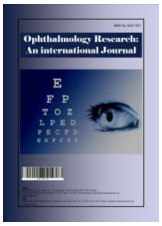

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Prevalence and Risk Factors of Retinopathy of Prematurity (ROP): A Cross-Sectional Study

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Background and Aim: Despite considerable progress made in the treatment of Retinopathy of prematurity (ROP), it is still a common cause of reduced vision in children in developed countries, and its prevalence is increasing. This is a preventable disease and responds to treatments appropriately if diagnosed at early stages, but in case of delayed diagnosis and treatment, it may lead to blindness. The aim of the present study is to describe the incidence, severity, and risk factors of ROP in a tertiary healthcare center.
Material and Methods: This was a prospective, observational, nonrandomized study conducted in a tertiary-level neonatal intensive care unit (NICU) of a teaching hospital in Gujarat. A total of 130 preterm neonates admitted in the NICU during the study period were screened for ROP as per the guidelines of NNF of India. Screening was done under topical anesthesia, and findings were documented according to the International Classification for Retinopathy of Prematurity recommendations. The data were analyzed for gestational age, birth weight, and systemic factors predisposing to ROP.
Results: Of the 130 neonates, 37 neonates were found to have ROP, with the incidence of ROP being 28.4%. The mean birth weight (1388 ± 312 g) and the mean gestational age (32.21 ± 2.50 wk) Out of the 37 neonates with ROP, 14 had a gestational age of > 32 weeks and/or birth weight of >

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1500 g. ROP was classified into type 1 and type 2 as per the ETROP study, 14 (39.39%) neonates had type 1 or treatable ROP; there were no cases of APROP in our study; ROP regressed without any intervention in 13 neonates; 7 neonates were defaulters; and 11 neonates were treated with laser.

Conclusion: ROP is strongly associated with smaller, more immature, and sicker neonates. However, in our study, about 40% of neonates who developed ROP were of higher gestation (> 32 wk) and birth weight (> 1500 g). The analysis of risk factors for ROP development will help to understand and predict it in severe preterm infants.

Keywords: Birth weight; infants; neonates; retinopathy of prematurity.

1. INTRODUCTION

Retinopathy of prematurity (ROP) refers to the developmental disorder of the retina in premature infants and is one of the most serious and most dangerous complications in premature infants. Embryonic retinal arteries start to grow in the third month of pregnancy and their development ends at birth. Therefore, the stages of evolution of the eye are defective in premature infants, and the growth of the vessels is either stopped or unusual, and ultimately, the vessels become very fragile, which can lead to visual impairment in severe cases [1]. Early identification of retinal damage and the institution of appropriate treatment prevent blindness and offer child better overall development [2].

ROP is characterized by abnormal neovascular development in the retina of premature infants. These abnormal blood vessels are fragile and can leak or bleed, scarring the retina and pulling it out of position. This causes a tractional retinal detachment, which is the main cause of visual impairment and blindness in ROP [3]. The stages of ROP describe the ophthalmoscopic findings at the junction between the vascularized and avascular retina; stage 1 is a faint demarcation line, stage 2 is an elevated ridge, stage 3 is an extraretinal fibrovascular tissue, stage 4 is a subtotal retinal detachment, while stage 5 is a total retinal detachment. In addition, Plus disease, which indicates significant vascular dilation and tortuosity observed at the posterior retinal vessels, may be present at any stage and reflects the increased blood flow through the retina [4].

In 1942, Terry [5] first described retrolental fibroplasia with implication of oxygen therapy as the causative agent. However, reports have found ROP in cases without oxygen therapy and even after oxygen therapy, not all premature infants develop ROP [6]. Three factors have shown consistent and significant association with ROP: low gestational age, low birth weight and prolonged exposure to supplementary oxygen following delivery [7]. Other putative risk factors include mechanical ventilation, [8] sepsis, [9] intraventricular hemorrhage, surfactant therapy, [10] anemia, [11] frequent blood transfusions, and apnea. The precise roles of these factors individually in the progression of the disease have not yet been determined [12].

Despite considerable progress made in the treatment of ROP, it is still a common cause of reduced vision in children in developed countries, and its prevalence is increasing [13-15]. This is a preventable disease and responds to treatments appropriately if diagnosed at early stages, but in case of delayed diagnosis and treatment, it may lead to blindness [16].

The aim of the present study is To describe the incidence, severity, and risk factors of ROP in a tertiary healthcare center.

2. MATERIAL AND METHODS

This was a prospective, observational, nonrandomized study conducted in a tertiary-level neonatal intensive care unit (NICU) of a teaching hospital in Gujarat.

