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Risk Factors and Outcome of Retinopathy of Prematurity (ROP) in A Tertiary Referral NICU at Malappuram District: A Prospective Analytical Study

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ABSTRACT

Background: Retinopathy of prematurity (ROP) is a potentially preventable cause of childhood blindness and remains a major public health concern in preterm neonates, especially in developing countries like India. With improving survival of premature infants, early identification of risk factors and timely intervention are essential to reduce visual morbidity.

Methods: This prospective analytical study was conducted over two years (January 2023 to January 2025) in a Level III NICU of a tertiary care hospital in Malappuram district, Kerala. A total of 151 preterm neonates fulfilling standard ROP screening criteria were enrolled. Serial retinal examinations were performed using indirect ophthalmoscopy starting at 3–4 weeks of postnatal age and continued until complete retinal vascularisation or up to 6 months of corrected gestational age. Clinical variables and neonatal morbidities were recorded and analyzed for association with ROP severity.

Results: Among the 151 infants screened, 16 (10.6%) developed Type 1 ROP, 57 (37.7%) developed Type 2 ROP, and 78 (51.6%) had no ROP. Type 1 ROP was significantly associated with lower gestational age, lower birth weight, invasive mechanical ventilation, surfactant therapy, inotrope use, sepsis, patent ductus arteriosus, and blood transfusion ($p<0.05$). No significant association was observed with intrauterine growth restriction. Laser photocoagulation and intravitreal anti-VEGF therapy were required in 11% of infants each, with complete regression noted in all treated cases.

Conclusion: Severe ROP is strongly associated with extreme prematurity, very low birth weight, respiratory morbidity, sepsis, PDA, and blood transfusion. Early screening and timely treatment result in favorable anatomical and visual outcomes.

Key-words: Blinding disease; Retinopathy of prematurity (ROP); Extreme prematurity; Patent ductus arteriosus

INTRODUCTION

Retinopathy of prematurity is a potentially blinding disease that affects preterm neonates born before 34 weeks of gestation or with a birth weight of less than 2 kg and who have received intensive neonatal care.

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According to the World Health Organization, ROP has emerged as the third epidemic of childhood blindness in India and other middle-income countries [1]. In preterm infants, ROP presents with a wide clinical spectrum, ranging from mild retinal changes that may regress spontaneously to severe progressive vasoproliferation leading to retinal detachment and irreversible blindness. The maturity of the retina is primarily dependent on gestational age, as normal retinal vascular development proceeds from the optic nerve head anteriorly toward the peripheral retina during intrauterine life. Premature birth interrupts this orderly vascularization process, rendering the immature retina vulnerable to abnormal

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vascular responses. The incidence of ROP in India has been reported to range between 38% and 47% among low-birth-weight infants, largely attributed to improved neonatal survival rates and advancements in intensive care practices [2].

Although unregulated oxygen therapy was initially considered the principal causative factor, it is now well established that ROP is a multifactorial disease. Several antenatal and postnatal factors influence its pathogenesis, including prematurity, low birth weight, prolonged and fluctuating exposure to oxygen, recurrent apnea, sepsis, respiratory distress syndrome, multiple blood transfusions, and cardiac conditions such as hemodynamically significant patent ductus arteriosus and critical congenital heart disease [3]. These risk factors often coexist in extremely preterm neonates, increasing the likelihood of progression to severe ROP.

ROP has a lifelong impact on visual acuity and ocular development, significantly affecting quality of life. However, timely screening, early identification of high-risk infants, and prompt intervention can substantially reduce disease-related morbidity. Standardized classification systems and evidence-based treatment strategies have played a crucial role in improving outcomes in infants diagnosed with ROP [4].

MATERIALS AND METHODS

Study Design and Setting- This prospective analytical study was conducted over 2 years, from January 2023 to January 2025, in the Department of Neonatology, Level III Neonatal Intensive Care Unit (NICU) of a tertiary care teaching hospital in Malappuram district, Kerala, India.

Study Population- A total of 151 preterm neonates admitted to the NICU during the study period and fulfilling the unit criteria for ROP screening were enrolled in the study after obtaining informed written consent from parents or guardians.

