RESEARCH PAPER

Incidence and Risk Factors of Retinopathy of Prematurity in Infants <1800 g: A Tertiary Care Study from West Bengal

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Abstract

Background

Retinopathy of prematurity (ROP) is a major cause of preventable childhood blindness. Improvements in neonatal survival in developing countries have increased the number of preterm infants at risk, including those with relatively higher birth weights. Identification of local incidence and risk factors is essential for optimizing screening strategies.

Objective

To determine the incidence of ROP and identify associated perinatal and neonatal risk factors among infants weighing less than 1800 g in a tertiary care center.

Methods

This prospective observational study was conducted over 12 months in the ROP clinic of a tertiary hospital in eastern India. Two hundred preterm infants with birth weight <1800 g underwent serial ophthalmic examinations using indirect ophthalmoscopy. Data on oxygen exposure, metabolic parameters, perinatal status, and neonatal morbidities were recorded. Statistical associations between these variables and development of ROP were analyzed.

Results

ROP was detected in 56 of 200 infants, giving an incidence of **28%**. Among infants weighing 1501–1800 g, 24.76% developed ROP. Most cases were Stage 1 (46.45%) or Stage 2 (42.85%), and no infant had plus disease. Oxygen therapy showed strong association with ROP; affected infants had higher maximum oxygen saturation, lower minimum saturation, and longer duration of oxygen exposure ($p<0.05$). Hyperglycemia and lower APGAR scores at one and five minutes were significantly associated with ROP. Respiratory distress syndrome, apnea of prematurity, septicemia, anemia, and need for blood transfusion were also significantly more common in infants who developed ROP. No association was observed with surfactant therapy, necrotizing enterocolitis, intraventricular hemorrhage, patent ductus arteriosus, or maternal risk factors.

Conclusion

ROP affected more than one-fourth of preterm infants, including a substantial proportion with birth weight above 1500 g. Careful oxygen monitoring, metabolic stability, and early identification of high-risk neonates are critical for preventing disease progression. Screening protocols in similar settings may need to include heavier infants.

Keywords: Retinopathy of prematurity; prematurity; low birth weight; oxygen therapy; neonatal risk factors; hyperglycemia; APGAR score; anemia; blood transfusion; neonatal intensive care.

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Introduction

Retinopathy of prematurity (ROP), previously known as retrolental fibroplasia (RFL), is a vaso-proliferative disorder of the developing retina that primarily affects preterm infants. The condition arises due to abnormal retinal vascularization and is strongly associated with immaturity of the retinal vasculature. Preterm neonates, particularly those with low birth weight (LBW), are especially vulnerable to this disease, more so when exposed to supplemental oxygen (O_2) during the neonatal period. ROP remains one of the leading causes of preventable blindness in infants worldwide[1]. ROP is closely linked to prematurity, low birth weight, oxygen administration, and several other contributing factors that are still being explored[2]. It is a potentially blinding disorder with a variable incidence across different neonatal intensive care units[3]. Reported incidence rates range from 21% to 65.8% in Western

studies[4] and from 34.9% to 60.1% in Indian studies[2]. Screening guidelines formulated by the American Academy of Pediatrics (AAP) and the American Association for Pediatric Ophthalmology and Strabismus (AAPOS), based on the CRYO-ROP and LIGHT-ROP trials, recommend screening infants with birth weight ≤1500 g or lower gestational age[5].

However, the epidemiology of ROP differs considerably between developed[6] and developing countries[7]. In many low- and middle-income settings, especially in rural and semi-urban regions, the survival rate of very low birth weight (VLBW) and extremely low birth weight (ELBW) infants has traditionally been lower, contributing to an apparently reduced incidence of ROP in these groups as reported in Indian studies. Conversely, with improving neonatal care and survival, infants with birth weight <1501 g in developing countries are now more likely to develop ROP compared to their counterparts in Western nations[6,8]. Furthermore, recent studies have reported an increasing incidence of ROP in infants weighing more than 1501 g; however, these infants are still largely excluded from routine screening programs.

