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Risk Factors for Retinopathy of Prematurity in Rural Tertiary Health Care Center North India

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Abstract

Objective: Retinopathy of prematurity (ROP) poses a significant challenge in the area of neonatal care, characterized by an aberrant retinal vasculature, often culminating in irreversible vision loss in childhood. **Methodology**: This prospective observational study was conducted at UPUMS Saifaiafter obtaining ethical clearance in the UPUMS, Saifai, Uttar Pradesh, India. The study spanned one year and enrolled a total of 250 neonates admitted to the Neonatal Intensive Care Unit (NICU) between March 2023 and March 2024. **Results:** Of the 20 infants weighing less than 1000 grams, 11 developed stage 1 or 2 ROP, highlighting a significant risk for ROP among extremely low-birth-weight infants. Among the 79 infants weighing between 1000 and 1500 grams, 26 developed ROP, with stage 2 being the most common, suggesting that infants in this weight category have a moderate risk of ROP development, with many progressing to advanced stages. Out of the 98 infants weighing between 1500 and 2000 grams, 14 developed ROP, with the majority of cases being stage 1 or 2, indicating that even among infants with slightly higher birth weights, there is still a notable risk of ROP development. Interestingly, out of the 53 infants weighing more than 2000 grams, only 5 developed ROP, all of which were limited to stages 1 or 2, suggesting that infants in this category have the lowest risk of developing ROP due to their higher birth weights. We examined a total of 250 infants across all weight categories, and 56 of them developed ROP. Stage 1 and 2 ROP were most common, indicating that the condition is more prevalent in its milder forms. **Conclusion**: Lower birth weight is associated with a higher probability of ROP occurrence, emphasizing the significance of monitoring and managing ROP in extremely low-birth-weight infants. Categories: Pediatrics, Ophthalmology

Keywords: ROP, visual impairment, intraventricular haemorrhage, irreversible vision loss, aberrant retinal vasculature, premature retinopathy.

Introduction

Retinopathy of prematurity (ROP) is a significant challenge in neonatal care, characterized by an aberrant retinal vasculature that often culminates in irreversible vision loss in childhood. Despite considerable strides in medical science, ROP persists as a preventable cause of visual impairment, affecting thousands of infants worldwide every year [1]. Tracing back its origins to the mid-20th century under the guise of retrolental fibroplasia, ROP emerged as an alarming epidemic primarily affecting premature infants, particularly evident in industrialized nations such as the United States and Western Europe. Unregulated oxygen administration supplementation marked the first epidemic wave, largely responsible for this initial surge [2]. Subsequent waves, particularly the second one in the 1970s, demonstrated the close relationship between ROP incidence and advancements in neonatal care. They showed how there is a paradoxical link between higher survival rates for babies born very early and a higher risk of developing ROP [3]. In recent years, a disturbing trend has emerged, marked by a surge in ROP incidence documented in developing countries, indicative of what is now termed the third epidemic

of ROP [4]. The driving forces behind this resurgence are numerous, including constantly increasing premature birth rates, very limited access to comprehensive neonatal care, and evolving medical practices. Initial theories mostly suggested that high oxygen levels were the main cause of ROP [5-8]. However, new evidence has called this idea into question, showing that the cause of ROP is complex and that many risk factors work together in a complicated way [9]. Central among these risk factors are low birth weight (BW) and gestational age (GA), extensively documented as predisposing factors for ROP development [5-8, 10, 11]. Moreover, researchers have identified gender, phototherapy, multiple gestations, intraventricular haemorrhage, and blood transfusions as additional factors that contribute to heightened ROP susceptibility [11-13]. The heterogeneity in ROP prevalence and screening outcomes across different geographical regions emphasizes the need for tailored screening programs that are sensitive to local contextual nuances [14] India, notably, bears a substantial burden of ROP-related blindness, with an estimated 500 cases reported annually [1]. Improved survival rates among very low-birth-weight preterm neonates contribute to the escalating incidence, highlighting the critical importance of robust prenatal care initiatives aimed at preventing premature births. ROP is a complicated disease that starts with abnormal vascular proliferation in the developing retina happens because oxygen kills endothelial cells and VEGF is blocked, which causes retinal ischemia and new blood vessels to grow [4-6]. Effective screening protocols serve as the cornerstone of ROP management, with guidelines advocating for comprehensive screening of at-risk infants, including those born prematurely or with low birth weights [12]. The stages of ROP progression, from demarcation lines to total retinal detachment, give us useful information about how bad the disease is. The later stages of Plus disease and aggressive posterior ROP are associated with higher risks of permanent blindness [9]. The present study endeavors to contribute to the existing body of research on ROP prevalence and incidence, with a particular focus on infants born prematurely or with low birth weights, especially those born before 34 weeks of gestation or weighing under 2000 g. This study aims to improve our knowledge of ROP epidemiology by looking at all the different demographic, clinical, and environmental risk factors that influence its development. Our study will help us come up with more effective ways to prevent and treat this debilitating condition so that it has a smaller effect on early childhood health outcomes

