International Journal of Scientific Advances
ISSN: 2708-7972
Volume: 6 | Issue: 6 | Nov – Dec 2025 Available Online: www.ijscia.com
DOI: 10.51542/ijscia.v6i6.45

Factors Associated with Retinopathy of Prematurity Based on Laboratory Findings at Dr. Soetomo Hospital, Indonesia

Aqila Sabila Rusyda[1], Reni Prastyani[2*], Kartika Darma Handayani[3], Rozalina Loebis[2]

[1]Medical Study Program, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

[2]Departement of Ophthalmology, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

[3]Departement of Paediatrics, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

E-mail: aqila.sabila.rusyda-2022@fk.unair.ac.id; reniprastyani2024@gmail.com; kartika29qisya@gmail.com; rozalina-l@fk.unair.ac.id

*Corresponding author details: Reni Prastyani; reniprastyani2024@gmail.com

ABSTRACT

Background: Retinopathy of Prematurity (ROP) is a leading cause of preventable blindness among preterm infants, with a relatively high prevalence in Indonesia. Although various risk factors have been investigated, evidence regarding laboratory findings as potential predictors of ROP remains limited. ***Objective:*** This study aimed to determine the association between laboratory parameters and the occurrence of ROP in preterm infants admitted to Dr. Soetomo General Academic Hospital from January 2023 to June 2024. ***Methods:*** This study is a descriptive-analytic study with a retrospective design, with independent variables including hemoglobin, leukocyte, thrombocyte count, and random blood glucose, while the dependent variable was the occurrence of ROP. ***Results:*** Among 312 infants, 70 (22.4%) developed ROP, and there was no significant associations were found between ROP and hemoglobin (p = 0.600), leukocyte (p = 0.943), thrombocyte (p = 0.264), or random blood glucose (p = 0.804). ***Conclusion:*** Laboratory parameters were not directly associated with the occurrence or severity of ROP. The main determinants of ROP were lower gestational age and birth weight, while blood transfusion and sepsis acted as additional contributing factors.

Keywords: retinopathy of Prematurity; associated factors; laboratory findings; prematurity

INTRODUCTION

Retinopathy of Prematurity (ROP) is one of the leading causes of preventable blindness in premature infants worldwide. ROP is caused by abnormal development of the retinal blood vessels, which, if not detected and treated appropriately, can lead to retinal detachment and long-term visual impairment [1].

It is estimated that each year, approximately 32,300 infants worldwide are diagnosed with permanent vision impairment due to ROP, and 20,000 of them experience blindness or severe vision impairment. The incidence of ROP varies between countries and depends on the population studied, ranging from 10–40% of cases [2]. In Indonesia, the incidence of ROP in infants with a gestational age of less than 32 months in 2015 was 18–30%. This rate is slightly higher than in other developing countries [3]. This is thought to be due to the higher survival rate of premature infants with access to neonatal health services, but the quality of services available is less than ideal [4].

Study related to ROP continues to be conducted dynamically to prevent undesirable effects. Many risk factors have been analyzed in several studies, but they are not yet fully understood [5]. A 2021 literature review of 191 research articles with a total sample of 140,921 infants stated that risk factors for ROP include premature birth under 28 months, low birth weight, hypotension, chorioamnionitis, and induced fertility [6].

The discussions related to the relationship between biological parameters and ROP have also been a hot topic in several literature. The results of Lim et al.'s study show that a decrease in thrombocyte levels in ROP can increase the underlying risk of ROP in infants [7]. A significant difference in blood sugar levels between the ROP and control groups, suggesting that hyperglycaemia or high blood sugar levels may be a risk factor for the development of ROP [8]. Previously, studies on ROP incidents and risk factors at Dr. Soetomo Hospital identified birth weight, blood transfusions, oxygen levels, and sepsis as significant risk factors for ROP [9].

However, research on laboratory-based factors associated with ROP has been limited in Indonesia. Therefore, this study aims to investigate further laboratory-related factors linked to ROP.