The pathogenesis of ROP is complex and multifactorial[9]. Several antenatal and postnatal risk factors have been implicated, including prematurity, sepsis, necrotizing enterocolitis, hyperoxia, intraventricular hemorrhage (IVH), severe respiratory distress requiring mechanical ventilation, shock, hypoxia, prolonged ventilatory support, blood transfusions, prolonged oxygen exposure, severity of neonatal illness, anemia, high ambient light exposure, metabolic acidosis, and vitamin E deficiency. In contrast, breast-feeding has been proposed to have a protective effect against the development of ROP[10,11].

In view of the evolving neonatal survival patterns in developing countries, the increasing recognition of ROP in relatively heavier preterm infants, and the limited data from eastern India, the present study was undertaken to determine the incidence of retinopathy of prematurity in infants weighing less than 1800 g and to identify the associated neonatal risk factors in a tertiary care setting.

Aims and Objectives

Aim

To evaluate the incidence of retinopathy of prematurity (ROP) and identify the associated risk factors among preterm infants weighing less than 1800 g attending a tertiary care centre.

Objectives

1. To determine the incidence of retinopathy of prematurity in infants with birth weight <1800 g.
2. To assess the association between various perinatal and neonatal risk factors and the development of ROP.

METHODOLOGY

Study Design

This was a **prospective, observational, hospital-based study** conducted to assess the occurrence of ROP and its associated risk factors in preterm neonates.

Study Setting

The study was carried out at the **ROP clinic of the Ophthalmology Outpatient Department, Nil Ratan Sircar Medical College and Hospital, Kolkata**, a tertiary care referral center catering to both urban and rural populations. Infants were referred from the neonatal intensive care unit (NICU) and postnatal wards for routine ROP screening.

Study Duration

The study was conducted over a period of **12 months**, from **March 2019 to February 2020**.

Study Population

The study population comprised **preterm infants with birth weight less than 1800 g** who presented to the ROP clinic either for initial screening or for scheduled follow-up examinations.

Sample Size

A total of **200 eligible infants** were enrolled consecutively during the study period.

Eligibility Criteria

Inclusion Criteria

- Preterm infants with **birth weight <1800 g**
- **Gestational age <36 completed weeks**, assessed by maternal obstetric history or Expanded New Ballard Scoring System
- Both male and female infants
- Infants whose parents or legal guardians provided **written informed consent**

Exclusion Criteria

- Infants with **birth weight ≥1800 g**
- Gestational age **≥36 weeks**
- Infants who failed to complete scheduled ROP follow-up for any reason
- Presence of congenital ocular anomalies or media opacities interfering with fundus examination
- Infants with known congenital retinal disorders

Operational Definitions of Risk Factors

For uniformity and consistency, the following definitions were adopted:

- **Low gestational age:** Gestational age <36 weeks.
- **Low birth weight:** Birth weight <1800 g.
- **Oxygen exposure:** Duration (hours), mode (oxygen hood, nasal prongs, CPAP, or mechanical ventilation), and flow rate of supplemental oxygen received.
- **Hypoxia and hyperoxemia:** Evaluated using arterial blood gas analysis and continuous pulse oximetry monitoring; oxygen saturation values between 88% and 92% were considered the reference range.
- **Hyperglycemia:** Random blood glucose level >125 mg/dL, recorded daily during the first seven days of life.
- **Thrombocytopenia:** Platelet count $<1.5 \times 10^5$ cells/mm³.
- **Severe respiratory illness:** Requirement of mechanical ventilation, with documentation of duration, fraction of inspired oxygen (FiO_2), peak inspiratory pressure, and positive end-expiratory pressure.
- **Septicemia:** Proven by positive blood culture for bacterial or fungal organisms or supported by laboratory parameters such as leukopenia, neutropenia, or elevated band cell ratio.
- **Anemia:** Hemoglobin or hematocrit values more than two standard deviations below the mean for postnatal age.
- **Blood transfusion:** Administration of whole blood or blood products (packed red blood cells, platelets, or fresh frozen plasma), recorded in mL/kg.

ROP Screening Procedure

Timing of Screening

Initial ROP screening was performed as per **AAP 2013 guidelines**, based on postmenstrual age and chronological age. Follow-up examinations were scheduled according to retinal findings and ICROP recommendations.