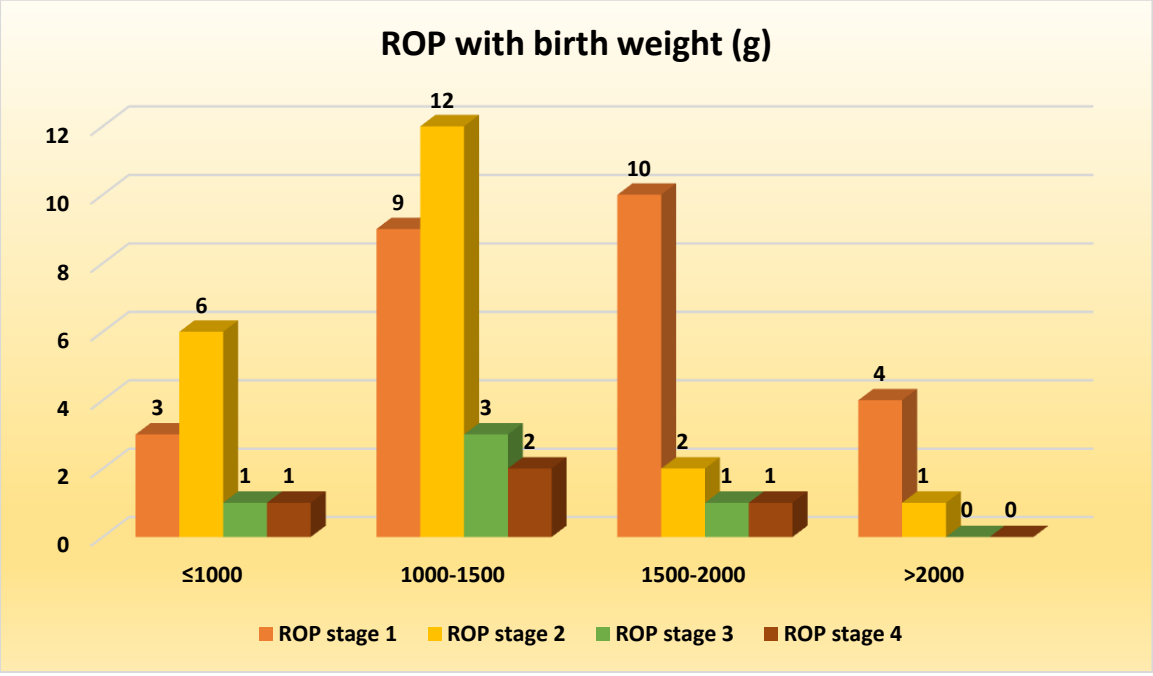
Materials And Methods

We conducted this prospective study in the Neonatal Intensive Care Unit (NICU) of a rural tertiary care university hospital in North India. The study was a collaboration between the Departments of Pediatrics and Ophthalmology. The study cohort comprised 250 neonates, specifically all preterm newborns hospitalized in the Neonatal Intensive Care Unit (NICU) between March 2023 and March 2024. The study included infants who received oxygen therapy for more than seven days, had a gestational age greater than 32 weeks, or had a birth weight greater than 2000 g. We assessed infants born between 32 and 34 weeks gestational age for signs of instability, such as infection, hypoxia, or ventilation. We did not include neonates who died before the initial ophthalmologic test. The study excluded infants with congenital malformations, chromosomal abnormalities, or inborn errors of metabolism. All newborns involved in this study underwent the following procedures: Neonatal history includes identifying risk factors such as prematurity, sepsis (foul-smelling amniotic fluid, premature rupture of membranes lasting more than 18 hours, maternal urinary tract infection, maternal fever during labor exceeding 38°C), and neonatal asphyxia. The current medical record includes the typical manifestations of respiratory distress necessitating oxygen therapy, sepsis, phototherapy, congenital heart disease, and blood transfusion. The ophthalmologist conducted routine examinations of all infants at intervals of 1-2 weeks, starting from the 4th week after birth. One hour before the examination, the ophthalmologist enlarged the pupils with a mixture of topical phenylephrine 2.5% and tropicamide 0.5% eye drops. We used a 20-diopter lens for indirect ophthalmoscopy, a speculum, and scleral depression. The ophthalmologist performed a retinal examination, using retinal drawing and RetCam 2 fundus imaging as needed. Retinopathy of prematurity (ROP) is characterized by the incomplete or abnormal growth of blood vessels in the retina. The International Committee for ROP Classification classifies ROP based on its location on the retina (zones 1-3) and severity (stages 1-5). All patients diagnosed with stage 3 ROP