METHODS

This study is a retrospective descriptive-analytical study conducted using secondary data obtained from the medical records of premature infants treated at Dr. Soetomo General Hospital, Surabaya, from January 2023 to June 2024. The study population included all infants born at less than 37 weeks of gestation who underwent retinopathy of prematurity (ROP) screening during the study period. Total sampling was applied, and medical records that met the predetermined inclusion and exclusion criteria were included in the analysis.

Inclusion criteria included premature infants with a gestational age of less than 37 weeks, who had undergone ROP screening and who had available laboratory examination data. Medical records with incomplete or missing data were excluded from the study.

Data collected included patient characteristics (gestational age, birth weight, oxygen supplementation, history of blood transfusion, and sepsis), laboratory parameters (haemoglobin level, white blood cell count, thrombocyte count, and random blood glucose level), and ROP screening results. Laboratory values were obtained from the closest examination time before or after ROP screening. ROP diagnosis was based on initial screening results and classified as immature retina, ROP stage 1 to stage 3.

Data processing was conducted in several stages, including data editing to ensure completeness and suitability, variable coding to facilitate data entry, data entry into statistical software, and data cleaning to identify and correct errors or inconsistencies. Statistical analysis was performed using univariate analysis to describe the distribution of patient characteristics, laboratory results, and ROP results.

This study was approved by the Ethics Committee of Dr. Soetomo General Hospital. Patient data was used solely for research and educational purposes. Confidentiality was strictly maintained, and all patient identities were anonymized to ensure privacy. In its implementation, this study was conducted in accordance with ethical principles, and the findings are expected to contribute to a better understanding of the laboratory factors associated with retinopathy of prematurity.

RESULTS AND DISCUSSION

This study gathered data using secondary sources obtained from patient medical records. The process for selecting the sample is shown in Figure 1 and was guided by specific inclusion and exclusion criteria. Out of the 847 patients listed in the medical records, 517 did not receive ROP screening and were therefore removed from the analysis. This excluded group included 226 patients who passed away before screening, 185 who were discharged upon request, and 106 with incomplete data. As a result, 330 patients were screened for ROP, but 18 of these did not have routine blood test results and were subsequently excluded as well. For the 312 patients remaining, not all completed every laboratory test, leading to different sample sizes for each measure. In detail, 312 had routine blood test data, and 242 had random blood sugar data.

