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Prevalence and Risk Factors of Retinopathy of Prematurity in Premature Born Infants

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ABSTRACT

Background: Retinopathy of prematurity (ROP) poses a serious challenge to the health of preterm infants. Given that blindness caused by this disease is treatable—and considering its higher incidence in developing countries—we investigated the prevalence and identified risk factors associated with ROP.

Methods: This cross-sectional study included 100 premature infants with a gestational age of less than 37 weeks and a birth weight of less than 2500 g. All infants were examined for ROP by an ophthalmologist beginning from the fourth postnatal week. Comparisons were made between two groups: those with ROP and those without.

Results: The prevalence of ROP in this study was 21%. The analysis showed a significant association between the occurrence of ROP and gestational age (P = 0.031), as well as the number of ventilator days (P = 0.05). However, no significant relationship was found between ROP occurrence and sex, age, birth weight, sepsis, oxygen therapy, Apgar score, intraventricular hemorrhage (IVH), pneumothorax, corticosteroid use, or surfactant administration (all P > 0.05).

Conclusion: Preventive measures should be taken to reduce the incidence of premature deliveries. Additionally, clinicians should be aware of the increased risk of ROP when providing ventilation and adopt intelligent oxygen therapy and appropriate management strategies.

Keywords: Retinopathy of prematurity, Risk Factors, Prematurity, Prevalence, Ventilation

Introduction

Retinopathy of prematurity (ROP) is a pathological ocular condition characterized by retinal neovascularization. It specifically affects preterm neonates and is a leading cause of avoidable vision loss worldwide (1). Due to advances in neonatal care and the resulting increase in survival rates of premature infants, the global population at risk for ROP has risen (2, 3).

The primary risk factors associated with ROP include lower gestational age, low birth weight, and oxygen supplementation (4, 5). Additional contributing factors include intraventricular hemorrhage (IVH), sepsis, necrotizing enterocolitis (NEC), respiratory distress syndrome (RDS), mechanical ventilation, poor postnatal weight gain, treatment-requiring patent ductus arteriosus (PDA), thrombocytopenia, antenatal

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corticosteroid administration, low Apgar scores, anemia, blood transfusions, and erythropoietin therapy (6, 7). While a genetic predisposition is suspected, the specific monogenic mutations influencing ROP onset and severity remain unidentified (8).

The incidence of ROP and the resulting blindness is higher in developing countries compared to developed nations (2). This difference is influenced by economic conditions, healthcare quality, and access to neonatal care (9). Routine eye screening for ROP is essential in neonatal intensive care units (NICUs) to identify infants at risk of blindness due to retinal detachment (10). Common treatments for ROP include laser photocoagulation and intravitreal anti-VEGF injections (11).

Given the treatable nature of blindness caused by ROP, this study aimed to assess the prevalence and associated risk factors of ROP among hospitalized preterm infants at Kowsar Medical Education Center. Identifying these risk factors can support early detection, guide local screening and intervention strategies, and reduce treatment costs.

Methods

This cross-sectional study was conducted on premature infants born at Kowsar Medical Education Center, affiliated with Qazvin University of Medical Sciences, during 2018–2019. Based on an estimated ROP prevalence of 20%, a sample size of 100 infants was selected, with a 10% margin of error. The infants were divided into two groups: those who developed ROP (n = 21) and those who did not (n = 79).

Eligible participants were infants born before 37 completed weeks of gestation and weighing less than 2500 grams at birth. Gestational age was categorized into three groups: <28 weeks, 28–32 weeks, and 32–36 weeks, to evaluate its impact on ROP development. Infants who died before the first ophthalmologic exam or had congenital anomalies, chromosomal or metabolic disorders (as diagnosed by amniocentesis or ultrasound), eye tumors, or congenital cataracts were excluded.

Data collected included sex, age, birth weight, gestational age, sepsis (diagnosed clinically and confirmed by either a C-reactive protein level >4 mg/dL or a positive blood culture), oxygen therapy, need for mechanical ventilation (based on clinical findings, O2 saturation, and ABG results), ventilator days, Apgar scores, IVH (diagnosed by cranial ultrasound), pneumothorax (based on clinical signs and chest X-ray), corticosteroid use, and surfactant administration.