2.1 Inclusion Criteria

Preterm neonates with ≤ 34 weeks of gestational age and/or birth weight ≤ 1750 g, Preterm neonates with 34 to 36 weeks of gestational age and/or birth weight between 1751 and 2000 g who are at a high risk developing ROP with risk factors such as need for cardiorespiratory support or prolonged oxygen therapy, blood transfusion, apnea of prematurity, anemia needing blood transfusion, or neonatal sepsis.

2.2 Exclusion Criteria

Neonates who died before full vascularization of retina or who were lost to follow-up were excluded.

A total of 130 preterm neonates admitted in the NICU during the study period were screened for ROP as per the guidelines of NNF of India [3]. The screening was done by a trained ophthalmologist in the NICU. The first screening was performed between 20 and 30 days of life. Pupils were dilated with 0.4% tropicamide and 2.5% phenylephrine eye drops instilled twice or thrice at an interval of 10 minutes. Retinal screening was done using an indirect ophthalmoscope with a 20D lens under topical anesthesia along with monitoring of vital signs. Pediatric speculum with scleral depression was used to examine the retina. Screening was carried out until (1) full retinal vascularization, (2) regression of ROP was noted with full retinal vascularization, or (3) zone-III retinal vascularization was attained without previous zone I or II ROP. Systemic risk factors and ocular findings were documented. ROP was classified according to the International Classification of ROP (ICROP) [4,5]. Follow-up examinations were recommended by the examining ophthalmologist on the basis of retinal findings and carried out until full vascularization in neonates without ROP and/or regression of ROP with full vascularization in those with ROP.6,7

ROP was determined as severe/treatable based on the following recommendations of the Early Treatment of ROP (ETROP) study.

Type 1 ROP

- Zone I, any stage ROP with plus disease
- Zone I, stage 3 ROP with or without plus disease
- Zone II, stage 2 or 3 ROP with plus disease

Type 2 ROP

- Zone I, stage 1 or 2 ROP without plus disease
- Zone II, stage 3 ROP without plus disease

As per the ICROP revisited, a condition characterized by a typical posterior location, prominence of plus disease, and the ill-defined nature of the retinopathy was diagnosed as aggressive posterior ROP (APROP). This rapidly progressing retinopathy was previously referred to as type II ROP and Rush disease [9-11].

2.3 Statistical Analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

3. RESULTS

The birth weight of the 130 neonates, screened for ROP, ranged from 700 to 2800 g (mean 1.48 kg) and their gestational age ranged from 28 to 42 weeks (mean 33.1 wk) (Table 1).. Of the 130 neonates, 37 neonates were found to have ROP, with the incidence of ROP being 28.4%. The mean birth weight (1388 ± 312 g) (Table 2) and the mean gestational age (32.21 ± 2.50 wk) (Table 3) of neonates with ROP was significantly on the lower side. It was noted that of the 37 neonates with ROP, 14 had a gestational age of > 32 weeks and/or birth weight of > 1500 g. ROP was classified into type 1 and type 2 as per the ETROP study, 14 (39.39%) neonates had type 1 or treatable ROP; there were no cases of APROP in our study; ROP regressed without any intervention in 13 neonates; 7 neonates were defaulters; 4 neonates died before ROP regressed; and 11 neonates were treated with laser.

Respiratory distress syndrome (RDS), sepsis, blood transfusion, apnea of prematurity, and oxygen with ventilator support were the significant risk factors, whereas multivariate analysis showed that birth weight, gestational age, oxygen with ventilator support, and blood transfusion were statistically significant risk factors for the development of ROP (Table 4).

Table 1. Distribution of Preterm Neonates Screened for ROP as per Birth Weight and Gestational Age

Variables	Mean	Standard Deviation
Birth Weight, g	1496	0.44
Gestational Age, wk	33.01	2.10
Postconceptional Age, wk	35.90	3.24

Table 2. Distribution of Neonates Based on Birth Weight and Incidence of ROP

ROP	N	Birth Weight, g Mean ± SD	P value
Present	37	1388 ± 312	
Absent	93	1568 ± 354	0.02*

**indicates statistically significance at p≤0.05*

Table 3. Distribution of Neonates Based on Gestational Age and Incidence of ROP

ROP	N	Gestational Age, wk Mean±SD G	P value
Present	37	32.21 ± 2.50	
Absent	93	33.68 ± 2.92	0.001*

**indicates statistically significance at p≤0.05*

Table 4. Multivariate Analysis of Risk Factors of ROP

Variables	β Constant	Standard Error	P value
Constant	0.6	0.42	0.01*
Birth weight	0.007	0.09	0.01*
Gestational Age	-0.02	0.001	0.09
Oxygen With Ventilator Support	-0.13	0.08	0.001*
Blood Transfusion	0.24	0.08	0.02*
RDS	0.16	0.07	0.05*
Sepsis	**0.21**	**0.07**	**0.04***

**indicates statistically significance at p≤0.05*

4. DISCUSSION

Retinopathy of prematurity is a disorder of retinal vascular development in preterm infants. It continues to be a significant complication in preterm neonates despite advances in neonatal care and remains a major cause of childhood blindness worldwide [17]. The birth weight of neonates ranged from 700 to 2800g and their gestational age ranged from 28 to 42 weeks. The incidence of ROP in our study was found to be 28.4% of the 37 neonates, 14 had type 1 ROP.