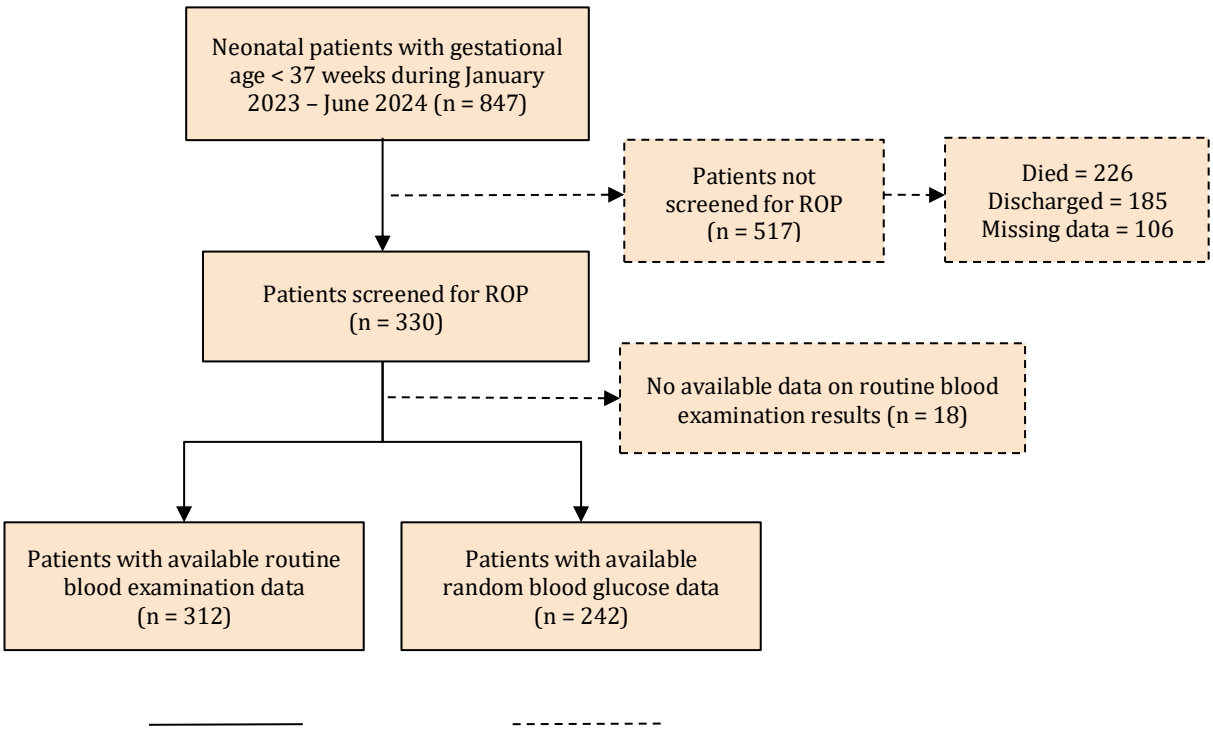

FIGURE 1: Sampling Procedure.

Sample Characteristics

A total of 312 infants were included in the study. Among these, 242 (77.6%) were diagnosed with an immature retina that was categorized as non-ROP, whereas 70 (22.4%) were diagnosed with ROP. Infants with ROP had a lower mean gestational age (31.54 ± 2.53 weeks) than those without ROP (33.07 ± 2.11 weeks). In the ROP group, 44.3% were classified as very or extremely preterm, whereas this classification accounted for only 19.8% of the non-ROP group. A similar trend was observed for birth weight: the mean birth weight in the ROP group (1526.43 ± 441.28 grams) was lower than in the non-ROP group (1833.64 ± 526.56 grams). Furthermore, 50% of infants with ROP had very low or extremely low birth weights, compared to 23.2% in the non-ROP group. In contrast, gender (p = 0.650) and oxygen concentration (FiO_2) (p = 0.242) did not differ significantly between groups, as indicated by p-values> 0.05. Both groups had a similar gender distribution, and the majority of infants received oxygen at a concentration of 21-30%. Blood transfusions were more frequent in the ROP group (35.7%) than in the non-ROP group (20.2%), and the incidence of sepsis was also higher among infants with ROP (48.6% versus 35.5%).

This research demonstrated a strong link between both gestational age and birth weight and the risk of developing retinopathy of prematurity (ROP). Infants diagnosed with ROP tended to be born at earlier gestational ages and had lower birth weights, most often falling into very preterm and very low birth weight categories. These results underscore the importance of prematurity and growth restriction as markers for immature retinal development and reduced intrauterine growth factor exposure, which are fundamental to the mechanisms underlying ROP [10]. From a biological perspective, when birth occurs before retinal vascularization is complete, there is disruption of VEGF regulation: this initially produces vessel loss and later leads to abnormal new vessel growth in response to hypoxic conditions [11]. The data also identified blood transfusions and sepsis as significant risk factors for ROP, acting respectively through increased oxidative stress from iron overload [12] and inflammation that interferes with the control of VEGF and IGF-1[13]. In contrast, neither sex nor mean FiO_2 level showed a significant association with ROP, in agreement with earlier studies [14, 15]. Current research points to oxygen fluctuations, rather than average FiO_2, as more relevant to ROP development, and this may be a result of tighter oxygen control in the NICU setting [16]. In summary, gestational age and birth weight remain primary predictors of ROP, while blood transfusion and sepsis further increase risk.

TABLE 1: Sample Characteristics.