ROP screening began between 4–6 weeks after birth and followed the guidelines of the American Academy of Pediatrics (AAP) (12). Using an indirect ophthalmoscope with a 20D lens and a neonatal-appropriate speculum, a single drop of cyclopentolate hydrochloride/ phenylephrine (2 mg/mL / 2.5 mg/mL) was instilled in each eye 30 minutes prior to examination to induce mydriasis. Exams continued until full retinal vascularization was observed or until the infant reached a post-conceptional age of 40 weeks. Treatment was provided based on disease severity and established diagnostic criteria (13, 14). Comparative analysis was conducted between infants with and without ROP.

Data were analyzed using SPSS version 24. The prevalence of ROP was calculated as a simple proportion, and group comparisons were conducted using Chi-square or Fisher's exact tests. A P-value ≤ 0.05 was considered statistically significant.

Ethical approval

This study was approved by the Ethics Committee of Qazvin University of Medical Sciences (ethical code: IR.QUMS.REC.1396.156). Parental consent was obtained prior to the ophthalmologic examination or chart review.

Results

In this study, the prevalence of ROP was 21%, with 21 out of 100 premature infants developing the condition. There were no significant differences in sex, age, or birth weight between the groups with and without retinopathy. However, the difference in gestational age between the two groups was statistically significant (p = 0.035) (Table 1).

In the ROP group, six infants required mechanical ventilation. Among them, one infant (16.7%) required ventilation for less than 7 days, while five (83.3%) required ventilation for more than 7 days. In the non-ROP group, only 28.6% of infants required ventilation for more than 7 days, which was significantly different between the two groups (p = 0.05).

No significant differences were observed between the two groups in terms of sepsis, oxygen therapy, Apgar scores at 1 and 5 minutes, IVH, pneumothorax, corticosteroid use, or surfactant administration (Table 2).

Table 1. Analysis of demographic characteristics of infants in two groups with and without retinopathy

Demographic Information	Subgroups	Retinopathy Number: 21 Number(Percentage)	Non-Retinopathy Number: 79 Number(Percentage)	p-value
Sex	Male	11(52.4%)	44 (55.7%)	0.828
	Female	10(47.6%)	34 (43.0%)	
	Ambiguous	۰	1 (1.3%)	
Age	Less than 28 days	4(19.0%)	26 (32.9%)	0.288
	1-2 months	17(81.0%)	53 (67.1%)	
Birth weight	<1000	6(28.6%)	35 (44.3%)	0.367
	1500-1000	14(66.7%)	39 (49.4%)	
	1500-2500	1(4.8%)	5 (6.3%)	
Gestational age at termination of pregnancy	<28	3(14.3%)	28 (35.4%)	۰.035
	32-28	17(80.9%)	41 (51.9%)	
	32-37	1(4.7%)	10 (12.7%)	

Table 2. Examination of clinical characteristics of infants in two groups with and without retinopathy of prematurity

Risk Factors		With ROP Number: 21 Number (Percentage)	Without ROP Number: 79 Number (Percentage)	p-value
Sepsis		۴(19%)	17(21.5%)	0.805
Oxygen	Less than 7 days	8(38.1%)	30(38%)	0.992
	7 days or more	13(61.9%)	49(62%)	
Ventilator		6(28.6%)	14(17.9%)	0.282
Ventilator day	Less than 7 days	1(16.7%)	10(71.4%)	0.024
	7 days or more	5(83.3%)	4(28.6%)	
Apgar minute 1	Less than 7	10(50%)	31(39.2%)	0.450
	7 or more	10(50%)	48(60.8%)	
Apgar minute 5	Less than 7	4(20%)	7(8.9%)	0.225
	7 or more	16(80%)	72(91.1%)	
IVH		4(19%)	21(26.6%)	0.478
Pneumothorax		1(4.1%)	۴(5%)	۰/۹۵۵
Corticosteroids		17(81%)	56(70.9%)	0.420
Surfactant		19(90.5%)	73(93.6%)	0.673

Discussion

In our study, the prevalence of ROP was 21%. This finding aligns with other studies conducted in Iran (15–18). Differences in the incidence and prevalence of ROP in various regions may be attributed to genetic factors, quality of NICU care, social and economic conditions, and differences in research methodology (19). Compared to other countries, the prevalence of ROP in our study was higher than that reported in China and the United States (20, 21), but lower than that in Saudi Arabia, Pakistan, and India (22–24).