received laser photocoagulation. The prenatal factors included gestational age, birth weight, sex, and mode of delivery. We observed information about respiratory distress syndrome, oxygen therapy, phototherapy for jaundice, the number of blood transfusions, sepsis, low blood pressure, intraventricular hemorrhage and patent ductus arteriosus after birth. Results Table 1 presents data on infant birth weight categories and the occurrence of Retinopathy of Prematurity (ROP) at various stages. We observed that 11 out of 20 infants in the ≤1000g category developed ROP. In this category, the majority of ROP cases are either stage 1 or stage 2, indicating a significant risk of ROP development among extremely low-birth-weight infants. Among the 79 infants with a birth weight of 1000 1500 g, 26 developed ROP. The distribution across ROP stages is relatively spread out, with stage 2 being the most common, suggesting that infants in this weight category have a moderate risk of ROP development, with a significant number progressing to more advanced stages. Out of 98 infants weighing 1500-2000 g, 14 developed ROP. 2

Birth Weight (g)	No. of infants	Infants with ROP	ROP Stage 1	Rop stage 2	Rop stage 3	Rop stage 4
≤1000	20	11	3	6	1	1
1000-1500	79	26	9	12	3	2
1500-2000	98	14	10	2	1	1
>2000	53	5	4	1	0	0
Total	250	56	26	21	5	4

TABLE 1:Association of ROP and birth weight(g)



Interestingly, most ROP cases in this category are stage 1 or 2, similar to the ≤1000g category, indicating that even among infants with slightly higher birth weights, there is still a notable risk of ROP development, albeit at a lower rate. Only 5 out of the 53 infants weighing over 2000 g developed ROP, with all cases falling into either stage 1 or stage 2. Infants in this category have the lowest risk of ROP development, likely due to their higher birth weights. Among the ROP cases, stage 2 ROP is the most prevalent across all birth weight categories, followed by stage 1, suggesting that while ROP is more common in lower-birth-weight infants, it tends to progress to stage 2 more frequently than other stages. We examined 250 infants across all weight categories, and 56 developed ROP. Most ROP cases are in