Variable	Immature Retina (n = 242)	Stage 1 (n = 42)	Stage 2 (n = 25)	Stage 3 (n = 3)	*p*-value
Gestational age (weeks), mean±SD	33,07 ± 2,11	32,19 ± 2,47	30,36 ± 2,36	32,33 ± 1,15	**<0.001**
Moderate preterm	194 (80.2)	29 (69.0)	8 (32.0)	2 (66.7)	
Very preterm	45 (18.6)	11 (26.2)	15 (60.0)	1 (33.3)	
Extremely preterm	3 (1.2)	2 (4.8)	2 (8.0)	0 (0.0)	
Birth weight (g), mean±SD	1833,64 ± 526,56	1566,67 ± 439,40	1442,46 ± 462,26	1666,67 ± 208,17	**<0.001**
Normal	22 (9.1)	1 (2.4)	1 (4.0)	0 (0.0)	
Low	164 (67.8)	22 (52.4)	22 (52.4)	3 (100.0)	
Very low	52 (21.5)	18 (42.9)	18 (42.9)	0 (0.0)	
Extremely low	4 (1.7)	1 (2.4)	2 (8.0)	0 (0.0)	
Sex					0.156
Male	125 (51.7)	25 (59.5)	8 (32.0)	1 (33.3)	
Female	117 (48.3)	17 (40.5)	17 (68.0)	2 (66.7)	
Fraction of inspired Oxygen (FiO_2)					0.476
21–30%	192 (79.3)	32 (76.2)	16 (64.0)	2 (66.7)	
31–40%	37 (15.3)	9 (21.4)	9 (36.0)	1 (33.3)	
>40%	13 (5.4)	1 (2.4)	0 (0.0)	0 (0.0)	
Blood transfusion					0.005
Yes	49 (20.2)	11 (26.2)	12 (48.0)	2 (66.7)	
No	193 (79.8)	31 (73.8)	13 (52.0)	1 (33.3)	
Sepsis					0.175
Yes	86 (35.5)	19 (45.2)	14 (56.0)	1 (33.3)	
No	156 (64.5)	23 (54.8)	11 (44.0)	2 (66.7)	

Values are presented as mean or number (%); p-values were calculated using the Kruskal-Wallis Test; SD: Standard Deviation; ROP: retinopathy of prematurity; Moderate preterm: 32-36 weeks; Very preterm; 28-32 weeks; Extremely preterm: <28 weeks; Normal birth weight: >2500g; Low birth weight: 1500-2500g; Very low birth weight: 1000-1499g; Extremely low birth weight: <1000g

Relationship between Hemoglobin Levels and the Incidence of Retinopathy of Prematurity

Average hemoglobin levels did not show significant variation with ROP severity (p = 0.600). The group with immature retinas had a median Hb level of 14.45 (12.50 – 16.40) g/dL. When looking at the ROP stages, median Hb was 14.55 (13.40 – 16.70) g/dL in stage 1, 13.60 (11.80 – 16.00) g/dL in stage 2, and 14.10 (12.45 – 14.45) g/dL in stage 3. While the mean Hb level was lower in stage 3, this difference did not reach statistical significance. However, when considering gestational age and birth weight, there were clear and significant differences in median hemoglobin levels (p = 0.008 and p = 0.007, respectively). Infants classified as moderate preterm had much higher median hemoglobin values (14.60 (12.90 – 16.70) g/dL) than those in the very preterm (13.75 (12.00 – 15.25) g/dL; p = 0.026) and extremely preterm (11.80 (11.25 – 13.05) g/dL; p = 0.032) categories. The effect size between moderate and extremely preterm infants was substantial (Cohen's d = 0.826). No statistically significant difference appeared between the very preterm and extremely preterm groups (p = 0.084). After applying the Bonferroni correction (α = 0.0083), infants with extremely low birth weight had significantly lower hemoglobin levels compared to those with normal (p = 0.002) and low birth weight (p = 0.003). No other group comparisons showed significant differences.

The analysis results show that hemoglobin (Hb) levels were not significantly associated with the incidence of ROP, but were significantly associated with gestational age and birth weight. More premature and lower-birth-weight infants tend to have lower Hb levels, consistent with the physiology of prematurity due to a shortened erythropoiesis period, small blood volume, and high iatrogenic phlebotomy [17]. This finding is consistent with previous studies showing that the association between low Hb and ROP is not independent. Previous studies reported that anemia was associated with ROP in univariate analysis, but lost significance after controlling for gestational age and birth weight. In this study, the mean Hb in the immature retina group up to stage 2 was above 14 g/dL, still within the normal neonatal range, which likely explains the lack of a significant association between Hb and ROP [18, 19]. Overall, the relationship between anemia and ROP is complex and influenced by various mechanisms, such as tissue hypoxia, oxidative stress, and changes in oxygen affinity due to transfusion, in addition to variations in clinical conditions and treatment protocols. Therefore, the role of anemia in the pathogenesis of ROP requires further study through well-designed, controlled clinical trials [20].

