Student's Journal of Health Research Africa
e-ISSN: 2709-9997, p-ISSN: 3006-1059
Vol.7 No. 2 (2026): June 2026 Issue
https://doi.org/10.51168/sjhrafrica.v7i2.2716
Original Article

A Prospective Analytical Observational Study on the Correlation of Weekly Postnatal Weight Gain with the Development of Retinopathy of Prematurity in Premature Babies.

Dr. Bighneswar Senapati, Dr. Mohammed Abdul Wasiq*, Dr. Soumya Ranjan Samal
Asst Professor, Dept of Pediatrics, IMS & SUM Hospital, Campus 2, Phulnakhara, BBSR

ABSTRACT
Background:
Retinopathy of Prematurity (ROP) is a major cause of preventable childhood blindness among premature infants. Poor postnatal weight gain has emerged as an important predictor of ROP and may facilitate early identification of high-risk neonates.

Aim:
To evaluate the relationship between weekly postnatal weight gain and the development of Retinopathy of Prematurity in premature babies.

Materials and Methods:
This prospective observational study was conducted in the Neonatal Intensive Care Unit of IMS & SUM Hospital, Bhubaneswar, from January 2019 to June 2020 among 80 preterm neonates fulfilling ROP screening criteria. Weekly postnatal weight gain was monitored, and ophthalmologic screening for ROP was performed according to standard guidelines. Associated risk factors, including oxygen therapy, mechanical ventilation, anemia, blood transfusion, hypoxemia, sepsis, and delayed regain of birth weight, were analyzed using appropriate statistical methods.

Results:
The median gestational age was 30.05 weeks, and the median birth weight was 1200 g. Most infants (66.25%) had a birth weight between 1001 and 1500 g. ROP was significantly associated with supplemental oxygen therapy, hypoxemia, mechanical ventilation, anemia, blood transfusion, late-onset sepsis, Candida sepsis, and delayed regain of birth weight. Infants with poor weekly postnatal weight gain had a significantly higher incidence of ROP than those with adequate weight gain.

Conclusion:
Weekly postnatal weight gain is a simple, cost-effective, and reliable predictor for the early identification of Retinopathy of Prematurity in premature infants. Regular monitoring of postnatal weight gain can facilitate timely recognition of neonates at increased risk.

Recommendation:
Routine weekly postnatal weight gain monitoring should be incorporated into neonatal care and ROP screening protocols, particularly in resource-limited settings, to improve risk stratification, enable earlier referral for ophthalmologic evaluation, and reduce the burden of preventable childhood blindness.

Keywords: *Retinopathy of Prematurity, Postnatal Weight Gain, Prematurity, Low Birth Weight, Neonatal Intensive Care Unit.*
Submitted: April 20, 2026 **Accepted:** May 22, 2026 **Published:** June 30, 2026

Corresponding author: *Dr. Mohammed Abdul Wasiq*
Email: ***mohammedwasiq03@gmail.com***
Assistant Professor, Dept of Pediatrics, IMS & SUM Hospital, Campus 2, Phulnakhara, BBSR

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INTRODUCTION

Retinopathy of Prematurity (ROP) is a vasoproliferative disorder of the immature retina and is one of the leading causes of preventable childhood blindness worldwide. The increasing survival of premature and low birth weight neonates due to advances in neonatal intensive care has simultaneously increased the burden of ROP, particularly in developing countries such as India. WHO Vision 2020 has recognized ROP as an important avoidable cause of childhood blindness. India contributes significantly to the global burden because of the large number of preterm births occurring annually.[1]

ROP develops due to incomplete vascularization of the retina at birth in premature infants. Various prenatal and postnatal factors interfere with normal retinal vascular growth, leading to abnormal neovascularization and retinal damage. The disease generally evolves 4–6 weeks after birth and may range from mild disease with spontaneous regression to severe retinal detachment and permanent blindness. Early diagnosis and timely treatment, therefore, play a crucial role in the prevention of visual disability.[2]

The major established risk factors for the development of ROP include low gestational age, low birth weight, prolonged oxygen exposure, mechanical ventilation, anemia, blood transfusion, sepsis, and unstable clinical condition. Hyperoxia after birth suppresses vascular endothelial growth factors essential for normal retinal vascularization, resulting in retinal ischemia and pathological neovascularization. Extremely premature infants are especially vulnerable to aggressive forms of ROP.[3]

Recent research has increasingly focused on postnatal growth as a predictor of the development of ROP. The ideal extrauterine growth pattern in premature infants should approximate intrauterine growth, which is approximately 15–25 g/kg/day during the neonatal period. Failure to achieve adequate postnatal weight gain has been associated with increased risk of ROP. Several predictive models, such as WINROP, CHOP-ROP, CO-ROP, and G-ROP, incorporate postnatal weight gain as an important screening parameter.[4]

