



TO STUDY VARIOUS RISK FACTORS ASSOCIATED WITH DEVELOPMENT OF RETINOPATHY OF PREMATURITY IN A TERTIARY CARE CENTRE IN CENTRAL INDIA

Ophthalmology

Dr. Minal Vyawahare	Associate Professor, Department Of Ophthalmology, Government Medical College, Nagpur
Dr. Piyush Madan	Assistant Professor, Department Of Ophthalmology, Government Medical College, Nagpur
Dr. Shivani Shadangri*	M.B.B.S, Third Year Junior Resident, Department Of Ophthalmology Government Medical College, Nagpur *Corresponding Author

ABSTRACT

Purpose: To evaluate the prevalence and associated risk factors for Retinopathy of Prematurity (R.O.P) in preterm infants in a tertiary care centre in Central India. **Methods:** A prospective observational study was conducted over 18 months involving 240 preterm infants (<34 weeks gestation or weight less than 2000g). Infants were screened for R.O.P as per R.B.S.K. Detailed data regarding various risk factors were collected and analysed using chi-square and odds ratio methods. **Results:** R.O.P was diagnosed in 88 infants (36.7%). Significant associations were found with gestational age <32 weeks (OR=11.03, $p<0.003$), birth weight <1500 g (OR=2.82, $p=0.022$), oxygen therapy (OR=1.87, $p=0.037$), sepsis (OR=2.69, $p=0.020$), blood transfusion, hypoglycemia, IVH, RDS, and congenital heart disease (CHD). Gestational age and low birth weight were the strongest predictors. **Conclusion:** R.O.P continues to be a significant neonatal morbidity in India, particularly among extremely premature and low birth weight infants. Early identification of modifiable risk factors and structured screening protocols are essential to prevent vision-threatening complications.

KEYWORDS

Retinopathy of Prematurity, Preterm, Low Birth Weight, Neonatal Screening

INTRODUCTION

Retinopathy of Prematurity (R.O.P) is a vaso-proliferative disorder of the developing retinal vasculature in preterm infants and is a leading cause of preventable childhood blindness worldwide.¹ The pathogenesis involves disrupted vascular development due to premature birth, followed by abnormal neovascularization, which may result in retinal detachment and permanent visual loss if left untreated.² R.O.P incidence varies globally, with higher prevalence reported due to improved neonatal survival but inconsistent N.I.C.U care and inadequate screening programs.³ In India, R.O.P rates range from 21% to 52%, influenced by differences in healthcare access, oxygen monitoring, and neonatal outcomes.^{4,5} Several neonatal and systemic risk factors contribute to R.O.P development. Among the most significant are gestational age <32 weeks and birth weight <1500 g.^{6,7} Other implicated factors include prolonged oxygen supplementation, neonatal sepsis, Intraventricular hemorrhage (I.V.H), blood transfusions, metabolic derangements (e.g., hypoglycemia), and congenital anomalies such as Congenital Heart Disease (C.H.D).⁸⁻¹¹

Understanding these risk factors in specific populations is critical for formulating effective screening and preventive strategies. The present study evaluates the prevalence and risk profile of R.O.P in preterm infants admitted to a tertiary care N.I.C.U in Central India.

MATERIALS AND METHODS

This observational study was conducted in the Neonatal I.C.U., paediatric, and emergency wards of a tertiary care centre. A total of 240 neonates were enrolled based on a calculated sample size using an R.O.P incidence of 18.8%. Inclusion criteria comprised infants with gestational age ≤ 34 weeks, birth weight ≤ 2000 grams, or >36 weeks with specific risk factors such as oxygen therapy, sepsis or blood transfusions. Exclusion criteria included term/post-term infants, incomplete data, and ocular or hereditary retinal disorders, other than R.O.P.

Following institutional ethical approval and informed consent from parents or guardians, preterm infants admitted to the N.I.C.U and pediatric wards were screened weekly for Retinopathy of Prematurity (R.O.P) as per R.B.S.K guidelines. A single vitreo-retinal surgeon conducted dilated fundus examinations using indirect ophthalmoscopy. Detailed maternal and neonatal data, including gestational age, birth weight, oxygen therapy, and hemoglobin levels, were documented. Infants were categorized into R.O.P and non-R.O.P groups based on retinal findings. Follow-up and management were carried out according to E.T.R.O.P guidelines, and parents were counselled for timely follow-up visits.

Statistical analysis was performed using SPSS v25. Chi-square test and Fisher's exact test were used for association. Odds ratios (OR) with 95% confidence intervals (CI) were calculated. A p -value <0.05 was considered statistically significant.

