

INCIDENCE, PREVALENCE AND RISK FACTORS OF RETINOPATHY OF PREMATURITY: A SYSTEMATIC REVIEW

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Abstract

The present study is a review article on Retinopathy of Prematurity (ROP) and its incidence, prevalence and risk factors. Although early stages of ROP typically regress or heal on their own, more advanced stages can cause serious vision impairment or blindness and hence require treatment. Premature newborns are highly vulnerable to ROP. Fifteen articles were selected to compile this review and the search engines used were pub med, Google scholar and Scopus using keywords ROP, associated risk factors of ROP and ROP related childhood blindness.

Review indicates all infants born in underdeveloped nations, such as India, who weight less than 2,000 gm and born at a gestational age of less than equal to 36 weeks are having very high chance of developing ROP and should always be screened. Risk factors of ROP could be linked to both the infant as well as maternal health. Because ROP in newborns is often asymptomatic in its early stages before progressing this disease to advanced condition, early screening is recommended for very low birth weight and extremely premature infants.

Key words: ROP, Blindness, New-born, Incidence, Prevalence, Risk-factor

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Introduction

One of the leading preventable causes of blindness in children is retinopathy of prematurity (ROP), according to the World Health Organization. Low birth weight preemies have abnormal vascular development due to a malfunction of the retinal blood vessels.¹

According to (WHO 2022), there are over 15 million preterm births annually, Where India being in the top ten countries.²

Around the world, ROP is majorly responsible for blindness in children in a percentage of 10% to 37.4%. ROP is one of the leading causes of childhood blindness in both high- and low-income nations, affecting at least 50,000 children each year around the world. Eastern Europe, Asian countries like India, and China are some of the developing region in the world, making them leading areas for occurring ROP.³

The retina performs its role of vision via specialised structures including the macula, fovea, and optic nerve, among others. These structures aid in our ability to see things in a variety of conditions, "including day and night vision, depth perception, colour vision, and static and dynamic phase vision, among others." Any discrepancy from the retina's structures' typical operation will result in poor eyesight. These disorders, such as macular degeneration, retinal detachment, and diabetic retinopathy.

The retina, which is the eyes inner thinnest, most delicate layer of nerve tissue, is crucial to our ability to see. It detects light, creates an inverted image, and transmits it to our brain for interpretation, through the optic nerve. The ICROP3 states that there are three zones in the retina ("International Classification of Retinopathy of Prematurity"). The estimated distance for Zone 1 between the centre of the optic disc and the fovea is shown by a circle with a radius of twice that amount. Oval in shape, zone II begins at the outer edge of zone 1 and continues in a superior and inferior direction all the way to the nasal oraserrata. It is the remaining crescent of zone II that is called zone III.⁴

Most recently, the concept of aggressive ROP (A-ROP) was devised to replace aggressive-posterior ROP, as described in the "International Classification of Retinopathy of Prematurity, Third Edition" (APROP). This was done because doctors as well as researcher were beginning to realise that in some parts of the globe with fewer resources, severe illness may strike bigger preterm newborns and could also manifest itself in locations other

than the posterior retina. The retinal arteries in the A-ROP are severely tortuous, dilated, and looped, with the illness progressing quickly to an advanced level (stage 4 or 5 ROP).⁴

Screening all preterm babies for ROP is commonplace now as a result of the efforts of the CRYO-ROP cooperative group ("Multicentre trial of cryotherapy for retinopathy of prematurity") to lower the rate of childhood blindness. Earlier study (preliminary findings, 1988) indicated the value of treating ROP at the threshold of illness.⁵

As the infant develops, prematurity-related retinal disease often self-limits. But in a few instances, if not identified and treated in the early stages, this illness might result in retinal detachment and as a result, lifelong blindness.

No significant data are available from rural India, despite the fact that the country as a whole has experienced an uptick in the survival rate of preterm infants with highly efforts of the Special Neonatal Care Unit in providing better treatment for these newborns (SNCU).

Methodology

This document provides an overview of incidence, prevalence and risk factors of Retinopathy of Prematurity. To write this work, we relied on previously published materials, or secondary sources. Secondary studies can collect information in a number of different methods. Secondary research includes information obtained from sources such as websites, libraries, and published statistics, studies, and surveys. The fifteen publications that formed the basis of systematic review all deal with final outcome.

Aim and Objective:

To Review on Incidence, Prevalence and Risk factors of Retinopathy of prematurity through the systematic review of published papers.