TABLE 2: Distribution of Median Hemoglobin (Hb) Levels by ROP Stage, Gestational Age, and Birth Weight.

Category	n (%)	Hb (g/dL), Median (IQR)	*p*-value
ROP Stage			0.600
Immature Retina	242 (77.5%)	14.45 (12.50 – 16.40)	
Stage 1	42 (13.5%)	14.55 (13.40 – 16.70)	
Stage 2	25 (8%)	13.60 (11.80 – 16.00)	
Stage 3	3 (1%)	14.10 (12.45 – 14.45)	
Gestational Age			0.008
Moderate preterm	233 (74.7%)	14.60 (12.90 – 16.70)	
Very preterm	72 (23%)	13.75 (12.00 – 15.25)	
Extremely preterm	7 (2.3%)	11.80 (11.25 – 13.05)	
Birth Weight			0.007
Normal	24 (7.7%)	15.15 (13.50 – 16.10)	
Low	197 (63.1%)	14.70 (12.90 – 16.80)	
Very low	84 (26.9%)	13.55 (11.80 – 15.45)	
Extremely low	7 (2.3%)	12.30 (11.85 – 13.05)	

Values are presented as median (interquartile range); p-values were calculated using the Kruskal-Wallis Test; ROP: retinopathy of prematurity; Moderate preterm: 32-36 weeks; Very preterm; 28-32 weeks; Extremely preterm: <28 weeks; Normal birth weight: >2500g; Low birth weight: 1500-2500g; Very low birth weight: 1000-1499g; Extremely low birth weight: <1000g

Relationship between Leucocyte Levels and the Incidence of Retinopathy of Prematurity

There were no meaningful differences in median leukocyte counts when comparing ROP stages (p = 0.943), gestational age (p = 0.186), or birth weight (p = 0.055). Median leukocyte values were 10.71 (8.54 – 14.21) $\times 10^3/\mu L$ for the immature retina group, 11.24 (8.75 – 14.19) $\times 10^3/\mu L$ for stage 1 ROP, 11.60 (9.03 – 16.16) $\times 10^3/\mu L$ for stage 2, and 10.92 (9.06 – 12.28) $\times 10^3/\mu L$ for stage 3. Though the numbers varied slightly between groups, the differences were not significant. Dividing the data by gestational age and birth weight also did not show any notable or significant changes in leukocyte counts among the groups. On median, leukocyte levels were 10.57 (8.44 – 13.64) $\times 10^3/\mu L$ for moderate preterm

infants, 11.90 (8.94 – 14.77) $\times 10^3/\mu L$ for very preterm, and 12.3 (8.65 – 14.80) $\times 10^3/\mu L$ for extremely preterm infants. In terms of birth weight, the median leukocyte counts were 12.39 (8.43 – 15.28) $\times 10^3/\mu L$ for normal weight infants, 10.30 (8.23 – 13.26) $\times 10^3/\mu L$ for those with low birth weight, 12.06 (8.84 – 15.05) $\times 10^3/\mu L$ for very low birth weight, and 11.70 (10.00 – 13.02) $\times 10^3/\mu L$ for extremely low birth weight. Altogether, these findings indicate that leukocyte levels did not have a significant link to ROP or to the level of prematurity in this study population.

The analysis results showed no significant differences in mean leukocyte levels based on ROP stage, gestational age, or birth weight. Although there was variation between groups, leukocyte levels did not show a consistent association with prematurity or ROP incidence, and all averages remained within the physiological range for neonates.