RESULTS

Among the 240 preterm infants evaluated, 88 cases (36.7%) were diagnosed with retinopathy of prematurity (R.O.P). In this study, a total of 240 neonates were included, of which 88 (36.7%) developed retinopathy of prematurity (R.O.P), and 152 (63.3%) did not (No R.O.P). Table 1 shows that among infants with No-R.O.P, 68 (44.7%) were female (FCH) and 84 (55.3%) were male (MCH). Among infants with R.O.P, 40 (46.0%) were female and 48 (54.0%) were male. There was no statistically significant association between sex and the presence of R.O.P ($p = 0.8529$). The mean gestational age was 32.73 ± 2.97 weeks in the no-R.O.P group and 30.83 ± 2.73 weeks in the R.O.P group, with statistically significant difference ($p = 0.007936$). (shown in table 1)

Table 1 Shows Demographic Details Among Infants Of Both The Groups

Particulars		NO R.O.P	R.O.P	p- value
Sex (MCH/FCH)	FCH	68 (44.7%)	40 (46.0%)	0.8529
	MCH	84 (55.3%)	48 (54.0%)	
	Total	152 (100.0%)	88 (100.0%)	
Gestational age (In weeks)		32.73 ± 2.97	30.83 ± 2.73	0.007936
Birth Weight (kg)		$1.67 \pm .79$	$1.51 \pm .51$	0.061

A significantly higher proportion of R.O.P cases was observed in infants born at <32 weeks gestation and those with a birth weight below 1500 g ($p < 0.01$). Other risk factors—such as supplemental oxygen use, sepsis, blood transfusion, intraventricular hemorrhage, hypoglycemia, respiratory distress syndrome, and congenital heart disease—were also more frequent among infants with R.O.P, with p -values between 0.012 and 0.037. Of all factors, gestational age <32 weeks exhibited the strongest correlation with R.O.P, followed by low birth weight, sepsis, and oxygen therapy.

Table 2: Risk Factor Distribution in R.O.P and Non-R.O.P Infants

Risk factors	DIAGNOSIS GROUP				p-value
	History (yes/no)	NO R.O.P (n=152)	R.O.P (n=88)	TOTAL (n=240)	
LBW	No	122 (80.26)	52 (59.09)	174 (72.5%)	0.02
	Yes	30 (34.0%)	36 (23.7%)	66 (27.5%)	
Prematurity	No	121 (79.06%)	23 (26.13%)	144 (60%)	0.00
	Yes	31 (35.2%)	65 (42.8%)	96 (40.0%)	

Oxygenation	No	119 (78.3%)	58 (65.9%)	177 (73.8%)	0.03
	Yes	33 (21.7%)	30 (34.1%)	63 (26.3%)	68
Respiratory distress syndrome	No	122 (80.3%)	65 (73.9%)	187 (77.9%)	0.03
	Yes	30 (19.7%)	23 (26.1%)	53 (22.1%)	28
Blood transfusion	No	112 (73.7%)	56 (63.6%)	168 (70.0%)	0.03
	Yes	40 (26.3%)	32 (36.4%)	72 (30.0%)	12
Intraventricular haemorrhage	No	136 (89.5%)	74 (84.1%)	210 (87.5%)	0.02
	Yes	16 (10.5%)	14 (15.9%)	30 (12.5%)	24
Hypoglycemia	No	122 (80.3%)	65 (73.9%)	187 (77.9%)	0.02
	Yes	30 (19.7%)	23 (26.1%)	53 (22.1%)	87
Congenital Heart Disease	No	139 (91%)	73 (82%)	212 (88.3%)	0.01
	Yes	13 (8.6%)	15 (17.0%)	28 (11.7%)	24
Sepsis	No	142 (93.4%)	74 (84.1%)	216 (90.0%)	0.02
	Yes	10 (6.6%)	14 (15.9%)	24 (10.0%)	02
	Total	152 (100.0%)	88 (100.0%)	24000.0%)	

Significant risk factors for ROP included low birth weight, gestational age <32 weeks, supplemental oxygen, sepsis, CHD, and transfusions, with gestational age showing the strongest association (OR 11.03).

Table 3- Shows Risk factors of R.O.P with Odds ratios (OR) with 95% confidence intervals (CI)

Risk Factor (History "Yes")	p-value	Odds Ratio (95% CI)
Low birth weight (<1500 g)	0.022	2.82 (1.57–5.04)
Gestational age <32 weeks	0.003	11.03 (5.95–20.46)
Supplemental oxygen	0.037	1.87 (1.04–3.35)
Respiratory distress syndrome	0.033	1.44 (0.77–2.68)
≥1 packed-cell transfusion	0.031	1.60 (0.91–2.81)
Intraventricular hemorrhage (IVH)	0.022	1.61 (0.74–3.48)
Symptomatic hypoglycemia	0.029	1.44 (0.77–2.68)
Congenital heart disease (CHD)	0.012	2.20 (0.99–4.86)
Culture-positive sepsis	0.02	2.69 (1.14–6.34)

DISCUSSION

Our study was a hospital-based observational study conducted over 24 months in the neonatal I.C.U, wards, and emergency department of a tertiary care centre. A total of 240 neonates were enrolled, of which 152 belonged to the No R.O.P group and 88 to the R.O.P group.