stages 1 and 2, indicating that the condition is more prevalent in its milder forms, which suggests that early detection and intervention may help prevent the progression of ROP to more severe stages. Table 2 presents data on Retinopathy of Prematurity (ROP) across different gestational age groups. ROP is a potentially blinding eye disorder that primarily affects premature infants. The data is divided into three gestational age categories: ≤28 weeks, 29-32 weeks, and >32 weeks. This categorization helps to understand how prematurity relates to ROP development. Within each gestational age category, the table indicates the number of infants included in the study. For instance, there were 29 infants born at or before 28 weeks, 134 infants born between 29 and 32 weeks, and 87 infants born after 32 weeks. In the ≤28-week gestational age group, out of 29 infants, 12 (approximately 41%) developed ROP. Among them, ROP stage 2 is the most common. The gestational age category of 29-32 weeks exhibits the highest incidence of ROP, affecting 36 out of 134 infants. ROP stage 1 is the most prevalent, followed by stage 2. ROP incidence is relatively lower in infants with gestational age >32 weeks, with only 8 out of 87 infants affected. As gestational age increases, the incidence of ROP decreases, and in this group, we observe ROP stages 1 and 2. Overall, out of the total 250 infants studied, 56 (approximately 22%) developed ROP. The majority of cases are in stages 1 and 2. The data suggests a correlation between a lower gestational age and a higher risk of ROP development. Infants born prematurely, especially those below 32 weeks, are more susceptible to ROP. These findings highlight the increased vulnerability of premature infants to ROP, particularly those born between 28 and 32 weeks of gestation.

Gestational age(weeks)	No. of infants	Infants with ROP	ROP Stage 1	ROP Stage 2	ROP Stage 3	ROP Stage 4
≤28	29	12	2	6	2	2
29-32	134	36	19	12	3	2
>32	87	8	5	3	0	0
Total	250	56	26	21	5	4

TABLE 2: Association of ROP and gestational age(weeks)

Discussion

Our study aimed to investigate the prevalence and risk factors associated with retinopathy of prematurity (ROP) in neonates admitted to a tertiary care center in North India. In the screened population, we found a ROP prevalence of 18.8%. Previous studies conducted in India and other developing countries have reported a similar range [5-9]. However, it is concerning to note that this prevalence rate continues to exceed that of developed nations [7] significantly. The distribution of ROP stages in our study cohort mirrored findings from prior research [6, 9, 12]. Stage 1 3 of 5 ROP was the most prevalent, followed by stages 2, 3, and 4, with no cases progressing to stage 5 [12], suggesting that a significant proportion of the identified cases may be amenable to preventive measures or early intervention. Our analysis confirmed a strong association between ROP and gestational age (GA) and birth weight (BW). Neonates born at less than 32 weeks gestation with a BW below 1500 grams were significantly more likely to develop ROP than their counterparts [2, 6, 8]. These findings underscore the vulnerability of premature and low-birth-weight infants to ROP and highlight the importance of prioritizing close monitoring and timely interventions for this high-risk group. The current study aligns with previous research highlighting the crucial role of gestational age and birth weight as risk factors for ROP [7-10]. Our findings emphasize the need for implementing effective strategies in North India to improve neonatal care, particularly for premature and low-birth-weight infants. They could include ensuring access to advanced monitoring technologies, optimizing oxygen therapy practices, and potentially implementing prophylactic measures where appropriate. By focusing on these areas, we can work towards reducing ROP's burden and safeguarding the vision of this vulnerable population. Our study has certain limitations. First, we conducted the study at a single center with a relatively modest

sample size, which limited the generalizability of the findings. Secondly, the study design was observational, precluding the establishment of causal relationships between risk factors and ROP development. Future multicenter studies with larger sample sizes and possibly a case-control design could provide more robust data.

Conclusions

In conclusion, there is a relationship between birth weight as well as gestational age and the risk of ROP development, with lower birth weights correlating with a higher likelihood of ROP occurrence. It also underscores the importance of monitoring and managing ROP, especially among highly low-birth-weight infants.

Limitations

Our study has certain limitations as the sample size was relatively modest, and the study was conducted at a single center, limiting the generalizability of the findings. Future multicenter studies with larger sample sizes and potentially employing a case-control design could provide more robust data.

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