Insulin-like Growth Factor-1 (IGF-1), an important somatic growth factor, plays a permissive role in vascular endothelial growth factor-mediated retinal vascularization. Premature infants lose maternal IGF-1 supply after birth and have poor endogenous production, resulting in impaired retinal vascular growth and increased risk of neovascularization. Since postnatal weight gain indirectly reflects IGF-1 levels and overall neonatal growth, it has emerged as a simple and inexpensive marker for identifying high-risk infants.[5]

ROP screening in developing countries remains challenging because of limited resources and a shortage of trained ophthalmologists. Identifying simple clinical markers that can help stratify risk and optimize screening programs is therefore highly important. Weekly postnatal weight monitoring is inexpensive, non-invasive, and feasible even in resource-limited neonatal units. If proven effective, it can supplement existing screening criteria and improve early identification of infants at risk.[6]

The present study was therefore conducted to evaluate the correlation between weekly postnatal weight gain and the development of retinopathy of prematurity among premature babies admitted to a tertiary care neonatal intensive care unit.

Aim

To study the correlation between weekly postnatal weight gain and the development of Retinopathy of Prematurity (ROP) in premature babies admitted to the neonatal intensive care unit.

Objectives

1. To evaluate the association between weekly postnatal weight gain and the occurrence of Retinopathy of Prematurity in premature neonates.
2. To determine the incidence of ROP among preterm and low birth weight babies.
3. To assess the relationship between gestational age, birth weight, and the development of ROP.

MATERIALS AND METHODS

Study Design

This is a Prospective Analytical Observational Study

Study Setting

Institute of Medical Sciences and SUM Hospital, Siksha 'O' Anusandhan (Deemed to be University)

Level of care

Level III NICU

Geographic context

Bhubaneswar, Odisha, India

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Facility description

Tertiary care teaching hospital and referral center providing comprehensive neonatal intensive care services.

Study Duration

over a period of 18 months from January 2019 to June 2020.

Sample size

The sample size was calculated using the single population proportion formula, $n = Z^2pq/d^2$, assuming an expected prevalence of Retinopathy of Prematurity (ROP) of **19.2%** based on a previous Indian study (Study by Abdel H A A Hakeem et al) with a **95% confidence level** and **9% absolute precision**. The minimum calculated sample size was **74**. Considering an anticipated attrition/non-response, the final sample size was rounded to **80 preterm neonates**, who were enrolled consecutively during the study period.

A total of 80 premature neonates fulfilling the inclusion criteria were enrolled in the study after obtaining informed consent from parents or guardians.

Bias

Selection bias was minimized by enrolling consecutive eligible preterm neonates. Measurement bias was reduced by using a calibrated digital weighing scale and standardized ROP screening performed by an experienced ophthalmologist. Potential confounders were recorded and adjusted for during statistical analysis.

Ethical Considerations:

The study was approved by the Institutional Ethics Committee, Institute of Medical Sciences and SUM Hospital, Siksha 'O' Anusandhan (Deemed to be University), Bhubaneswar, Odisha, India**.** The study was conducted in accordance with the Declaration of Helsinki.

Informed Consent:

Written informed consent was obtained from the parents or legal guardians of all enrolled neonates before participation. Confidentiality was maintained, and participation was voluntary.

Study Population

Premature infants admitted to the NICU were screened according to the inclusion criteria:

1. Gestational age ≤34 weeks
2. Birth weight <1750 grams
3. Preterm infants between 34 and 36+6 weeks gestation or birth weight between 1750–2000 grams with unstable clinical course or requiring cardiorespiratory support

Exclusion Criteria

1. Major congenital malformations
2. Parents not willing to provide consent for participation

Data Collection

Detailed demographic and clinical information was collected for all enrolled premature neonates at the time of admission to the Neonatal Intensive Care Unit (NICU). Baseline neonatal characteristics, including gestational age, birth weight, sex, anthropometric classification, and order of birth, were documented systematically. Based on growth parameters, babies were categorized as Small for Gestational Age (SGA), Appropriate for Gestational Age (AGA), or Large for Gestational Age (LGA). Gestational age assessment was performed using obstetric history and clinical examination. Birth weight was measured immediately after delivery using calibrated neonatal weighing scales. These demographic variables were analyzed to determine their association with the development of Retinopathy of Prematurity (ROP).

Serial monitoring of body weight was carried out throughout the neonatal period using standardized electronic neonatal weighing machines. Weekly postnatal weight gain was carefully recorded for each infant to assess extrauterine growth patterns. Special emphasis was placed on identifying delay in regaining birth weight beyond 14 days of life, as inadequate postnatal weight gain is considered an important predictor for the development of ROP. Weight measurements were performed under uniform conditions to minimize measurement errors, and growth trends were analyzed in relation to retinal findings.