Inclusion Criteria- Preterm neonates with a birth weight less than 2 kg or gestational age less than 34 weeks were included in the study. Neonates with gestational ages between 34 and 36 weeks were also screened for associated risk factors, including cardiorespiratory support, prolonged oxygen therapy, respiratory distress syndrome, chronic lung disease, blood transfusion, exchange transfusion, or intraventricular hemorrhage.

Exclusion Criteria- Neonates who expired before completion of the initial ROP screening, those lost to follow-up before completion of retinal vascularisation, and neonates with congenital ocular anomalies interfering with retinal examination were excluded from the study.

ROP Screening and Follow-up Protocol- The first screening examination for retinopathy of prematurity was performed at 3–4 weeks of postnatal age. In neonates with gestational age less than 28 weeks or birth weight below 1.2 kg, or when gestational age at birth was not conclusively confirmed, the initial screening was postponed to 2–3 weeks of postmenstrual age. Subsequent retinal examinations were performed at weekly to biweekly intervals until complete retinal vascularisation up to zone 3 or until features of established ROP regression were observed. All ROP screenings were performed by a vitreoretinal surgeon using indirect ophthalmoscopy.

Classification and Treatment of ROP- The staging of ROP was recorded according to the revised International Classification of Retinopathy of Prematurity, including the zone, stage, extent, and the presence or absence of plus disease. Treatment with diode laser photocoagulation was initiated when the disease progressed to Type 1 ROP as per the Early Treatment for Retinopathy of Prematurity (ETROP) guidelines. Infants who progressed to Stage 3 ROP were treated with intravitreal anti-VEGF therapy or laser photocoagulation.

Data Collection- Demographic details, antenatal risk factors, neonatal clinical course, comorbidities, and treatment details were recorded prospectively using a structured proforma.

Statistical Analysis- Data were entered into Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (SPSS), version 25.0. Categorical variables were expressed as frequencies and percentages, while continuous variables were summarized as means and standard deviations. Associations between categorical variables and ROP severity were assessed using the Chi-square test. A p-value of less than 0.05 was considered statistically significant.

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Ethical Considerations- The Institutional Ethics Committee of the participating hospital approved the study. Written informed consent was obtained from parents or legal guardians before enrollment of the neonates in the study.

RESULTS

Table 1 shows the demographic and clinical details of 151 neonates in the study. Males (51%) were slightly more than females (49%). Most babies (55%) were born between 32 and 33+6 weeks. More than half (55.6%) required CPAP, while 23.8% needed a ventilator. About 56% of the babies weighed less than 2.5 kg. Few required Avastin (11%) or laser therapy (11%) for eye problems. Most mothers (78.1%) received antenatal steroids, and 30.5% of babies were given surfactant. Around 22.5% had intrauterine growth restriction. Common problems included respiratory distress syndrome (28.5%), patent ductus arteriosus (27.2%) and sepsis (15.2%). About 16.6% required a blood transfusion. Other conditions included BPD (6.6%), PVL (2.6%), IVH (1.3%), and asphyxia (0.7%). Around 3.3% needed inotropes.

Table 1: Descriptive statistics of study population

		Frequency	Percentage (%)
Gender	Female	74	49
	Male	77	51
Gestational Age	<28	18	12
	28-31+6	33	22
	32-33+6	83	55
	34-36+6	16	11
	>37	1	01
Respiratory support	BIPAP	15	9.90
	CPAP	84	55.60
	NPO_2	16	10.60
	Ventilator	36	23.80
Weight	<1	18	12
	<1.5	37	25
	<2.5	84	56
	>2.5	12	8
Avastin	No	133	88
	Yes	17	11
Laser	No	134	89
	Yes	16	11
Antenatal steroids	No	32	21.20
	Yes	118	78.10
Surfactant	No	105	69.50
	Yes	46	30.50
IUGR	No	117	77.50
	Yes	34	22.50
PROM	No	90	59.60
	Yes	61	40.40
RDS	No	108	71.50
	Yes	43	28.50
Asphyxia	No	150	99.30
	Yes	1	0.70

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PDA	No	110	72.80
	Yes	41	27.20
Sepsis	Absent	128	84.80
	Present	23	15.20
Blood Transfusion	No	126	83.40
	Yes	25	16.60
BPD	No	141	93.40
	Yes	10	6.60
PVL	No	147	97.40
	Yes	4	2.60
IVH	No	149	98.70
	Yes	2	1.30
Inotrope	No	146	96.70
	Yes	5	3.30

Table 2 illustrates the association between maternal and natal covariates and the development of ROP. A significant association ($p<0.05$) was observed between ROP type and gestational age, birth weight, respiratory support, inotrope use, surfactant, blood transfusion, PDA, and sepsis. However, no significant association ($p>0.05$) was observed between ROP type and IUGR.