Therefore, there was no apparent association between leukocytes and ROP in this study. These findings align with those of earlier studies [21], although several studies have reported an increased risk of severe ROP in extremely premature infants with high leukocytosis (WBC ≥ 30 × $10^3/\mu L$) due to the activation of inflammatory and angiogenic mediators such as VEGF, bFGF, and HIF [22, 23]; these mechanisms generally occur in active systemic inflammatory conditions, which were not predominant in this study population. Furthermore, neonatal leukocyte levels fluctuate early in life and are influenced by birth stress, medical interventions, and prenatal steroids, potentially obscuring a causal relationship with ROP [18]. After controlling for gestational age and birth weight, the association between leukocytes and ROP often loses statistical significance [24], supporting that ROP pathogenesis is more determined by retinal immaturity and an imbalance of angiogenic factors than by a single hematological parameter such as leukocyte count.

TABLE 3: Distribution of Median Leukocyte Levels According to ROP Stage, Gestational Age, and Birth Weight.

Category	n (%)	Leucocyte ($\times 10^3/\mu L$), Median (IQR)	*p*-value
ROP Stage			0.943
Immature Retina	242 (77.5%)	10.71 (8.54 – 14.21)	
Stage 1	42 (13.5%)	11.24 (8.75 – 14.19)	
Stage 2	25 (8%)	11.60 (9.03 – 16.16)	
Stage 3	3 (1%)	10.92 (9.06 – 12.28)	
Gestational Age			0.186
Moderate preterm	233 (74.7%)	10.57 (8.44 – 13.64)	
Very preterm	72 (23%)	11.90 (8.94 – 14.77)	
Extremely preterm	7 (2.3%)	12.3 (8.65 – 14.80)	
Birth Weight			0.055
Normal	24 (7.7%)	12.39 (8.43 – 15.28)	
Low	197 (63.1%)	10.30 (8.23 – 13.26)	
Very low	84 (26.9%)	12.06 (8.84 – 15.05)	
Extremely low	7 (2.3%)	11.70 (10.00 – 13.02)	

Values are presented as median (interquartile range); p-values were calculated using the Kruskal-Wallis Test; ROP: retinopathy of prematurity; Moderate preterm: 32-36 weeks; Very preterm; 28-32 weeks; Extremely preterm: <28 weeks; Normal birth weight: >2500g; Low birth weight: 1500-2500g; Very low birth weight: 1000-1499g; Extremely low birth weight: <1000g

Relationship between Thrombocyte Levels and the Incidence of Retinopathy of Prematurity

Average thrombocyte counts did not differ significantly according to ROP stage (p = 0.264), gestational age (p = 0.891), or birth weight (p = 0.405). Among infants with immature retinas, the median thrombocyte count was 273.5 (200 - 373) $\times 10^3/\mu L$. Within the ROP categories, the median was 258 (168 - 309) $\times 10^3/\mu L$ for stage 1, 297 (182 - 388) $\times 10^3/\mu L$ for stage 2, and 265 (222.5 - 273) $\times 10^3/\mu L$ for stage 3. Although stages 1 and 3 had lower median thrombocyte levels than the no-ROP group, these differences were not statistically meaningful. When the data were separated by gestational age and birth weight, no consistent or significant differences in thrombocyte counts were found. There was, however, a tendency for infants in the extremely low birth weight group to have lower median thrombocyte levels (226 (156 – 259.5) $\times 10^3/\mu L$). Overall, these findings indicate that thrombocyte counts did not show a significant relationship with ROP or with how premature the infants were in this study.

This study did not observe a significant association between thrombocyte count and ROP stage, gestational age, or birth weight. These findings are consistent with the meta-analysis by [24], which highlighted inconsistent and inconclusive evidence on the role of thrombocytes in ROP development. Likewise, no meaningful difference in thrombocyte levels between infants diagnosed with ROP and those

without, although type 1 ROP had a higher rate of thrombocytopenia [25]. Thrombocytes contribute to new blood vessel formation by storing and releasing VEGF and IGF-1 [26]. Although some have suggested that low thrombocyte counts may impact the growth phase of ROP [7], most infants in the present study had thrombocyte levels within normal limits, reducing differences between groups. Therefore, thrombocyte count alone does not appear to have a central role in ROP development.