In addition to anthropometric data, several neonatal clinical risk factors known to influence the occurrence of ROP were evaluated in detail. Supplemental oxygen therapy was assessed because prolonged oxygen exposure can suppress normal retinal vascularization and contribute to abnormal neovascular proliferation. Episodes of hypoxemia were documented, as fluctuations in oxygen saturation are recognized contributors to retinal vascular injury. Requirement of mechanical ventilation was recorded as it reflects the severity of respiratory illness and increased exposure to oxygen therapy.

Other systemic risk factors, including hypotension, anemia, and blood transfusion, were also studied. Anemia may impair oxygen delivery to tissues, while repeated blood transfusions expose neonates to adult hemoglobin, altering

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oxygen dissociation dynamics and increasing oxidative stress, thereby increasing susceptibility to ROP. Neonatal infections such as late-onset sepsis and candida sepsis were evaluated because systemic inflammatory responses can adversely affect retinal vascular development. Hypercarbia was documented due to its association with unstable respiratory status and altered retinal blood flow. Babies with unstable clinical courses requiring intensive cardiorespiratory support were identified separately, as critically ill neonates are at significantly higher risk for severe ROP. All these risk factors were analyzed statistically to determine their relationship with the development and severity of Retinopathy of Prematurity.

Ophthalmologic Examination

ROP screening was conducted by trained ophthalmologists according to standard screening guidelines. The first ophthalmologic examination was performed based on gestational age and birth weight criteria. Subsequent follow-up examinations were scheduled depending on retinal findings until complete retinal vascularization or regression of disease.

ROP staging and classification were performed according to the International Classification of Retinopathy of Prematurity (ICROP). Disease severity was categorized into stages 1 to 5, with documentation of plus disease and zone involvement wherever applicable.

Outcome Measures

The primary outcome of the study was the development of ROP among screened premature infants. Secondary outcomes included evaluation of the association between weekly postnatal weight gain and other clinical risk factors with the occurrence of ROP.

Statistical Analysis

All collected data were entered into Microsoft Excel and analyzed using SPSS software version 17. Quantitative variables were expressed as mean and standard deviation. Categorical variables were presented as frequency and percentage. Pearson correlation coefficient and Z-test were used to determine statistical significance between various risk factors and the development of ROP. Multivariate binary logistic regression analysis was performed to assess the association between weekly weight gain per kilogram per week and risk of ROP. Odds ratios and confidence intervals were calculated. A p-value less than 0.001 was considered statistically significant.