Our results showed that gestational age and ventilator duration were the most important factors associated with the development of ROP. Other factors—including sex, age, birth weight, sepsis, oxygen therapy, Apgar score, IVH, pneumothorax, corticosteroids, and surfactants—were not found to be significant risk factors.

Regarding the effect of sex, our study found it to be a non-significant risk factor for ROP, consistent with findings from other studies (25, 26). However, some studies have reported male sex as a significant risk factor (15, 27). It has been proposed that higher maternal levels of pro-inflammatory cytokines and angiogenic factors, including VEGF, during pregnancy may adversely affect male infants, potentially increasing the risk of ROP (28).

Gestational age was found to be a significant risk factor for ROP in our study, consistent with previous research (29, 30). This association can be explained by the retina's increased susceptibility to oxidative stress, perinatal hypoxia and

hyperoxia, and sepsis in infants with immature vascularization (29). A multicenter study (CRYO-ROP) reported that each additional week of gestational age reduced the odds of reaching the ROP threshold by 19% (31).

We did not find a significant correlation between birth weight and ROP in our study, which contrasts with findings from other research (27, 30). For instance, CRYO-ROP found that every 100-g increase in birth weight reduced the odds of reaching the ROP threshold by 27% (31). The lack of significance in our findings may be due to the wide range of birth weights included in our sample.

No significant association was found between sepsis and ROP severity in our study. However, neonatal sepsis has been widely recognized as a risk factor for ROP (29, 30), and perinatal inflammation may adversely affect retinal development (32).

Oxygen therapy also showed no significant association with ROP in our study. This finding contrasts with other studies that identified supplemental oxygen use and prolonged oxygen therapy as significant risk factors for severe ROP (33). Instead, we found that the duration of mechanical ventilation had a significant effect on ROP occurrence. This finding is supported by multiple studies that identified prolonged ventilation as a risk factor for ROP (17, 34, 35). Flynn et al. (1992) reported that every 12 hours of transcutaneous PO_2 ≥80 mmHg nearly doubled the risk of severe ROP (36).

While many studies have shown that low Apgar scores are not directly associated with ROP, infants with lower scores generally exhibit poorer neonatal health, which may correlate with increased ROP risk (6). However, it is important to note that the Apgar score alone is not a reliable predictor of neonatal neurological outcomes and should not be used as a sole diagnostic criterion for asphyxia (37).

Other variables—such as IVH, pneumothorax, corticosteroids, and surfactants—also did not show significant associations with ROP in our study. Similarly, Taqui et al. reported no significant relationship between ROP and IVH but did observe associations with sepsis and gestational age (24). In contrast, Al-Armo et al. reported a significant association between ROP and IVH (35). While corticosteroids have shown mixed results in previous research, one study analyzing 1,472 infants with birth weight <500 g found corticosteroid use to be a significant risk factor for any stage of ROP (38).

This study has several limitations, including a small sample size, single-center design, and the omission of several relevant variables such as necrotizing enterocolitis (NEC), respiratory distress syndrome (RDS), patent ductus arteriosus (PDA), thrombocytopenia, anemia, and blood transfusion. Future studies should address these limitations by incorporating a broader set of risk factors, larger sample sizes, and multi-center designs.

Although our study identified gestational age and ventilator duration as significant risk factors based on univariate analysis, a major limitation is the lack of multivariable logistic regression analysis to adjust for potential confounders. Future research should use multivariable models and expanded datasets to yield more robust and reliable conclusions.

Conclusion

Our findings indicate that low gestational age and prolonged ventilation are significantly associated with the development of ROP and Preventive strategies to reduce premature deliveries and increase gestational age are essential.

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Conflicts of interest

The authors declare no conflict of interest.

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