Review of papers:

"Worldwide incidence and prevalence"

Due to the high number of patients "which would allow a global registry to collect more precise data," it can be challenging to determine the prevalence of ROP globally. Only a few nations, including "Kenya, Nigeria, India, the United States, and Romania, for example, follow proper ROP screening methodology" as can be shown in Table 1. It is important to take notice of the many risk factors that can be managed to prevent ROP progression to severe vision impairment or blindness.

| Country | Notes |
|---|---|
| | ROP affects around 7.8%-10.7% of the 14,000 preterm newborns |
| | identified each year, with the majority of these infants not reaching a |
| | severe enough stage of the illness to warrant treatment. 400-600 children |
| | a year go blind from ROP, "ROP was present in 66% of children weighing |
| United States (Bashinsky | less than 1,250 gm at birth and 82% of newborns weighing less than 1,000 |
| 2017) ¹ | gm at birth, as reported by the CRYO-ROP Group Study." |
| | The reported prevalence was 41.7%. The majority of cases were classified |
| | as either early or moderate ROP. It was estimated that 20.9% of people |
| Kenya (Onyango et al. | in the world suffer with sight-threatening ROP. |
| 2018) (Wang et al. 2019) ⁶ | It was found that prevalence was 16.7%. In 2018, new rules for screening |
| 7 | were established. |
| | The reported prevalence was 47.2%. |
| Nigeria (Wang et al. 2019) | After the 2014 study by Adios et al., researchers in 2015 found that the |
| (Adio et al. 2014) ^{7 8} | prevalence of ROP was 15%, with 50% of patients requiring treatment. |
| | The incidence of ROP differed significantly across metropolitan and rural |
| | regions. The frequency in Madhya Pradesh was 30.1%, with 15.8% |
| | having moderate ROP and 14.2% having severe ROP. The newborns |
| | diagnosed with ROP, 27.7% had an aggressive form, and the vast |
| | majority (83.3%) were determined to have been born before the 32 weeks |
| | of pregnancy. Also, blindness or severe vision impairment developed in |
| | 2.2% of instances. The Incidence between 20% to 51.9% of the Indian |
| | population suffers from ROP. "There is a wide variation in the rate of |
| | severe ROP, from 4.7% to 13.2%." |
| | This investigation uncovered a frequency of 32.6% in Tamil Nadu. |
| | Nearly all patients presented with signs of illness on both eyes. Those |
| | with birth weights of less than 1,000 gm had the greatest incidence. The |
| India (Dwivedi et al. 2019) | greatest rate of ROP, 62.8%, was found in infants delivered at less than |
| (Ahuja AA, V Reddy YC, | 28 weeks of gestation. About 13% of individuals required some sort of |
| Adenuga OO, Kewlani D, | treatment. |
| Ravindran M 2018) | Depending on where you lived, the prevalence of ROP was anything from |
| ,(Bowe, BS et al. 2019) ^{9 10} | 38.2 to 47. Eighty percent of patients experienced spontaneous remission, |
| ,11 | whereas 1.8% developed severe ROP, required early treatment. |
| | In 2002, the ROP screening programme began operation. It was |
| Romania (Bowe, BS et al. | hypothesised that between 40% to 50% of preterm infants will affected |
| 2019) 11 | with any stage of ROP. |

"Table 1: "General information on the prevalence

of ROP from various countries across the world" This developmental condition is especially prevalent in premature infants whose retinas are still developing. This disease is referred to medically as premature retinopathy. ROP frequently affects both eyes. Beginning at 20 weeks of pregnancy and continuing until the baby is born, the normal growth of retinal vessels begins. As preterm new-borns are exposed to a number of variables, including as medicines, oxygen, blood transfusions, and temperature fluctuations, all of which can affect eye development, this process may be temporarily stopped in preterm infants, resulting in a temporary delay in the growth of retinal blood vessels. ¹² ¹³ ¹⁴

Population-based studies on ROP have been carried out in a number of nations, with various definitions and reported outcomes. Studies using publicly accessible paediatric inpatient care datasets found that ROP prevalence among infants in the United States with LOS longer than 28 days ranged from 12.8% to 19.9%. In a recent Taiwanese study using the National Health Insurance Research Database, it was discovered that the prevalence of ROP was 36.6% among preterm new-borns with a LOS of more than 28 days (NHIRD). ROP was detected in 31.9% of Swedish infants delivered at exactly 31 weeks gestation in 2011, but in England it affected just 12.6% of infants born at exactly 1500 gm. Babies in a Turkish NICU network were more likely to be diagnosed with ROP at any time (27-30%) "if they had a birth weight (BW) below 1500 g, a gestational age (GA) below 32 weeks, or an unstable clinical course. A study of the Korean Neonatal Network (KNN) database, a national registry for VLBWIs," found that the overall prevalence of ROP among VLBWIs (less than 1500 g BW) in South Korea was 34.1%. Even though about 70% of VLBWIs born in South Korea at the time were included in the KNN data.