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RESULTS

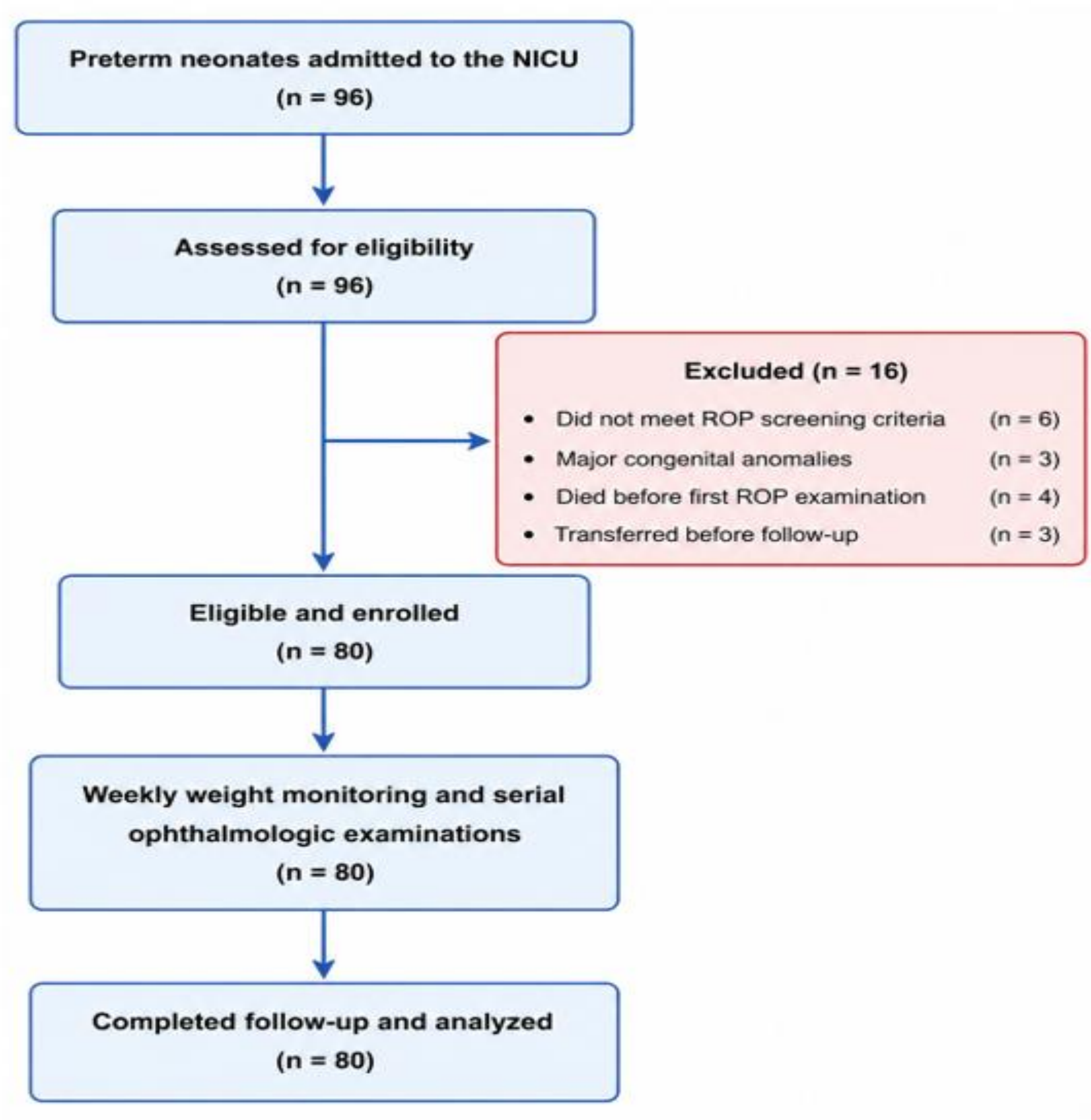

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Table 1: Distribution of Study Population According to Gestational Age

Gestational Age (Weeks)	*n*	%
23–26	3	3.75
26–29	27	33.75
29–32	29	36.25
32–35	19	23.75
35–38	2	2.50
Total	**80**	**100.00**

The study population comprises a total of 80 babies, with the vast majority falling into the moderate-to-extreme prematurity categories. The largest cohort belongs to the 29–32 weeks gestational age group, accounting for 36.25% (n = 29) of the population, closely followed by the 26–29 weeks group at 33.75% (n = 27). Together, these two subsets represent 70% of all observed subjects. Conversely, the extremes of the spectrum—the most vulnerable 23–26 weeks group (3.75%, n = 3) and the near-term 35–38 weeks group (2.50\%, n = 2)—make up the smallest proportions of the study population.

Graph 1: Distribution According to Gestational Age

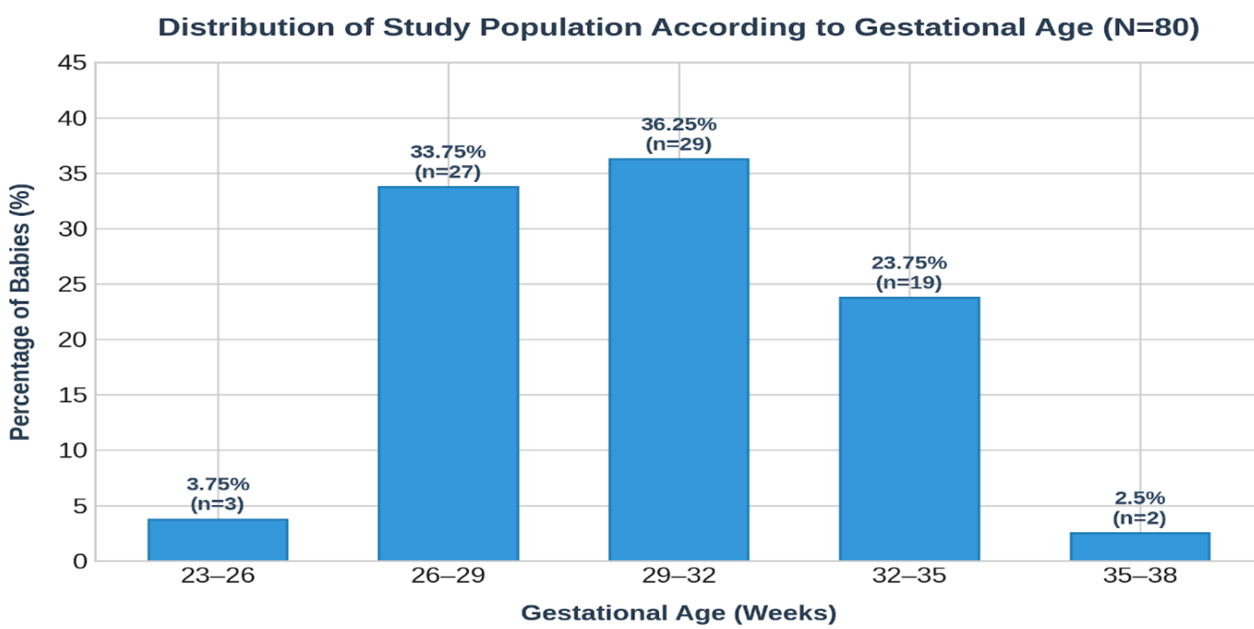

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Table 2: Distribution According to Birth Weight

