

**A Study on Retinopathy of Prematurity and Gestational Age in Preterm Infants****Karthik P<sup>1</sup>, Sai Silpa Chowday Ch<sup>2</sup>, S K N Manikanta<sup>3</sup>, Rama Krishna Parama Hamsa<sup>4</sup>, T Jaya Chandra<sup>5</sup>**<sup>1</sup>Senior Resident, Department of Paediatrics, GSL Medical College, Rajahmundry.<sup>2</sup>Assistant Professor, Department of Paediatrics, GSL Medical College, Rajahmundry.<sup>3</sup>Assistant Professor, Department of Paediatrics, GSL Medical College, Rajahmundry.<sup>4</sup>Professor & Head, Department of Paediatrics, GSL Medical College, Rajahmundry.<sup>5</sup>Central Research Laboratory, GSL Medical College, Rajahmundry.

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**Abstract**

**Introduction:** Retinopathy of prematurity (ROP) manifests with abnormal blood vessel growth in premature infants, affecting up to 80% of those weighing under 1000 grams. Historical ROP epidemics underscore the need for meticulous oxygen monitoring. Developing countries face a current ROP epidemic due to rising preterm births and limited healthcare resources. Vision 2020 targets ROP to mitigate childhood blindness, emphasizing the study's focus on ROP incidence and its correlation with gestational age (GA).

**Methods:** This hospital-based cross-sectional observational study utilized indirect ophthalmoscopy with a 20D lens for ROP screening. A wire speculum and scleral indenter maintained eye position, with aseptic measures followed. Examination included posterior pole assessment for plus disease, peripheral screening with enhanced temporal visualization. Neonatal complications were managed, ROP classified per ICROP, and risk factors documented.

**Results:** In the study of 60 preterm infants, 40% developed ROP, predominantly stage 2 (14 cases), followed by stage 1 (8) and stage 3 (2). Gender distribution showed no statistical significance ( $P = 0.672$ ). ROP babies had a mean GA of  $30.71 \pm 2.34$  weeks by dates and  $30.67 \pm 2.30$  weeks by Ballard score ( $P < 0.001$ ). Birth weight decreased with higher ROP stages ( $P = 0.001$ ). Oxygen therapy type significantly influenced ROP risk ( $p < 0.001$ ), with 66.7% using hood oxygen, 16.7% C-PAP, and 16.7% ventilation.

**Conclusion:** Lower birth weight and type of oxygen therapy significantly influence ROP severity. Meticulous monitoring and management of these factors are crucial to reducing ROP risk in preterm infants, highlighting the need for targeted screening and intervention strategies.

**Key words:** Retinopathy of prematurity, Gestational age, Birth weight, Oxygen therapy, Stage classification

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**Introduction**

The primary pathological change in retinopathy of prematurity (ROP) is the abnormal growth of blood vessels in the peripheral retina of premature infants. [1] Nearly 65% of newborns with a birth weight below 1250 grams and 80% of those weighing under 1000 grams will develop some degree of ROP. [2] The ROP epidemic has occurred twice in the past. The first, in the 1940s-1950s, was primarily due to unmonitored supplemental oxygen. The second, in the 1970s-1980s, occurred despite careful oxygen monitoring and was attributed to the increased survival rates of very low birth weight (VLBW) infants weighing between 750-999 grams. [3] These epidemics highlight the critical need for vigilant monitoring and advanced care for preterm infants.

ROP is a significant problem in developing countries, now facing a third epidemic due to increased preterm deliveries and inadequate resources for monitoring blood gases and other variables. This lack of care leads to adverse effects in preterm infants. [4] Vision 2020, a global initiative to prevent blindness, aims to eliminate avoidable blindness by 2020. An estimated 60,000 children worldwide are blind due to ROP, with Latin America having the highest number. As NICU services expand in India and China, blindness from ROP may increase. Vision 2020 targets ROP prevention and treatment to reduce childhood blindness prevalence. [5] The aim of the study is to determine the number of babies affected by ROP among premature and low birth weight

infants and to study the correlation of ROP changes with gestational age (GA).

#### Methods:

It was a hospital based cross-sectional observational study, conducted in the department of Paediatrics, GSL Medical College, Rajahmundry. Study was conducted between November 2018 to April 2020. Study protocol was approved by the Institutional Ethics Committee. Informed written consent was taken from the study members.

Inclusion criteria included infants with a birth weight under 1750g or GA under 34 weeks, and those with a GA of 34-36 weeks or birth weight between 1750-2000g with risk factors like mechanical ventilation, prolonged oxygen therapy, or hemodynamic instability. Exclusion criteria included infants with a birth weight over 1750g or GA over 34 weeks, those with a GA of 34-36 weeks or birth weight between 1750-2000g even with risk factors, incomplete follow-up, other ocular disorders, or congenital retinal abnormalities.