Pupil Dilation

Pupillary dilation was achieved using **tropicamide 0.5%** instilled every 10–15 minutes for four doses beginning one hour prior to examination, followed by **phenylephrine 2.5%** instilled once immediately before examination. Repeated instillation of phenylephrine was avoided to minimize systemic side effects.

Examination Technique

ROP screening was performed by an experienced ophthalmologist using **binocular indirect ophthalmoscopy** with a +20 diopter lens. After instillation of topical anesthetic (proparacaine), a neonatal wire speculum was used to separate the eyelids. The anterior segment was examined first to assess pupillary dilation, tunica vasculosa lentis, and lens clarity.

The posterior pole was then evaluated for the presence of plus or pre-plus disease, followed by systematic examination of the peripheral retina in all clock hours using a scleral depressor. Findings were carefully documented after each examination.

Classification of ROP

ROP was classified according to the **International Classification of Retinopathy of Prematurity (ICROP)** based on:

- Zone of involvement
- Stage of disease
- Extent (clock hours)
- Presence or absence of plus or pre-plus disease

The timing of subsequent examinations was determined based on disease severity and progression.

Data Collection

Data were collected using a structured proforma and included:

- Demographic details (birth weight, gestational age, sex)
- Perinatal factors (APGAR scores at 1 and 5 minutes, mode of delivery)
- Oxygen exposure parameters
- Metabolic and hematological variables
- Neonatal morbidities such as respiratory distress syndrome, apnea of prematurity, septicemia, necrotizing enterocolitis, intraventricular hemorrhage, and patent ductus arteriosus
- Details of blood transfusion and supportive therapies

Ethical Considerations

Approval for the study was obtained from the **Institutional Ethics Committee** prior to commencement. Written informed consent was obtained from parents or legal guardians after explaining the purpose, procedures, benefits, and potential risks of the study in their vernacular language. Confidentiality of patient data was strictly maintained.

Statistical Analysis

All collected data were entered into Microsoft Excel and analyzed using the **Statistical Package for Social Sciences (SPSS) version 26.0**. Continuous variables were expressed as mean ± standard deviation and compared using Student's *t*-test. Categorical variables were expressed as proportions and compared using the

chi-square test or Fisher's exact test, as appropriate. Multivariate logistic regression analysis was performed to identify independent risk factors associated with the development of ROP. A *p*-value <0.05 was considered statistically significant.

Results

Demographics

The present study is conducted at the ROP clinic of Eye-OPD of Nil Ratan Sircar Medical College and Hospital, Kolkata from March 2019 to February 2020 over a period of 12 months. Two hundred (200) babies having birth weight <1800g visiting ROP clinic and those referred from NICU were enrolled in this study. The details are shown in Table 1

Table 1. Baseline Characteristics of the Study Population

Variable	Number (%)
Total infants screened	200
Birth weight <1500 g	95 (45%)
Birth weight 1501–1800 g	105 (55%)
Male	103 (51.5%)
Female	97 (48.5%)
Gestational age <32 wk	58 (29%)
Gestational age 32–36 wk	142 (71%)

Incidence of ROP

56 babies out of 200 babies (28%) were having ROP. In babies having birth weight between 1501-1800g, 26 out of 105 babies had ROP (24.76%). Regarding staging of ROP**,** out of 200 babies having birth weight <1800g in 144 babies no ROP were found. A detailed description of Stage 1 to 5. This is shown in Table 2.

Table 2: Staging of ROP

Stage of ROP	BW<1500g	BW1501-1800g	BW <1800g
No ROP	65	79	144
Stage 1	14 (46.65%)	12 (46.1%)	26 (46.45%)
Stage 2	12 (40%)	12 (46.1%)	24 (42.85%)
Stage 3	2 (6.66%)	1 (3.84%)	3 (5.35%)
Stage 4	1 (3.33%)	1 (3.84%)	2 (3.5%)
Stage 5	1 (3.33)	0	1 (1.78%)
Plus, disease	0	0	0
Any ROP	30	26	56

Need of oxygen administration

41 babies out of 56 babies (73.21%) having BW <1800g and 19 babies out of 26 babies (82.60%) required oxygen by any of the modes like through oxygen hood, oxygen prongs, bubble CPAP (continuous positive airway pressure) or mechanical ventilation. The requirement of oxygen was significant for both BW<1800g and BW 1501-1800g. This is shown in Table 3.