Birth Weight (grams)	Number of Babies	Percentage
<600	1	1.25%
601–750	3	3.75%
751–1000	16	20.00%
1001–1500	53	66.25%
1501–2500	7	8.75%

The dataset evaluates the birth weight distribution of 80 neonates, revealing a high concentration within the very low birth weight (VLBW) category. The prominent majority of the study population falls into the 1001–1500 grams range, constituting 66.25% (n = 53) of the cohort. The next most frequent interval is 751–1000 grams, which accounts for 20.00% (n = 16). Combined, these two categories represent over 86% of the total sample. Extreme low birth weights below 750 grams are less frequent, with 3.75% (n = 3) in the 601–750 grams bracket and only 1.25% (n = 1) weighing under 600 grams. Meanwhile, 8.75% (n = 7) of the neonates fall into the higher 1501–2500 grams range.

Graph 2: Distribution According to Birth Weight

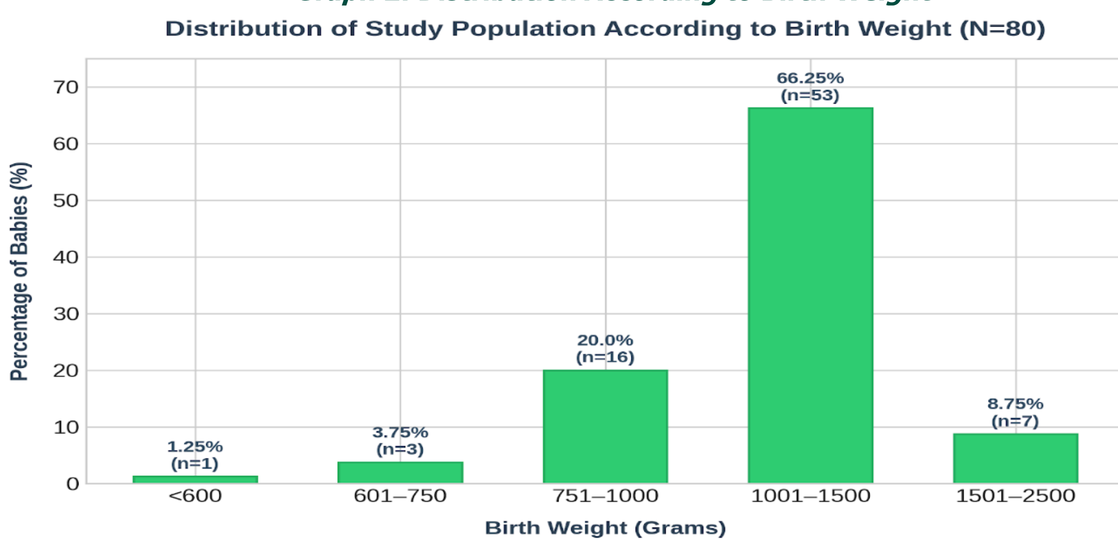

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Table 3: Distribution According to SGA/AGA/LGA Status

Category	Number of Babies	Percentage
SGA	22	27.50%
AGA	58	72.50%
LGA	0	0%

Table 3 shows the distribution of study subjects according to anthropometric classification. The majority of the premature babies were Appropriate for Gestational Age (AGA), accounting for 72.5% of the study population, while 27.5% were Small for Gestational Age (SGA). None of the neonates were categorized as Large for Gestational Age (LGA). This indicates that most preterm infants included in the study had birth weights appropriate for their gestational age, whereas a smaller proportion exhibited intrauterine growth restriction.