Table 2: Analysis of maternal and natal covariates and the development of ROP

		NO ROP (%)	**Type 1 ROP (%)**	**Type 2 ROP (%)**	**Total (%)**	**p-value**
Gestational Age	<28	4(22.23)	10(55.56)	4(22.23)	18(100)	0
	>37	0(0)	0(0)	1(100)	1(100)	
	28-31+6	17(51.52)	5(15.15)	11(33.34)	33(100)	
	32-33+6	42(50.60)	1(1.20)	40(48.19)	83(100)	
	34-36+6	15(93.75)	0(0)	1(6.25)	16(100)	
Total		78(51.66)	16(10.60)	57(37.75)	151(100)	
Weight	<1	5(27.78)	6(33.33)	7(38.89)	18(100)	0
	<1.5	18(48.64)	9(24.32)	10(27.03)	37(100)	
	<2.5	50(59.52)	1(1.19)	33(39.29)	84(100)	
	>2.5	5(41.67)	0(0)	7(58.34)	12(100)	
Total		78(51.66)	16(10.60)	57(37.75)	151(100)	
Respiratory Support	BIPAP	10(66.67)	1(6.67)	4(26.67)	15(100)	0
	CPAP	49(58.34)	0(0)	35(41.67)	84(100)	
	NPO2	8(50)	1(6.25)	7(43.75)	16(100)	
	Ventilator	11(30.56)	14(38.89)	11(30.56)	36(100)	
Total		78(51.66)	16(10.60)	57(37.75)	151(100)	
Inotrope	No	77(52.74)	13(8.90)	56(38.36)	146(100)	1

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	Yes	1(20)	3(60)	1(20)	5(100)	
Total		78(51.66)	16(10.60)	57(37.75)	151(100)	
Surfactant	No	61(58.10)	2(1.90)	42(40)	105(100)	0
	Yes	17(36.96)	14(30.43)	15(32.60)	46(100)	
Total		78(51.66)	16(10.60)	57(37.75)	151(100)	
IUGR	No	63(53.85)	13(11.11)	41(35.04)	117(100)	0.44
	Yes	15(44.12)	3(8.82)	16(47.06)	34(100)	
Total		78(51.66)	16(10.60)	57(37.75)	151(100)	
Blood transfusion	No	73(57.94)	2(1.59)	51(40.48)	126(100)	0
	Yes	5(20)	14(56)	6(24)	25(100)	
Total		78(51.66)	16(10.60)	57(37.75)	151(100)	
PDA	No	65(59.09)	1(0.90)	44(40)	110(100)	0
	Yes	13(31.70)	15(36.68)	13(31.70)	41(100)	
Total		78(51.66)	16(10.60)	57(37.75)	151(100)	
Sepsis	Absent	73(57.03)	3(2.34)	52(40.62)	128(100)	0
	Present	5(21.74)	13(56.52)	5(21.74)	23(100)	
Total		78(51.66)	16(10.60)	57(37.75)	151(100)	

Fig. 1 depicts the association between birth weight and the type of retinopathy of prematurity. The majority of infants who developed Type 1 ROP had a birth weight below 1.5 kg, with a notable proportion belonging to the extremely low birth weight group (<1 kg). Infants with higher birth weights more commonly had Type 2 ROP or no ROP. This figure highlights low birth weight as a strong determinant of severe ROP.

