77, p = 0.029; RR = 0.32), suggesting that antenatal steroids may reduce the risk of ROP. On the other hand, birth asphyxia demonstrated a strong association with ROP, with 12 of the 18 ROP cases having a history of birth asphyxia. The statistical analysis confirmed a highly significant relationship (Chi-square = 18.48, p = 0.0001; RR = 5.78), indicating that neonates with birth asphyxia were nearly six times more likely to develop ROP.

Additional neonatal complications also showed significant links with ROP development. Respiratory distress syndrome (RDS) was present in 15 of the 18 ROP cases, showing a significant association (Chi-square = 5.42, p = 0.019; RR = 3.75). Similarly, requirement of ventilatory support (mechanical ventilation) was strongly associated with ROP, with 11 out of 20 ventilated neonates developing ROP compared to 7 out of 50 non-ventilated ones (Chi-square = 10.52, p = 0.0012; RR = 3.93), [Figure 3]. Neonatal sepsis was another significant factor, present in 13 of the 18 ROP cases (Chi-square = 5.50, p = 0.019; RR = 3.09), as were episodes of apnoea, which occurred in 8 neonates with ROP (Chi-square = 10.26, p = 0.0136; RR = 3.87), highlighting their substantial roles in increasing ROP risk.

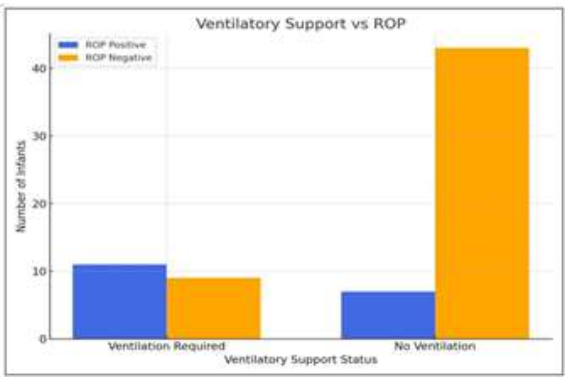

Figure 3: Distribution of ROP cases requiring VENTILATORY SUPPORT

In contrast, preterm premature rupture of membranes (PPROM) did not show a statistically significant association with ROP. Of the 23 neonates with a history of PPROM, 7 developed ROP compared to 11 cases among 47 neonates without PPROM (Chi-square = 0.116, p = 0.733; RR = 1.30). These findings collectively emphasize that while certain maternal factors may not significantly impact ROP incidence, several neonatal complications—especially those affecting respiratory function and systemic stability—are major contributors to ROP development and should be closely monitored during NICU care.

DISCUSSION

This prospective observational study was conducted to determine the incidence and risk factors associated with Retinopathy of Prematurity (ROP) among preterm neonates admitted to the NICU at Jorhat Medical College. Among 70 screened neonates, the incidence of ROP was found to be 25.7%, aligning with previous Indian studies such as Yadav et al. (2020) at 22.8% and Arora et al. (2023) at 33%.[11,12] The incidence lies within the reported national range of 20–52%, indicating a moderate burden compared to Western literature, where Yau et al. (2016) reported 18.5% ROP incidence.[13]

In terms of staging, most cases were detected early: 50% had Stage I ROP, followed by 27.7% with Stage II, which is comparable to findings by Shrestha et al. (2010) who reported 56.6% Stage I and 21.7% Stage II cases.[14] No Stage V ROP was found, reflecting effective early screening similar to results Shankar et al. (2014).[15]

Lower gestational age was a significant risk factor (p = 0.03). Infants <30 weeks had 50% ROP incidence, consistent with Rao et al. (2013), who reported 55.2% ROP in <30-week neonates, and Singh et al. (2016), who found a strong association for <32 weeks (p < 0.001).[16,17] Similarly, low birth weight (<1.5 kg) had a strong correlation with ROP (p = 0.003). All neonates <1 kg developed ROP in the present study, mirroring Singh et al. (2016), who found 100% ROP in <1 kg infants, and Yadav et al. (2020), who reported significant risk under 1.5 kg (p = 0.04).[11,17]

Maternal conditions like gestational hypertension, GDM, and PPROM did not show statistically significant associations. This is in line with Kubrey et al. (2023), who reported no link with PIH and GDM, while Raj et al. (2017) found GDM to be significant (p = 0.025), highlighting ongoing debate.[18,19] However, antenatal steroid use showed a significant protective effect (p = 0.029; RR = 0.32), consistent with Carlo et al. (2011), who documented reduced neonatal morbidity and ROP risk with antenatal corticosteroids.[20]

Birth asphyxia emerged as one of the strongest risk factors (p = 0.001; RR = 5.78), aligning with Kumar et al. (2023) and Steinkuller et al. (1999), who found hypoxic-ischemic events critical in ROP development.[21,22] Respiratory distress syndrome (RDS) was significantly associated with ROP (p = 0.019), consistent with findings by Shankar et al. (2014) and Chang et al. (2019), who both highlighted oxygen-related injury as a key factor.[15,23]

The need for invasive ventilatory support significantly increased ROP risk ($p = 0.0012$; RR = 3.93), as reported by Choi et al. (2024), who demonstrated the independent impact of ventilation on severe ROP.[24] Conversely, use of CPAP and oxygen via HFNC or nasal prongs showed no significant association ($p > 0.13$), in agreement with Suga et al. (2022), who found prolonged CPAP to be protective (OR = 0.84).[25]

Prolonged oxygen therapy was also a significant factor (mean duration 28.4 days in ROP group, $p < 0.0001$), emphasizing oxygen fluctuation as a major contributor. These findings support Wallace et al. (2007), who stressed that duration and variability in oxygen delivery matter more than mode alone.[26]

Lastly, apnoea episodes ($p = 0.0136$; RR = 3.87) and neonatal sepsis ($p = 0.019$; RR = 3.09) were strongly linked to ROP. These findings are consistent with Chaudhari et al. (2009) and Sathar et al. (2018), who also reported apnoea and systemic infections as significant contributors to abnormal retinal vascularization.[27,28]

CONCLUSION

This prospective observational study aimed to determine the incidence of Retinopathy of Prematurity (ROP) and its association with maternal and neonatal risk factors among preterm neonates. Among 70 screened neonates, the incidence of ROP was found to be 25.7%. The study revealed a significant association between ROP and lower gestational age, low birth weight, and postnatal complications such as respiratory distress syndrome, birth asphyxia, neonatal sepsis, apnoea, and the need for mechanical ventilation. These factors likely contribute to abnormal retinal vascular development through mechanisms of hypoxia and oxidative stress.

While maternal factors like gestational hypertension, gestational diabetes, and PPROM did not show significant statistical associations, the use of antenatal corticosteroids appeared protective, likely reducing neonatal morbidity and thus lowering ROP risk.

In conclusion, timely screening, meticulous neonatal care, judicious oxygen therapy, and preventive antenatal strategies can help reduce the burden of ROP in high-risk preterm neonates.

Limitations of the Study

1. Single-centre study with limited sample size (n=70), time, and resources — may limit generalizability to other settings.
2. Small sample size reduced the ability to detect weaker associations or assess rarer risk factors.
3. Potential confounders such as genetic factors, nutrition, cardiovascular anomalies, IVH, and post-discharge care were not accounted for.
4. Long-term visual outcomes and progression/regression of ROP post-neonatal period were not evaluated.
5. Observational design restricts the ability to establish causality between risk factors and ROP.
6. Treatment outcomes (e.g., laser therapy, anti-VEGF) were not assessed.

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