Table 4: Association of Clinical Risk Factors with ROP

Risk Factor	Association with ROP	Statistical Significance
Supplemental Oxygen	53% developed ROP	$p < 0.0001$
Mechanical Ventilation	65% developed ROP	$p < 0.0001$
Anemia	Significant association	$p < 0.0001$
Blood Transfusion	85% developed ROP	$p < 0.0001$
Late Onset Sepsis	60% developed ROP	$p < 0.0001$
Candida Sepsis	All developed ROP	$p < 0.0001$
Delayed Regain of Birth Weight	93% developed ROP	$p < 0.0001$

The data show an exceptionally strong link between specific clinical risk factors and the development of Retinopathy of Prematurity (ROP), with all analyzed parameters demonstrating extreme statistical significance ($p < 0.0001$). Among the studied cohort, infectious and metabolic stressors presented the highest vulnerabilities: Candida Sepsis resulted in a 100% incidence of ROP, closely followed by a 93% incidence in neonates with a Delayed Regain of Birth Weight. Invasive clinical interventions also carried substantial risk, as 85% of infants receiving a Blood Transfusion and 65% on Mechanical Ventilation went on to develop the condition. Furthermore, systemic infections and standard respiratory support showed prominent associations, with Late Onset Sepsis and Supplemental Oxygen exposure leading to ROP in 60% and 53% of cases, respectively. Anemia was also confirmed to have a highly significant qualitative association ($p < 0.0001$) with the onset of the disease.

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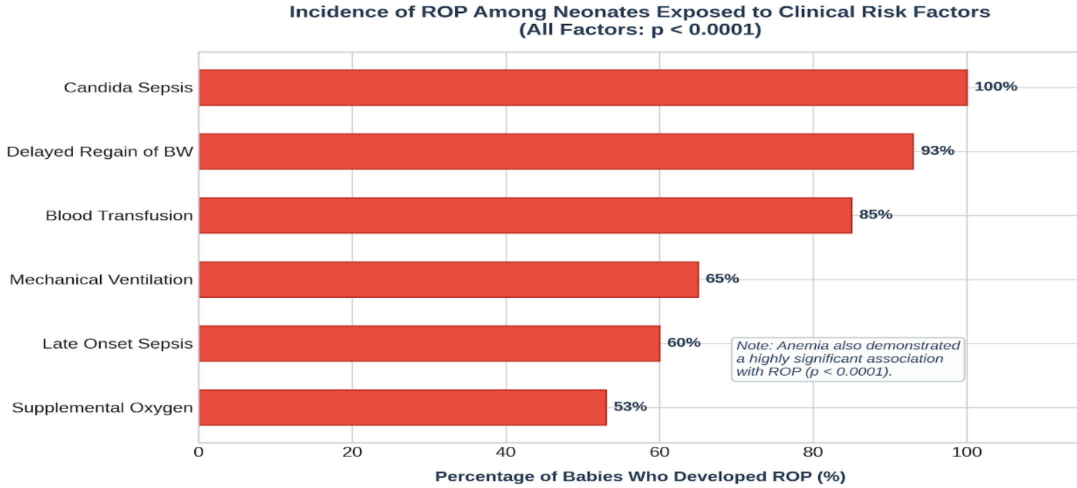
Graph 3: Clinical Risk Factors Associated with ROP



Discussion

In the present study, the majority of premature babies belonged to the gestational age group of 29–32 weeks, accounting for 36.25% of the study population, followed by 26–29 weeks (33.75%). The median gestational age was 30.05 weeks. These findings indicate that moderately preterm infants constituted the major proportion of neonates requiring ROP screening. Lower gestational age has been consistently recognized as one of the strongest predictors for the development of Retinopathy of Prematurity because retinal vascularization remains incomplete in extremely premature infants. Similar findings were reported by Binenbaum et al. (2022)[7], who observed that neonates born before 32 weeks of gestation had significantly higher susceptibility to severe ROP due to retinal immaturity and prolonged NICU exposure. Likewise, a multicentric Indian study by Dammann O et al[8] demonstrated that decreasing gestational age significantly increased the incidence and severity of ROP among preterm neonates. Another recent study by Koc E et al[9] also reported that infants with gestational age below 30 weeks had a markedly increased risk for severe ROP requiring treatment. These findings support the observations of the present study that prematurity itself remains a major determinant for ROP development.

The birth weight distribution in the present study showed that 66.25% of babies weighed between 1001 and 1500 grams, while 20% weighed between 751 and 1000 grams. The median birth weight was 1200 grams. Lower birth weight is a well-established risk factor for ROP because extremely low birth weight infants often require prolonged respiratory support, oxygen supplementation, and intensive neonatal care. Similar findings were reported by Gilbert C et al,[10] who observed significantly higher ROP incidence among neonates weighing less than 1500 grams. A recent study by Blencowe H et al[11] demonstrated that very low birth weight infants had an increased risk of retinal neovascularization and severe ROP due to immature retinal vascular growth. Furthermore, research conducted by Fierson WM et al[12] confirmed that birth weight below 1250 grams independently predicted severe ROP requiring laser therapy. The present study findings are therefore consistent with recent literature emphasizing low birth weight as a critical predictor of ROP.