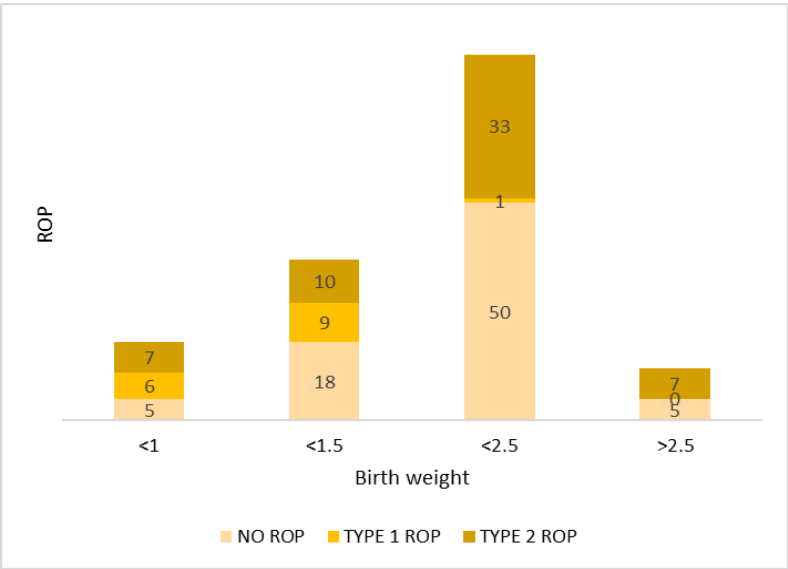

Fig. 1: Association between Birth weight and type of ROP

Fig. 2 depicts the association between gestational age and the type of retinopathy of prematurity. Among the 16 infants with Type 1 ROP, the majority were born at a gestational age below 32 weeks, with a substantial proportion belonging to the extremely preterm group (<28 weeks). Infants born between 28 and 31+6 weeks

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showed a mixed distribution of Type 1 and Type 2 ROP. In contrast, infants born at ≥32 weeks predominantly had either Type 2 ROP or no ROP. This Fig. demonstrates that the severity of ROP increases with decreasing gestational age.

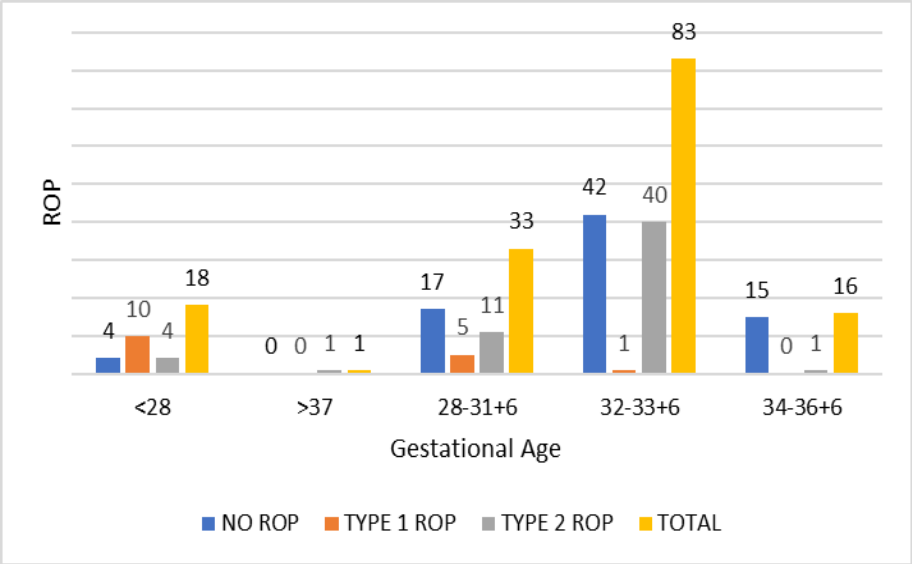

Fig. 2: Association between Gestational age and type of ROP

Fig. 3 shows that Type 1 ROP was most commonly seen in neonates who required ventilator support, while infants managed with CPAP or non-invasive oxygen support had a lower incidence of severe ROP, indicating a strong association between invasive ventilation and Type 1 ROP.