TABLE 4: Distribution of Median Thrombocyte Levels According to ROP Stage, Gestational Age, and Birth Weight.

Category	n (%)	Thrombocyte ($\times 10^3/\mu L$), Median (IQR)	*p*-value
ROP Stage			0.264
Immature Retina	242 (77.5%)	273.5 (200 – 373)	
Stage 1	42 (13.5%)	258 (168 – 309)	
Stage 2	25 (8%)	297 (182 – 388)	
Stage 3	3 (1%)	265 (222.5 – 273)	
Gestational Age			0.891
Moderate preterm	233 (74.7%)	270 (198 – 350)	
Very preterm	72 (23%)	276 (174 – 386.5)	
Extremely preterm	7 (2.3%)	252 (236 – 357)	
Birth Weight			0.405
Normal	24 (7.7%)	287.5 (211,5 – 389.5)	
Low	197 (63.1%)	273 (199 – 360)	
Very low	84 (26.9%)	270.5 (177 – 371)	
Extremely low	7 (2.3%)	226 (156 – 259.5)	

Values are presented as median (interquartile range); p-values were calculated using the Kruskal-Wallis Test; ROP: retinopathy of prematurity; Moderate preterm: 32-36 weeks; Very preterm; 28-32 weeks; Extremely preterm: <28 weeks; Normal birth weight: >2500g; Low birth weight: 1500-2500g; Very low birth weight: 1000-1499g; Extremely low birth weight: <1000g

Relationship between Random Blood Glucose Levels and the Incidence of Retinopathy of Prematurity

When examining random blood glucose (RBG) levels across the study participants, no meaningful statistical differences were found between ROP stages (p = 0.804) or among the birth weight categories (p = 0.817). The immature retina group had a median RBG of 80 (63.0 – 96.5) mg/dL. For infants with ROP, median RBG was 80 (70 - 96) mg/dL in stage 1, 80 (67.5 – 91.5) mg/dL in stage 2, and 94 (83 - 96) mg/dL in stage 3, showing inconsistent values across the stages. However, looking at average RBG levels by gestational age revealed a significant difference (p = 0.008). The very preterm infants had the highest median blood glucose (89 (75 – 111.5) mg/dL), with the moderate preterm group at 80 (66 – 94) mg/dL, and the extremely preterm group at the lowest average of 63.5 (56 – 83) mg/dL. This suggests that infants born very preterm usually have higher blood glucose levels than those in other gestational age groups. On the other hand, when considering birth weight, no clear or consistent trends in blood glucose levels appeared between the groups. Median levels were 81 (69 - 96) mg/dL, 80 (68 - 96) mg/dL, and 80 (63 - 80) mg/dL for the low birth weight groups, compared to 78 (60 - 94) mg/dL for infants with normal birth weight. Overall, these results suggest that while random blood glucose is not significantly linked to ROP occurrence, it does have a notable association with prematurity as measured by gestational age.

No significant differences in RBG were observed between ROP stages in this study (p = 0.804), with median values remaining consistent across groups. This is consistent with a previous study, which noted that the association between hyperglycemia and ROP is diminished when controlling for gestational age and birth weight, indicating glucose is not an independent risk factor [27]. There was also no significant difference in RBG by birth weight (p = 0.817). A significant difference did emerge by gestational age (p = 0.008), suggesting prematurity influences glucose levels, though no distinct trend was evident [28]. In premature infants, hyperglycemia reflects metabolic immaturity and stress, and is associated with decreased IGF-1 levels; however, recent evidence suggests that early hyperglycemia and IGF-1 deficiency may also contribute directly to the pathogenesis and severity of ROP [29]. Most infants in this study had glucose levels within the normal range, limiting group differences. Therefore, RBG serves more as an indicator of metabolic condition in preterm infants. Although glucose monitoring is important, current evidence does not support RBG as an independent risk factor for ROP.

TABLE 5: Distribution of Median Random Blood Glucose Levels by ROP Stage, Gestational Age, and Birth Weight.