In our study, male infants were slightly more common in both groups—55.3% in the No ROP group and 54.0% in the R.O.P group. However, this difference was not statistically significant ($p = 0.8529$). Similarly, a study by **Prasad N et al.62 (2023)** included 410 preterm infants with gestational age <36 weeks and birth weight <2.0 kg and also observed similar gender distribution. The mean gestational age was 32.73 ± 2.97 weeks in the no-ROP group and 30.83 ± 2.73 weeks in the R.O.P group. This difference was statistically significant ($p = 0.007936$). Other studies, such as **Manzoni et al.**, have reported gestational age as a significant independent predictor of ROP, particularly among extremely low birth weight infants. The mean birth weight was 1.67 ± 0.79 kg in the no-ROP group and 1.51 ± 0.51 kg in the ROP group. This difference was statistically significant ($p = 0.01061$). Low birth weight is widely acknowledged in literature as a critical risk factor **Manzoni P, et al. (2016)**. The incidence of ROP (36.7%) in this cohort is comparable to reported rates from other Indian centres, indicating a persistent burden despite improved neonatal care.^{4,5} The most significant independent predictor was **gestational age <32 weeks**, aligning with the findings of the CRYO-ROP and ETROP studies, both of which underscored the critical role of prematurity in ROP pathogenesis.^{6,7} **Low birth weight** also demonstrated a strong association. The correlation between immature vascular development and hypoxic stress in small preterm infants has been well documented.^{8,9} **Oxygen therapy**, while life-saving, can trigger vaso-obliteration followed by hypoxia-driven neovascularization. The significance of cautious oxygen regulation has been emphasized in trials such as SUPPORT and BOOST.^{10,11}

Neonatal sepsis emerged as a notable risk factor. It is postulated that systemic inflammation and oxidative stress exacerbate retinal vascular dysregulation, increasing susceptibility to ROP.^{12,13} **Blood transfusions** may introduce iron overload and free radicals, amplifying oxidative retinal injury, though their causal role remains debated.¹⁴ **IVH and hypoglycemia** were also significantly associated, possibly reflecting systemic instability and cerebral-ocular vascular

compromise.¹⁵ Emerging literature points to **CHD**, especially cyanotic defects, as a new contributor to ROP risk. Chronic hypoxemia and circulatory anomalies in CHD may disturb retinal perfusion, explaining the observed association in our study.¹⁵

CONCLUSION

Our study reinforces the multifactorial nature of R.O.P and highlights key modifiable and non-modifiable risk factors. Gestational age and birth weight remain the cornerstone predictors, while oxygen therapy, blood transfusion, sepsis, and CHD merit focused attention. Timely screening and management tailored to the local risk profile can significantly reduce the burden of R.O.P-related blindness. Strengthening neonatal care, oxygen monitoring, and awareness among healthcare workers remains paramount.

Key Message-

Antenatal education on preterm birth risks, maternal nutrition, infection prevention, and timely check-ups can help empower mothers, promotes early R.O.P screening, and play a vital role in preventing childhood blindness and lifelong psycho-social and financial dependency.

REFERENCES

- Blencowe H, Lawn JE, Vazquez T, et al. Preterm-associated visual impairment and estimates of retinopathy of prematurity at regional and global levels for 2010. *Pediatr Res.* 2013;74(Suppl 1):35–49.
- Hartnett ME, Penn JS. Mechanisms and management of retinopathy of prematurity. *N Engl J Med.* 2012;367(26):2515–26.
- Gilbert C. Retinopathy of prematurity: a global perspective. *Early Hum Dev.* 2008;84(2):77–82.
- Charan R, Dogra MR, Gupta A, et al. The incidence of ROP in a neonatal care unit. *Indian J Ophthalmol.* 1995;43(3):123–6.
- Vinekar A, Dogra MR, Sangtam T, et al. ROP in Indian babies >1250 g: ten-year data. *Indian J Ophthalmol.* 2007;55(5):331–6.
- ETROP Cooperative Group. Revised indications for ROP treatment. *Arch Ophthalmol.* 2003;121(12):1684–94.
- CRYO-ROP Group. Multicenter trial of cryotherapy for ROP. *Arch Ophthalmol.* 1990;108(2):195–204.
- Hungi B, Vinekar A, Datti N, et al. ROP in rural NICUs. *Indian J Pediatr.* 2012;79(9):911–5.
- Shah PK, Narendran V, Kalpana N. Severe ROP in large preemies in India. *Eye.* 2009;23(1):162–5.
- Askie LM, Henderson-Smart DJ, Irwig L, et al. Oxygen saturation and preterm outcomes. *N Engl J Med.* 2003;349(10):959–67.
- SUPPORT Study Group. Target ranges of oxygen saturation. *N Engl J Med.* 2010;362(21):1959–69.
- Özdemir R, Sarıcı D, Yüksel B, et al. ROP incidence and risk factors. *Indian Pediatr.* 2015;52(10):837–42.
- Bardin C, Ghirri P, Bassi L, et al. Severe ROP risk factors. *Ital J Pediatr.* 2020;46(1):59.
- Sivanandan S, Agarwal R, Suresh GK. ROP: current management. *Indian J Pediatr.* 2016;83(9):1057–64.
- Flynn JT, Bancalari E, Snyder ES, et al. Transcutaneous oxygen tension and ROP. *N Engl J Med.*