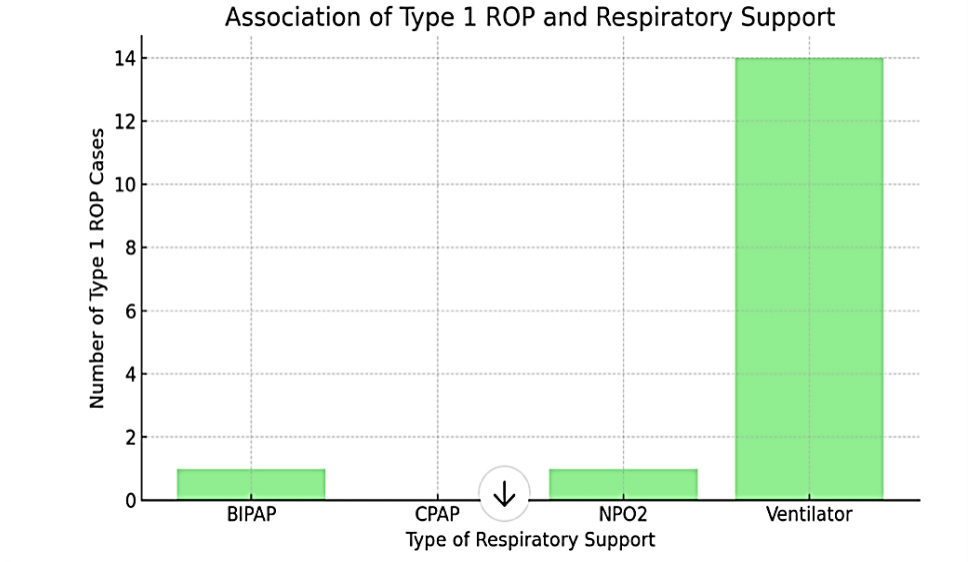

Fig. 3: Association of type 1 ROP and respiratory support

Fig. 4 illustrates the association between Type 1 retinopathy of prematurity and key clinical risk factors, including surfactant therapy, intrauterine growth restriction, blood transfusion, patent ductus arteriosus, and sepsis. Statistically significant associations ($p<0.05$) were observed for all factors except intrauterine growth restriction, indicating a strong correlation between systemic illness, intensive neonatal interventions, and the development of severe ROP.

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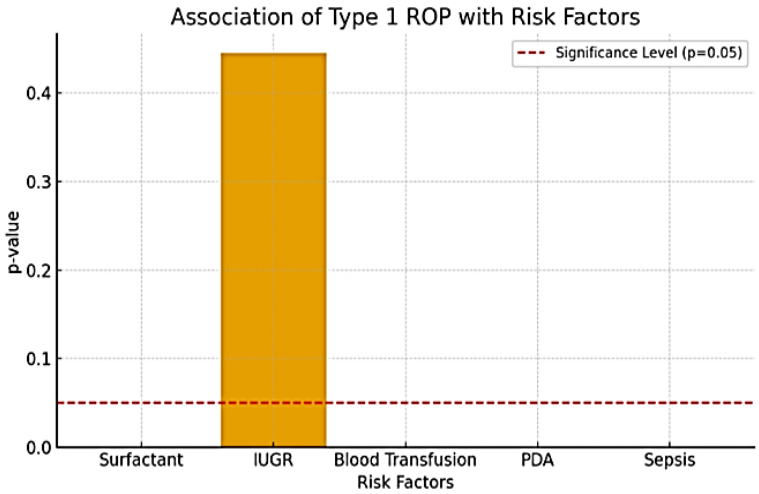

Fig. 4: Association of type 1 ROP and risk factors

Fig. 5 depicts the distribution of selected risk factors—surfactant therapy, inotrope use, blood transfusion, patent ductus arteriosus, sepsis, and intrauterine growth restriction—across infants with no ROP, Type 1 ROP, and Type 2 ROP. Type 1 ROP was predominantly observed among infants with multiple systemic risk factors such as surfactant use, blood transfusion, PDA, and sepsis. In contrast, infants without ROP were more frequently those with fewer or no associated risk factors, highlighting the role of illness severity in ROP progression.