With respect to anthropometric classification, 72.5% of neonates were Appropriate for Gestational Age (AGA), while 27.5% were Small for Gestational Age (SGA). None of the babies were categorized as Large for Gestational Age (LGA). Although most babies were AGA, a significant proportion of SGA infants suggests that intrauterine growth restriction may contribute to poor postnatal growth and increased risk of retinal vascular insufficiency. Similar observations were reported by Lundgren P et al. ([13], who found that SGA infants had a higher probability of developing severe ROP because of impaired fetal nutrition and reduced growth factor levels. Another study by Löfqvist C et al[14] concluded that SGA status significantly increased the need for ROP treatment among premature neonates. These findings indicate that fetal growth restriction may contribute to altered retinal vascular development and increased susceptibility to oxidative injury.

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The present study demonstrated a highly significant association between supplemental oxygen therapy and the development of ROP, with approximately 53% of oxygen-receiving infants developing disease. Oxygen therapy has historically been one of the most important contributors to ROP pathogenesis. Hyperoxia suppresses Vascular Endothelial Growth Factor (VEGF), leading to arrest of retinal vascular growth, followed by pathological neovascularization during hypoxic phases. Similar findings were reported by Jensen et al. (2021)[15], who demonstrated that prolonged oxygen exposure and fluctuations in oxygen saturation significantly increased severe ROP risk in extremely premature infants. A systematic review by Woods J et al [16] also confirmed that uncontrolled oxygen supplementation remains an independent risk factor for severe ROP. Likewise, a recent Indian neonatal study by Fleck BW et al [17] found that prolonged supplemental oxygen therapy was strongly associated with aggressive posterior ROP. These studies support the findings of the present study and highlight the importance of careful oxygen monitoring in NICUs.

Hypoxemia was also found to have a statistically significant relationship with ROP in the present study. Fluctuations in oxygen saturation contribute to retinal ischemia and vascular instability, thereby promoting abnormal retinal angiogenesis. Similar findings were observed by Askie LM et al [18], who reported that recurrent hypoxemic episodes were associated with severe ROP among ventilated preterm infants. Another study by Di Fiore JM et al [19] concluded that intermittent hypoxia significantly altered retinal vascular development and increased retinal oxidative stress. These observations reinforce the role of unstable oxygenation in ROP pathogenesis.

Mechanical ventilation showed a highly significant association with ROP, with 65% of ventilated neonates developing disease. Infants requiring ventilation are usually critically ill and exposed to prolonged oxygen therapy and hemodynamic instability. Similar findings were reported by Kim SJ et al. ([20], who demonstrated that mechanical ventilation duration independently correlated with severe ROP. Another recent study by Good WV et al [21] showed that prolonged respiratory support significantly increased the risk of treatment-requiring ROP. These findings are comparable to the present study and indicate that mechanically ventilated neonates require close retinal surveillance.

Anemia and blood transfusion were strongly associated with ROP in the present study. Approximately 85% of neonates receiving blood transfusions developed ROP. Blood transfusion exposes preterm infants to adult hemoglobin, which alters oxygen delivery and enhances oxidative stress. Similar observations were made by Wang J et al[22], who reported multiple transfusions as a major risk factor for severe ROP. Another study by Dani C et al[23] found that transfusion frequency significantly correlated with progression of retinal neovascularization. Furthermore, research by Cooke RW et al [24] concluded that severe anemia and repeated packed cell transfusions increased the likelihood of aggressive ROP. These findings support the strong association identified in the present study.

Late-onset sepsis and candida sepsis demonstrated extremely significant relationships with ROP development in the current study. All neonates with candida sepsis developed ROP. Neonatal infections produce inflammatory cytokines and endothelial injury, which adversely affect retinal vascularization. Similar findings were reported by Kim SJ et al. ([25], who observed neonatal sepsis as an independent predictor for severe ROP. Another recent study by Gantz et al. (2022)[26] showed that fungal sepsis substantially increased the risk of aggressive posterior ROP. Likewise, Arroe M et al[27] demonstrated that systemic infections prolonged NICU stay and enhanced retinal oxidative stress, thereby increasing ROP severity. These studies are in agreement with the present findings and underline the importance of infection prevention strategies in premature infants.

One of the most important observations of the present study was the significant association between delayed regain of birth weight beyond 14 days and the development of ROP. Nearly 93% of infants with delayed weight regain developed ROP. Poor postnatal weight gain reflects inadequate nutrition, impaired Insulin-like Growth Factor-1 (IGF-1) production, and disrupted retinal vascular development. Similar findings were reported by Hellstrom et al.[28] in the WINROP model, which established postnatal weight gain as an important predictor for severe ROP. More recently, Wu et al. (2022)[29] confirmed that poor early postnatal growth strongly predicted treatment-requiring ROP. Another study by Binenbaum et al. (2023)[7] validated seven growth-based prediction models, such as G-ROP and CHOP-ROP, showing excellent sensitivity for early detection of severe ROP. These findings strongly support the observations of the present study and emphasize the importance of serial weight monitoring in neonatal intensive care units.