"Retinopathy of prematurity (ROP) in India"

The risk of developing ROP is 65% higher in infants who weighed 1,250 gm or less at birth, while those of 1000 gm or less are at an 80% increased risk. Premature infants (those born with a birth weight of less than 2,000 gm and/or those whose gestational ages were less than and equal to 36 weeks) are encouraged to undergo ROP screening (Indian population data). The risk of ROP increases when the mother is only a few weeks along. Other variables include illness severity and oxygen exposure in addition to length and instability. ROP occurs at different rates in India's urban and rural areas as well as within each of them. Despite the fact that the country as a whole has seen an increase in the survival rate of preterm infants attributable to the Special Neonatal Care Unit's efforts in providing better treatment for these newborns, there are no data from rural India accessible (SNCU).

The number of SCNUs has expanded in many rural sections of the nation. Eight of the units were initially set up with aid from UNICEF, which provided both financial and technical support. Patient visual results have improved thanks to early treatment methods including "cryotherapy, laser photocoagulation, and Anti-Vascular Endothelial Growth Factor (AVEGF) therapy.¹⁵

A study done by (Patel and Shendurnikar 2019) investigate ROP's prevalence, related hazards, and long-term repercussions in Vadodara's high-risk infant population in a tertiary care hospital. Children born at >2000 gm and >34 weeks of gestation were screened for ROP 4 weeks after birth; infants born at >1200 gm and >28 weeks of gestation were screened 3 weeks after birth. Associated risk factors were included only for babies whose birth weight or gestational age was more than 34 weeks. Those at the greatest risk of developing ROP were provided preventative treatment. Among the 286 neonates tested, 24.1% were diagnosed with ROP; 12 of these babies were born weighing more than 2,000 gm. In a multivariate study, We identified the following conditions as contributors to ROP: birth asphyxia; Sepsis; recurrent blood transfusions; respiratory distress syndrome; multiple births; and phototherapy (p 0.05). From the 69 infants diagnosed with ROP, 6 needed immediate surgical intervention. ROP was linked to prematurity, low birth weight, advanced mother age, birth asphyxia, sepsis, multiple births, respiratory distress syndrome, and phototherapy. Prenatal steroid use can reduced chance of develop severe ROP. Increasing rates of ROP, which affect infants of all sizes, are prompting experts to re-evaluate the best practises for screening newborns in developing countries.¹⁶

A study done by (Parihar et al. 2022) observes, Increases in preterm birth survival pose a problem for ROP. Incidences of this avoidable cause of blindness are on the rise. There is a lack of data on its prevalence, severity, and outcome in rural areas. Births at a tertiary care facility were the focus of a prospective observational longitudinal research. Premature infants were not screened for ROP unless they were 32 weeks or heavier at birth. Premature infants (those born at less than 32 weeks) who need supplemental oxygen, had respiratory distress syndrome, used surfactant, had persistent pulmonary hypertension, needed phototherapy for neonatal hyperbilirubinemia, had septicaemia, required a red cell transfusion because of anaemia were also included. Infants with ROP were evaluated after 6 and 12 months to determine the severity of their condition and whether or not they required intervention. Fifty-one of the 211 newborns tested positive for ROP. There was no difference in frequency between the sexes after adjusting for birth weight or gestational age. "Important risk variables were the use of oxygen treatment (p 0.001), respiratory distress syndrome (p 0.005), mechanical ventilation (p 0.003)," and septicaemia (p 0.005). Phototherapy for hyperbilirubinemia of the new-born has been proven to be beneficial (p 0.0005). Photocoagulation with a laser was necessary in 15.68% of the instances. All individuals with ROP showed improvement during follow-up. Factors associated with ROP included oxygen treatment, distress syndrome, mechanical respiratory ventilation, and septicaemia. There was no correlation between the use of blood component and the final result. To a great extent, the infantile hyperbilirubinemia was beneficial to the infant. The prognosis for ROP is good if the condition is identified early.¹⁷

"Incidence and risk factors of retinopathy of prematurity in Western India – Report from A Regional Institute of Ophthalmology"