Table 3: Oxygen-Related Variables and ROP

Variable	ROP Present	No ROP	p-value
Oxygen required	41	30	<0.0001
Maximum SpO_2 (%)	98.87 ± 1.13	97.23 ± 1.98	0.024
Minimum SpO_2 (%)	81.95 ± 6.57	87.68 ± 3.33	0.002
Duration of oxygen (hrs)	60.15 ± 57.57	11.48 ± 24.46	<0.001

Perinatal and metabolic factors

Blood glucose level were measured for first seven days of life. Babies who were having ROP had higher blood glucose level (179+-12mg/dl) as compared to those who did not have ROP (120+-10mg/dl) (p=-0.0032). In subgroup of BW 1501-1800g, blood glucose level was higher among those having ROP as compared to those not having ROP (p=0.0035). Infants who developed ROP demonstrated significant differences in metabolic and immediate postnatal parameters when compared with those who did not develop the disease. Mean blood glucose levels during the first week of life were higher among infants with ROP. Similarly, lower APGAR scores at both one minute and five minutes were more frequently observed in the ROP group.

In the present study groups, no baby had one-minute APGAR score less than 3, but those having ROP had a lower APGAR at both 1 and 5 minutes when compared to those without ROP. There was a statistically significant difference in the distribution of APGAR score between those having ROP and not having ROP in both BW<1800g and BW1500-1800g subgroup recorded at first and fifth minute of life (P value<0.0001). This is shown in Table 4.

Table 4. Perinatal and Metabolic Factors

Variable	ROP Present	No ROP	p-value
Hyperglycemia (mg/dL)	179 ± 12	120 ± 10	0.003
APGAR <6 at 1 min	29	30	<0.0001
APGAR <7 at 5 min	26	24	<0.001

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Neonatal Morbidities

Several neonatal morbidities were significantly more common among infants who developed ROP. Respiratory distress syndrome and apnea of

prematurity were observed more frequently in the ROP group. In addition, septicemia, anemia, and the need for blood transfusion showed significant associations with the occurrence of ROP. A detailed comparison between infants with and without ROP is presented in Table 5**.**

Table 5. Neonatal Morbidities Associated with ROP

Variable	ROP Present	No ROP	p-value
Respiratory distress syndrome	38	23	<0.001
Apnea of prematurity	22	14	<0.001
Septicemia	30	20	0.003
Anemia	33	24	0.03
Blood transfusion	36	22	0.039

Certain maternal and neonatal variables were analyzed but did not demonstrate a statistically significant association with the development of ROP. These included surfactant therapy, necrotizing enterocolitis, intraventricular hemorrhage, patent ductus arteriosus, pregnancy-induced hypertension, antepartum hemorrhage, meconium-stained amniotic fluid, and birth order. These findings are shown in Table 6**.**

Table 6. Variables Not Showing Significant Association

Variable	p-value
Surfactant therapy	Not significant
Necrotizing enterocolitis	Not significant
Intraventricular hemorrhage	Not significant
Patent ductus arteriosus	Not significant
Pregnancy induced hypertension	Not significant
Antepartum hemorrhage	Not significant
Meconium-stained liquor	Not significant
Birth order	Not significant

Discussion

Retinopathy of prematurity (ROP) remains a leading and largely preventable cause of childhood visual impairment worldwide. Improvements in neonatal intensive care have increased survival of premature infants, but this has simultaneously expanded the population at risk for disordered retinal vascular development.[1] In the present study involving infants weighing less than 1800 g, the overall incidence of ROP was 28%, which lies within the range reported from many neonatal units in India and other middle-income countries.[2,3]

A noteworthy finding was the occurrence of ROP in nearly one-quarter of infants in the 1501–1800 g subgroup. Similar observations have been reported from Indian cohorts where heavier or more mature infants developed treatable disease, emphasizing that Western screening cutoffs may miss babies in developing settings.[7,8] These reports advocate tailoring screening criteria to regional neonatal practices and survival patterns.

With regard to severity, the majority of affected infants in our study had Stage 1 or Stage 2 ROP, and advanced disease was uncommon. Large multicenter natural history studies have shown that systematic screening programs often identify disease in earlier stages, allowing timely intervention and reducing progression to retinal detachment.[4] The absence of plus disease in our cohort may reflect early referral and close follow-up.