We found that low birth weight was a significant risk factor on univariate (P≤0.05) as well as multivariate analyses (P = 0.01), whereas gestational age was a significant risk factor only on univariate analysis (P = .0002) and not on multivariate analysis for the development of ROP, both type 1 and 2. The mean birth weight and gestational age of neonates with ROP were 1388 ± 312 g g and 32.21 ± 2.50 weeks, respectively. The mean birth weight and gestational age of neonates with type 1 ROP were 1448 ± 181 g and 30.05 ± 2.42 weeks, respectively. In studies conducted in Indian settings, the incidence of ROP varies—46%, 47%, 21.7%, 21%, and 22.3% in studies conducted by Charan et al. [18] (1995), Rekha et al. [19] (1996), Gupta et al. [9] (2004; ≤ 35 wk or ≤ 1500 g), Dutta et al15 (2004; ≤ 32 wk or ≤ 1700 g), and Chaudhari et al16 (2009; ≤ 32 wk or ≥ 1500 g), respectively. This was explained by immaturity of vascularization that induces an increased susceptibility of the retina to oxidative damage and to a number of perinatal factors which include hyper and hypoxia, blood transfusions, and sepsis.

Studies conducted in recent years with screening criteria including heavier and older neonates showed the incidence of ROP to be similar to or more than that in our study. Vinekar et al. [20] in 2007, studied neonates with mean birth weight of 1533.9 g (range = 1251–2750 g) and mean gestational age of 30.9 weeks (range = 26–35 wk) and found the incidence of ROP to be 41.5%. In a study conducted by Hungi et al. [21] (2012) in south India, the incidence of ROP was found to be 41.5% and that of type 1 ROP was found to be 26.4% in neonates with birth weight ≤ 2000 g and/or gestational age ≤ 34 weeks.

ROP is still a major cause of potentially preventable blindness around the world [22]. According to guidelines published by the American Academy of Ophthalmology, the American Academy of Children, and the American Association for Ophthalmology for Children and Strabismus for ROP screening, infants weighing less than 1500 g or GA ≤ 30 weeks, and infants weighing between 1500 and 2000 g or GA > 30 weeks with an unstable clinical course should receive dilated ophthalmoscopy examinations for ROP [23].

there was a significant association between the various risk factors and development of ROP in preterm neonates with gestational age up to 34 weeks and/or birth weight up to 1750 g; neonates with gestational age of 34 to 36 weeks and/or birth weight of 1751 to 2000 g who are at a high risk of developing ROP; and neonates believed to be at risk by the attending neonatologist. This was in agreement with Shah et al [8] and Vinekar et al. [20] which may be due to the effect of endotoxins on retinal blood vessels. On the other hand, this was in disagreement with the results of Chaudhari et al. [24] and Smith [25]. This was also stated in a study by Jalali et al, [26] which confirmed that severe ROP occurs in a significant number of neonates who fall outside the screening criteria of ROP in high-income countries. In their review on the incidence of ROP, Zin and Gole [27] found that in middle-income countries, high rates of preterm birth and thus the increasing rate of resuscitation, along with suboptimal care, have resulted in an increase in the incidence of ROP. It is essential to have ROP screening guidelines appropriate to middle-income countries and provide good-quality and timely care to mothers and neonates.

5. CONCLUSION

We are aware that a limitation of this study is the small number of patients. ROP is strongly associated with smaller, more immature, and sicker neonates. However, in our study, about 40% of neonates who developed ROP were of higher gestation (> 32 wk) and birth weight (> 1500 g). The analysis of risk factors for ROP development will help to understand and predict it in severe preterm infants. The timely retinal screening of highrisk preterm infants is important to prevent the development of advanced ROP. Since ROP may produce serious sequelae up to complete blindness, all efforts must be made to prevent the development of advanced ROP through elimination of preterm births, changes in the neonatal care, and improvement in detection of threatening ROP markers.

CONSENT

Written informed consent was taken from all the participants.

ETHICAL APPROVAL

Ethical approval was taken from the institutional ethical committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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