The purpose of this study is to report on ROP rates and risk factors in a western India ophthalmology centre and assess those rates and variables in the context of the current epidemic. Babies born between January 2012 and October 2013 with weight less than 1700 gm at birth were the subjects of a prospective observational study. Babies were checked for ROP and information on the delivery, such as how much oxygen was given, was documented in collaboration with a neonatologist. Risk variables for ROP of any severity and ROP

were identified needing treatment using multivariable logistic regression. There were 280 infants tested, and 54 of them (19.28%) were diagnosed with any ROP, while 28 (10.29%) were diagnosed with severe ROP. If oxygen treatment was given as prescribed, the risk of having any ROP risk of developing severe ROP increased. The odds of having a child with severe ROP were lower among women who gave birth at a later gestational age but not among women who gave birth at any age. Treatment with laser or Bevacizumab was successful for 24 of the 26 infants with severe ROP. "whereas 4 infants had retinal detachment. Finally, this paper is the first to provide incidence and risk factors for ROP in western India." A rate of any-ROP in infants of one in five is consistent with national data. Slightly arise more cases of severe ROP needing treatment, and they respond to therapy similarly to those documented in the literature.¹⁸

"Pattern, risk factors and prevalence of severe retinopathy of prematurity in eastern Madhya Pradesh"

The purpose of this study is to characterise the incidence of severe ROP in eastern Madhya Pradesh, India, and to define its prevalence, features, and pattern. This was a retrospective research that looked back over a period of 5 years, "noting baseline characteristics, systemic risk factors, and ROP test results." The causes of advanced ROP stages (IV and V) and aggressive posterior ROP (APROP) were examined. The current version of SPSS (version 20) was used for the statistical analysis. Thirty percent (30%) of the 763 infants examined were found to have ROP. There were 59 cases of classic ROP and 30 cases of APROP for a total of 14 percent (109) of cases of severe ROP. Advanced ROP was seen in 18 patients (16.6%). (Stage IV and V). Birth weight was inversely linked with severe ROP, with a mean of 1.34 kg and a mean GA of 31.05 weeks for babies born with severe ROP. However, 10% of kids born prematurely had severe ROP. These newborns were born at a gestational age of 34 weeks or less. APROP risk was significantly increased by low GA and RDS. The late screening presentation was the most relevant factor in ROP stages IV and V. Severe ROP, including APROP, was shown to be very common in this study. Nearly 7% of instances of severe ROP fell beyond NNF's recommended screening thresholds. The most significant risk factor for ROP-related blindness is a delay in screening.⁹

"Retinopathy of prematurity: a review of risk factors and their clinical significance"

In preterm newborns, a retinal vasoproliferative disease known as ROP can develop. Although there have been advancements in the care and management of newborns, ROP continues to be a major contributor to childhood blindness. "Many researchers have argued that screening standards should go beyond birth weight and gestational age to include additional risk variables such as maternal factors, prenatal factors and, demography, medical treatments, co morbidities of prematurity, awareness factor, nutrition, and genetic factors." We survey the existing research on ROP and analyse many probable contributors. Despite the fact that there are conflicting reports and that the risk may vary across populations, The pathogenesis of retinal vascular disorders and diseases of prematurity all depend on an understanding of the other risk factors for this condition.¹⁹

Retinopathy of prematurity in practice:

The researchers in this study set out to determine how effective a single ophthalmologist's ROP screening efforts were in the north of England over a period of 11 years. In order to study the effects of ROP severity on the gestational ages and birth weights of infants. Examining how much labour is needed to do a screening for threshold ROP and discovering that screening parameters had to be tightened in practise. Finding Infants Diagnosed with a Threshold Condition. Babies were tested prospectively according to national criteria and the findings were recorded into a computerised database from August 1987 to October 1998. Following that, these records were thoroughly examined. Among the 484 newborns for whom there was sufficient data, 203 (or 41%) developed ROP, 46 (9%) progressed to stage 3, and 25 (5%) met the criterion for ROP and required treatment. The average of 2.3 screening tests was needed for each of the 425 newborns analysed. As many as 39 screening examinations were required to find a single case with threshold ROP. Babies who were delivered prematurely or who weighed less at birth underwent more thorough checks. For this reason, we may have missed two of our threshold instances if we had relaxed the inclusion criteria for screening: both of these babies were born at 30 weeks gestation and weighed more than 1,400 gm. Successful treatment justifies the effort put into screening. When applied to newborns in Northern England, the existing national screening standards work well enough. The document included here presents the outcomes of therapy for the infants who were identified in this investigation.²⁰

"Risk Factors for Retinopathy of Prematurity in Premature Born Children"