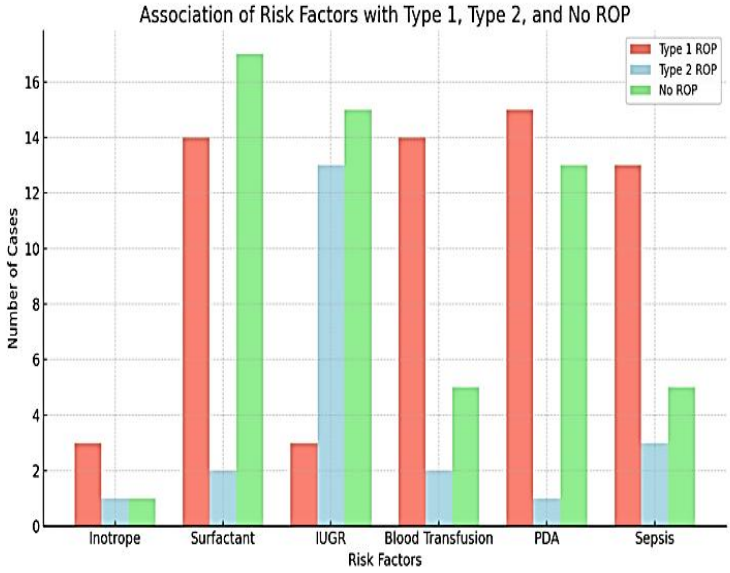

Fig. 5: Association of various risk factors with type 1, type 2 and no ROP

DISCUSSION

Retinopathy of prematurity continues to be a significant cause of preventable childhood visual impairment, particularly in resource-limited settings. In this prospective study conducted in a tertiary referral NICU, 151 preterm infants fulfilling ROP screening criteria were evaluated. The incidence of Type 1 ROP was 10.6%, which is comparable to reports from other Indian centres [5].

Previous studies from Northern India have reported an overall ROP prevalence of 18.5%, while Sujith *et al.* from Vadodara reported a higher incidence of 24% [6]. Studies from Tamil Nadu and Central India have documented Type 1 ROP rates of 6–12%, which closely align with our findings and suggest a similar epidemiological trend across Indian NICUs [7,8].

Gender distribution was nearly equal, and no significant association was observed between sex and the

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development of ROP, consistent with multiple Indian studies [5,6]. Prematurity emerged as the strongest and most consistent risk factor for severe ROP, with 94% of infants with Type 1 ROP born before 32 weeks of gestation and 62% being extremely preterm (<28 weeks), demonstrating a statistically significant association [9]. Immaturity of retinal vasculature predisposes extremely preterm infants to abnormal vascular proliferation under fluctuating oxygen conditions [10].

Low birth weight was similarly associated with disease severity; all infants with Type 1 ROP weighed less than 1.5 kg, and one-third were extremely low birth weight (<1 kg) [9,11]. Respiratory morbidity and oxygen exposure also played a crucial role. A significantly higher proportion of ventilated infants developed Type 1 ROP, whereas none managed exclusively with CPAP developed severe disease [12]. Surfactant therapy, reflecting the severity of respiratory distress, was also significantly associated with Type 1 ROP [14].

Blood transfusions were another highly significant risk factor, with more than half of transfused infants developing Type 1 ROP, consistent with previous reports [12,13]. Sepsis contributed to disease progression, with a higher proportion of septic neonates developing severe ROP [7,10]. Patent ductus arteriosus was similarly associated with Type 1 ROP, likely due to altered systemic perfusion and oxygen delivery [5]. No significant association was observed between intrauterine growth restriction, IVH, PVL, BPD, or NEC and ROP in this cohort [6,8].

Regarding management, 11% of infants required laser photocoagulation and 11% received intravitreal bevacizumab, with complete regression observed in all treated cases, highlighting the effectiveness of early screening and timely intervention [9,14].

CONCLUSIONS

This study confirms that Type 1 retinopathy of prematurity (ROP) predominantly affects the most vulnerable preterm infants, with extreme prematurity (<32 weeks) and very low birth weight (<1.5 kg) being the strongest predictors. Additional risk factors, including invasive mechanical ventilation, surfactant therapy, inotropic support, prolonged oxygen exposure, sepsis, hemodynamically significant patent ductus arteriosus, and blood transfusions, were significantly associated with progression to severe ROP, highlighting the roles of inflammation, hemodynamic instability, and oxidative stress. In contrast, intrauterine growth restriction showed no significant correlation with Type 1 ROP. Structured early screening and timely treatment—using intravitreal Avastin, laser photocoagulation, or combination therapy—resulted in complete disease regression without visual impairment on follow-up. These findings underscore the importance of rigorous ROP screening, meticulous respiratory and oxygen management, and prompt ophthalmic intervention to prevent progression to severe disease, advocating for mandatory screening of all at-risk preterm infants to reduce preventable childhood visual loss.

CONTRIBUTION OF AUTHORS

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Final approval: Vismaya Molly Siby, A. K. Jayachandran, Jayakumar, Vineeta Prakasam

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