Oxygen exposure emerged as one of the strongest associations with ROP. Infants who developed ROP were more likely to have received oxygen therapy, had higher maximum saturation levels, lower minimum levels, and longer duration of supplementation. The causal relationship between oxygen and ROP has been recognized since the early descriptions of retrolental fibroplasia.[11] Contemporary research has clarified that both hyperoxia and repeated fluctuations in oxygenation disturb vascular endothelial growth factor regulation, leading to abnormal neovascularization.[9] Reviews of modern NICU practice continue to emphasize careful oxygen targeting as a key modifiable preventive strategy.[1]

Metabolic instability was also evident. Hyperglycemia during the first week of life was significantly associated with ROP in our study. Previous analyses have similarly linked elevated glucose levels with increased oxidative stress and higher probability of severe disease, although the mechanism may be partly mediated by overall illness severity.[1]

Perinatal compromise, reflected by lower APGAR scores, showed a significant relationship with ROP. Infants requiring more resuscitative support at birth may experience hypoxic–ischemic stress that interferes with normal retinal vascularization. Associations between low APGAR scores and ROP have been noted in several observational datasets.[8]

Respiratory morbidities, particularly respiratory distress syndrome and apnea of prematurity, were markedly more frequent in affected infants. Recurrent hypoxia followed by re-oxygenation is believed to

intensify free radical injury and angiogenic drive within the immature retina, a mechanism strongly supported by experimental and clinical data.[8]

Septicemia was another significant factor. Systemic infection promotes inflammatory cascades and endothelial dysfunction, both of which may potentiate retinal vascular damage. Multiple contemporary studies have confirmed higher ROP rates in infants with culture-proven sepsis.[3]

Hematological variables further contributed to risk. Anemia and the need for blood transfusion were significantly associated with ROP. It has been proposed that transfusion increases oxygen delivery and oxidative stress by replacing fetal hemoglobin with adult hemoglobin, thereby exacerbating retinal injury.[12] Large population studies have repeatedly identified transfusion exposure as an important marker for disease development.

Conversely, maternal and neonatal variables such as surfactant therapy, necrotizing enterocolitis, intraventricular hemorrhage, patent ductus arteriosus, and hypertensive disorders of pregnancy did not demonstrate significant associations in our cohort. Similar inconsistencies are described in the literature, where these factors often lose statistical significance after controlling for gestational age and oxygen requirement.[1]

Overall, our findings reinforce that ROP is multifactorial but strongly linked to potentially modifiable aspects of neonatal care. The presence of disease in infants up to 1800 g supports the need for region-specific screening strategies and continued vigilance in NICU monitoring.[7,8] Optimizing oxygen delivery, preventing infection, and stabilizing systemic parameters remain essential to reducing ROP-related blindness.

Limitations

This study has certain limitations. It was conducted at a single tertiary care center, and the findings may not be generalizable to other neonatal units with different patient profiles or clinical practices. The sample size, although adequate to demonstrate significant associations, limits the strength of subgroup analyses. Multivariate modeling to determine independent predictors was not performed, and therefore potential confounding between variables such as gestational age, illness severity, and oxygen exposure cannot be completely excluded. In addition, long-term visual outcomes were not evaluated.

Future Directions

Future research should involve multicentric collaborations with larger and more diverse populations to validate these findings and improve generalizability. Development of predictive models incorporating oxygen metrics, metabolic parameters, and systemic morbidities may help identify infants at highest risk. Longitudinal follow-up studies evaluating visual and neurodevelopmental outcomes would provide further insight into the long-term impact of ROP. Continuous refinement of region-specific screening guidelines based on evolving neonatal survival patterns is also warranted.

Conclusion

The present study demonstrates that retinopathy of prematurity continues to affect a substantial proportion of preterm infants, including many weighing more than 1500 g. Oxygen exposure, glycemic instability, low APGAR scores, respiratory morbidity, septicemia, anemia, and blood transfusion were significantly associated with disease development. These findings highlight the importance of meticulous neonatal monitoring and timely ophthalmic screening. Adaptation of screening criteria to local epidemiology may be necessary to prevent avoidable blindness.

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