Retinopathy of prematurity is a condition more common in premature newborns. Prematurity, low birth weight, hypoxia, duration of oxygen supplementation, respiratory distress syndrome, multiple pregnancies, anaemia, blood transfusions, sepsis, intra-ventricular haemorrhage, hypotension , and hypothermia are all potential causes of retinopathy of prematurity. In youngsters, significant vision impairment and blindness can arise from untreated illnesses that go un-diagnosed; therefore early detection is important for avoiding these outcomes. One of the main reasons for doing this study is to pinpoint the exact number of cases with active retinopathy of prematurity that occurred throughout the study period. Another objective is to identify the specific risk factors that contributed most to the development of this illness. From January to May of 2015, observed 80 infants who were born preterm in relation to the indicated risk factors for eye examinations and performed a retrospective clinical study. Of the 80 premature infants included in the study, 48.8% were male and 51.2% were female. While 6.2% of cases developed into ROP's active form, the vast majority (93.8%) cleared up without treatment. Patients with active ROP were significantly more likely to be delivered prematurely (26.41.5 weeks), to weigh less than 974 gm at birth, to have an APGAR score of 7 at either the 1- or 5-minute intervals, and to require prolonged oxygen therapy (203.4 days). Premature birth, low birth weight, a poor APGAR score, and prolonged exposure to oxygen have all been linked to an increased likelihood of ROP's cases. (p 0.05).²¹

ROP in high-risk neonates at a tertiary care hospital in Vadodara in order to better understand the incidence, risk factors, and consequences of this condition. All infants weighing 1200 gm or more at birth or those born at 28 weeks of gestation were screened 3 weeks after birth, while all infants weighing 2000 gm or more at birth were screened 4 weeks after birth. Only infants who fulfilled these conditions were subjected to additional risk factors, such as a gestational age or birth weight greater than 34 weeks. High-risk individuals were given treatment for ROP. Out of 286 neonates, 24.1% were found to have ROP; 12 of these babies had a birth weight of above 2,000 gm. Multivariate study found that suffocation immediately following birth, sepsis, multiple birth, prenatal steroid usage, and phototherapy were all risk factors for ROP (P0.05). Only 8.7 percent (6/69) of the 69 kids diagnosed with ROP required invasive treatment. Gestational

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age and birth weight remained the major risk factors for ROP, although birth asphyxia, sepsis, blood transfusions, respiratory distress syndrome, multiple births, prenatal steroid use, and phototherapy were also important. Because ROP is more prevalent in infants delivered to mothers of greater birth weight and older gestational ages, screening criteria for newborns in developing nations need to be revised to account for this. ²²

Conclusion

Retinopathy of prematurity (ROP) is a disease of the retinal blood vessels that has caused blindness in millions of premature infants around the world. Untreated ROP can lead to complications such severe myopia, strabismus, cataracts, glaucoma, and retinal detachment. Due to the several risk connected with the delivery and early growth of preterm infants, ROP is an intriguing measure of the quality of a hospital's antenatal and postnatal care. Therefore, it is not shocking that ROP rates remain greater in low-income areas. The incidence, prevalence, and risk factors for ROP are reviewed in our study. ROP affects approximately 7.8% to 10.7% of people in the USA, and its prevalence ranges from 12.8% to 19.9%. The prevalence rate that was reported in Kenya was 41.7%. It was reported that 47.2% of people in Nigeria were affected. The total frequency of ROP among very low birth weight infants (less than 1500 gm BW) in South Korea was reported to be 34.1%, according to a study that used the database of the Korean Neonatal Network (KNN), which is a nationwide registry for VLBWIs. Even though almost 70 percent of VLBWIs who were born in South Korea at the time were included in the KNN data, additional study is necessary to fully understand the epidemiology of ROP across the country. The chance of having ROP is increased by 65% in newborns whose birth weight was 1,250 gm or less, while the risk is increased by 80% in children whose birth weight was 1000 gm or less. Premature infants are defined as those who were born with a birth weight of less than 2,000 gm and/or those whose gestational ages were less than equal to 36 weeks (Indian population data). The rate of ROP was significantly higher in urban regions than in rural ones. Thirty percent of inhabitants in Madhya Pradesh have ROP, with 15.8 percent having moderate ROP and 14.2 percent having severe ROP. In a multivariate analysis, we found that birth asphyxia, sepsis, frequent blood transfusions, respiratory distress syndrome, multiple birth and phototherapy all increased the risk of retinopathy of prematurity (ROP).

Abbreviations used:

ROP- Retinopathy of prematurity, LOS- length of stay

A-ROP- Aggressive retinopathy of prematurity,

VLBW- Very low birth weight

GM- Gram, GA- Gestational Age,

NICU- Neonatal Intensive Care Unit,

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