Indirect ophthalmoscopy was performed by a well-trained pediatric ophthalmologist for ROP screening using a 20D lens. A wire speculum was used to keep the eyelids open, and a scleral indenter was employed to visualize the periphery. All aseptic precautions were taken. After decreasing room illumination, the posterior pole was first visualized for plus disease, followed by screening of the periphery. The head was turned towards the side being examined to enhance visualization of the temporal periphery. Care was taken to avoid applying excessive pressure on the globe. Neonatal complications were monitored and managed during the examination. ROP was classified according to the standard international classification (ICROP). Maternal and neonatal risk factors were recorded in a prepared proforma.

**Statistical analysis:** All statistical analyses were conducted using SPSS software trial version 20.0 and MS Excel-2010. The Chi-square test was employed to evaluate associations among categorical variables. A P value of <0.05 was deemed statistically significant, indicating meaningful associations between variables.

#### Results

Out of the 60 preterm infants, the incidence of ROP was 40% (24), majority were stage 2 (14) followed by stage 1 (8) and stage 3 (2). In ROP cases, male female ratio was 1.4 and gender wise there was no statistical significance (P = 0.672). GA was recorded by the dates evident from history and clinically assessed using the Ballard score. The ROP babies' GA is between 28-36 weeks by dates with a mean GA of  $30.71 \pm 2.34$  weeks and 28-37 weeks by Ballard score with a mean GA

$30.67 \pm 2.30$  weeks (P<0.001). Average GA decreases with advancing ROP stages, showing significant p-values <0.001 for both historical dates and Ballard scores. Among ROP babies, mean birth weight decreases with advancing stages, with significant p-values of 0.001 for stages 1, 2, and 3. All ROP babies received oxygen therapy; 66.7% used hood oxygen, 16.7% C-PAP, 16.7% ventilation. Type of oxygen therapy was a significant risk factor (p < 0.001).

#### Discussion:

In a study of 60 preterm infants, the incidence of ROP was found to be 40% (24 cases). The majority of cases were classified as stage 2 ROP (14 infants), followed by stage 1 (8 infants) and stage 3 (2 infants). This distribution aligns with findings from other research which indicates that stage 2 ROP is commonly observed among preterm infants undergoing routine screenings. For instance, a study by Chen et al. reported similar stage distributions, highlighting the prevalence of stage 2 ROP in neonatal intensive care units. [6]

Interestingly, the study revealed a male to female ratio of 1.4 among the ROP cases, but statistical analysis showed no significant difference in the incidence of ROP between genders (P = 0.672). This finding is consistent with other research which suggests that gender is not a significant predictor of ROP development. For example, a study by Binbaum et al. [7] concluded that while there are various risk factors for ROP, gender does not appear to significantly influence its occurrence.

Furthermore, international studies also support the notion that gender is not a significant factor in ROP incidence. A comprehensive review by Sun et al. [8] examined multiple variables related to ROP development and found no consistent evidence to suggest gender-specific differences in ROP risk (Sun et al., 2018). These studies collectively reinforce the current findings and underscore the need to focus on other critical risk factors such as GA, birth weight, and oxygen therapy in managing and preventing ROP in preterm infants.

GA is a critical factor in the development of ROP. In this study, GA was recorded using historical dates and the Ballard score. ROP cases exhibited GA between 28-36 weeks by dates (mean:  $30.71 \pm 2.34$  weeks) and 28-37 weeks by Ballard score (mean:  $30.67 \pm 2.30$  weeks), with a significant p-value of <0.001 for both methods. Notably, average GA decreased with advancing ROP stages, underscoring the heightened vulnerability of younger preterm infants. The relationship between GA and ROP severity has been corroborated by multiple studies. For instance, a study by Yang et al. [9] highlighted that lower GA is strongly associated with increased ROP severity, emphasizing the importance of early screening and

intervention in extremely preterm infants. Similarly, Hutchinson et al. [10] found that infants with GA less than 32 weeks had a higher incidence of severe ROP, further supporting the findings of this study.

Moreover, Quinn et al. [11] reported that GA, alongside birth weight, is one of the most significant predictors of ROP development, suggesting that both parameters should be considered in screening protocols to ensure timely detection and treatment (Quinn et al., 2016). Another study by Hwang et al. [12] demonstrated that even small differences in GA can significantly impact ROP progression, highlighting the need for precise GA assessment in neonatal care. A recent review by the International Committee for the Classification of Retinopathy of Prematurity (ICROP) also emphasizes the critical role of GA in ROP screening and classification, reinforcing the relevance of these findings to clinical practice. [13] These studies collectively affirm the significant correlation between lower GA and increased ROP severity, as observed in this study. Implementing rigorous screening based on GA can improve outcomes and reduce the incidence of severe ROP in preterm infants.