Overall, the findings of the present study are consistent with recent national and international literature demonstrating that lower gestational age, low birth weight, poor postnatal weight gain, oxygen exposure, mechanical ventilation, anemia, blood transfusion, and neonatal sepsis significantly contribute to the development of Retinopathy of

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Prematurity. The study highlights the usefulness of weekly postnatal weight monitoring as a simple, economical, and practical screening adjunct for early identification of high-risk neonates, particularly in resource-limited settings.

CONCLUSION

Weekly postnatal weight gain is significantly associated with the development of Retinopathy of Prematurity in premature babies. Poor weight gain, delayed regain of birth weight, oxygen therapy, mechanical ventilation, anemia, blood transfusion, and neonatal sepsis are important predictors of ROP.

Routine monitoring of weekly postnatal weight gain is a simple, economical, and effective method for identifying high-risk neonates. Incorporation of serial weight monitoring into ROP screening strategies may improve early diagnosis and timely intervention, particularly in resource-limited settings.

Generalizability

The findings of this study are applicable to preterm infants admitted to tertiary care NICUs with similar demographic and clinical characteristics. The results may be generalized to comparable resource-limited healthcare settings; however, caution is required when extrapolating to different populations or healthcare systems.

Limitations

- Single-center study with a relatively small sample size.
- Limited follow-up period, preventing assessment of long-term visual outcomes.
- Some potential confounding factors, including nutritional practices and genetic predisposition, were not evaluated.
- Observational study design limits causal inference.

Recommendations

Clinical Practice: Routine weekly postnatal weight monitoring should be incorporated into standard NICU care as an adjunct to existing ROP screening protocols for early identification of high-risk infants.

Future Research: Large multicenter prospective studies are recommended to validate these findings and evaluate the incorporation of postnatal weight gain into predictive models for ROP screening.

Acknowledgment

The authors sincerely thank the Department of Pediatrics, Department of Ophthalmology, NICU staff, Institute of Medical Sciences, SUM Hospital, and the parents/guardians of the participating neonates for their cooperation and support during the study.

List of Abbreviations

Abbreviation	Full Form
ROP	Retinopathy of Prematurity
NICU	Neonatal Intensive Care Unit
AGA	Appropriate for Gestational Age
SGA	Small for Gestational Age
LGA	Large for Gestational Age
IGF-1	Insulin-like Growth Factor-1
ICROP	International Classification of Retinopathy of Prematurity
VLBW	Very Low Birth Weight
VEGF	Vascular Endothelial Growth Factor
SPSS	Statistical Package for the Social Sciences

Source of Funding

No external funding was received for this study.

Conflict of Interest

The authors declare that there are no conflicts of interest related to this study.

Author Contributions

- **Dr. Bighneswar Senapati:** Study conception and design, data collection, manuscript preparation.
- **Dr. Mohammed Abdul Wasiq:** Study supervision, statistical analysis, manuscript revision, corresponding author.
- **Dr. Soumya Ranjan Samal:** Literature review, data interpretation, critical review, and final approval of the manuscript.

Author Biographies

Dr. Bighneswar Senapati – MD Pediatrics, Assistant Professor, Department of Pediatrics, IMS & SUM Hospital, Campus 2, Bhubaneswar, Odisha, India.
Dr. Mohammed Abdul Wasiq – MD Pediatrics, Assistant Professor, Department of Pediatrics, IMS & SUM Hospital, Campus 2, Bhubaneswar, Odisha, India. Corresponding Author.
Dr. Soumya Ranjan Samal – MD Pediatrics, Assistant Professor, Department of Pediatrics, IMS & SUM Hospital, Campus 2, Bhubaneswar, Odisha, India.

Data Availability

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request and with institutional approval.

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Student's Journal of Health Research Africa
e-ISSN: 2709-9997, p-ISSN: 3006-1059
Vol.7 No. 2 (2026): June 2026 Issue
https://doi.org/10.51168/sjhrafrica.v7i2.2716
Original Article

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Student's Journal of Health Research Africa
e-ISSN: 2709-9997, p-ISSN: 3006-1059
Vol.7 No. 2 (2026): June 2026 Issue
https://doi.org/10.51168/sjhrafrica.v7i2.2716
Original Article

PUBLISHER DETAILS

Student's Journal of Health Research (SJHR)
(ISSN 2709-9997) Online
(ISSN 3006-1059) Print
Category: Non-Governmental & Non-profit Organization
Email: studentsjournal2020@gmail.com
WhatsApp: +256 775 434 261
Location: Scholar's Summit Nakigalala, P. O. Box 701432, Entebbe Uganda, East Africa