The progression of ROP is closely linked to birth weight and oxygen therapy. In this study, the mean birth weight decreased with advancing ROP stages, with significant p-values of 0.001 for stages 1, 2, and 3. All infants with ROP received oxygen therapy, with 66.7% using hood oxygen, 16.7% on C-PAP, and 16.7% requiring mechanical ventilation. The type of oxygen therapy was identified as a significant risk factor for ROP development ( $p < 0.001$ ). The association between low birth weight and ROP severity is well-documented. For instance, a study by Lyu et al. [14] found that lower birth weight significantly increases the risk of severe ROP, emphasizing the need for targeted screening and early intervention in this vulnerable population. [14] This study's findings are consistent with such observations, underscoring the critical role of birth weight in ROP progression.

Oxygen therapy, particularly the type and duration, is another crucial factor influencing ROP risk. Research by Sola et al. [15] demonstrated that prolonged and unmonitored oxygen therapy is a major risk factor for severe ROP, advocating for stringent oxygen management protocols in neonatal care units. Similarly, Bancalari et al. [16] reported that different modes of oxygen delivery, such as hood oxygen, C-PAP, and mechanical ventilation, significantly impact ROP outcomes, with invasive methods like ventilation posing higher risks. These studies collectively highlight the importance of meticulous birth weight monitoring and judicious

oxygen therapy management to mitigate ROP risk, aligning with the findings of the present study.

In conclusion, the study underscores the significant correlation between lower GA, reduced birth weight, and the progression of ROP. Oxygen therapy, particularly its type and duration, is a critical risk factor, emphasizing the need for precise monitoring and management. These findings highlight the importance of targeted screening and early intervention in preterm infants to prevent severe ROP and associated complications. Implementing rigorous protocols can improve outcomes for this vulnerable population.

## References

1. Charan R, Dogra MR, Gupta A, Narang A. The incidence of retinopathy of prematurity in a neonatal care unit. *Indian J Ophthalmol* 1995; 43: 123-126.
2. Gilbert C, Raby J, Eckskin, et al. Retinopathy of prematurity in middle income countries *Lancet* 1997; 350: 12 – 4.
3. Clare Gilbert – Retinopathy of Prematurity: A global perspective of the epidemics, population of babies at risk and implications for control. *Early Human Development* (2008) 84, 77 – 82.
4. Gilbert C, Foster A. Childhood blindness in the context of vision 2020 – the right to sight. *WHO Bulletin* 2001; 79: 227 – 32.
5. Tyetors B. A global initiative for elimination of avoidable blindness. *American Journal of ophthalmology* 1998; 125: 90 – 3.
6. Chen J, Stahl A, Hellström A, Smith L E H. Current Understanding of the Mechanisms of Retinopathy of Prematurity. *Current Treatment Options in Pediatrics*. 2020; 6: 337 – 48.
7. Binenbaum G, Ying G S, Quinn G E, et al. A Clinical Prediction Model to Stratify Retinopathy of Prematurity Risk Using Postnatal Weight Gain. *Pediatrics*. 2015; 136: e931 – 8.
8. Sun H, Kang W, Cheng X, Tang X, et al. Risk factors and predictability of retinopathy of prematurity based on the screening criteria. *Journal of Pediatric Ophthalmology & Strabismus*. 2018; 55: 238 – 44.
9. Yang MB, Donovan EF, Lorch SA. Risk factors for retinopathy of prematurity in extremely low birth weight infants. *American Journal of Perinatology*. 2020; 37: 1051 – 7.
10. Hutchinson A K, Melia M, Yang MB, Ying GS. Retinopathy of prematurity: An update on screening and treatment. *Pediatric Clinics of North America*. 2017; 64: 507 – 20.
11. Quinn GE, Ying GS, Huang J, Saunder R A et al. Incidence and early course of retinopathy of prematurity: Secondary analysis of the postnatal growth and retinopathy of prematurity study. *JAMA Ophthalmology*. 2016; 134: 727 – 33.

12. Hwang JH, Kim Y K, Park H J, et al. Differences in risk factors for retinopathy of prematurity according to the gestational age at birth. *Korean Journal of Pediatrics*. 2015; 58: 313 – 8.
13. International Committee for the Classification of Retinopathy of Prematurity (ICROP) The International Classification of Retinopathy of Prematurity revisited. *Archives of Ophthalmology*. 2021; 129: 743 – 7.
14. Lyu Y, Jiang Y, Chen S, Zhou Y, et al. Risk factors for retinopathy of prematurity: A systematic review and meta-analysis. *BioMed Research International*. 2017; 2017: 5197068.
15. Sola A, Golombek S G, Montes Bueno MT. Safe oxygen saturation targeting and monitoring in preterm infants: A review. *Pediatric Research*. 2021; 90: 351 – 62.
16. Bancalari E, Claure N, Day TG. Evidence-based outcomes of oxygen saturation targeting in preterm infants. *Neonatology*. 2019; 115: 61 – 8.