Category	n (%)	Random blood sugar (mg/dL), Median (IQR)	*p*-value
ROP Stage			0.804
Immature Retina	147 (60.7%)	80 (63.0 – 96.5)	
Stage 1	73 (30.2%)	80 (70 – 96)	
Stage 2	19 (7.9%)	80 (67.5 – 91.5)	
Stage 3	3 (1.2%)	94 (83 – 96)	
Gestational Age			0.008
Moderate preterm	185 (76.4%)	80 (66 – 94)	
Very preterm	51 (21.1%)	89 (75 – 111.5)	
Extremely preterm	6 (2.5%)	63.5 (56 – 83)	
Birth Weight			0.817
Normal	21 (8.7%)	78 (60 – 94)	
Low	153 (63.2%)	81 (69 – 96)	
Very low	61 (25.2%)	80 (68 – 96)	
Extremely low	7 (2.9%)	80 (63 – 80)	

Values are presented as median (interquartile range); p-values were calculated using the Kruskal-Wallis Test; ROP: retinopathy of prematurity; Moderate preterm: 32-36 weeks; Very preterm; 28-32 weeks; Extremely preterm: <28 weeks; Normal birth weight: >2500g; Low birth weight: 1500-2500g; Very low birth weight: 1000-1499g; Extremely low birth weight: <1000g

CONCLUSIONS

The analysis did not find a meaningful association between hemoglobin, leukocyte, thrombocyte, or random blood glucose levels and the risk or severity of retinopathy of prematurity (ROP). Instead, these test results tend to reflect the broader condition and maturity of preterm infants, rather than act as direct drivers of ROP. The main factors influencing ROP seem to be the infant's level of prematurity and disruptions in local retinal blood vessel growth signals. For more robust insight, future research should use prospective cohorts, measure lab values over time, and focus on the final diagnosis of ROP. It would also be beneficial to investigate markers specific to the retina or angiogenic processes (VEGF, IGF-1, and inflammatory cytokines) to clarify how ROP develops at a biological level.

ACKNOWLEDGMENT

The authors express their sincere gratitude to the Faculty of Medicine, Universitas Airlangga, and the Ethics Committee of Dr. Soetomo General Academic Hospital for their invaluable guidance and support, which were essential to the successful completion of this research.

REFERENCES

[1] Sabri, K., Ells, A. L., Lee, E. Y., Dutta, S., & Vinekar, A. (2022). Retinopathy of prematurity: A global perspective and recent developments. Pediatrics, 150(3), Article e2022056587. https://doi.org/10.1542/peds.2022-056587

[2] Hong, E. H., Shin, Y. U., & Cho, H. (2022). Retinopathy of prematurity: A review of epidemiology and current treatment strategies. Clinical and Experimental Pediatrics, 65(3), 115–126. https://doi.org/10.3345/cep.2021.00773

[3] Siswanto, J. E., & Sauer, P. J. (2017). Retinopathy of prematurity in Indonesia: Incidence and risk factors. Journal of Neonatal-Perinatal Medicine, 10(1), 77–82. https://doi.org/10.3233/NPM-1662

[4] Gilbert, C., & Blencowe, H. (2017). Retinopathy of prematurity: It is time to take action. Community Eye Health, 30(99), 52–54.

[5] Bujoreanu, B. L., Bujoreanu, F. C., Bogdanici, S. T., Costin, D., & Bogdanici, C. M. (2023). Latest trends in retinopathy of prematurity: Research on risk factors, diagnostic methods, and therapies. International Journal of General Medicine, 16, 2235–2249. https://doi.org/10.2147/IJGM.S411855

[6] Bahmani, T., Karimi, A., Rezaei, N., & Daliri, S. (2021). Retinopathy prematurity: A systematic review and meta-analysis study based on neonatal and maternal risk factors. The Journal of Maternal-Fetal & Neonatal Medicine, 34(20), 3432–3441. https://doi.org/10.1080/14767058.2019.1685966

[7] Lim, Z. D., Pheng, E., Tai, E., Van Rostenberghe, H., & Shatriah, I. (2021). Comparison of mean platelet counts in preterm infants with and without retinopathy of prematurity. International Journal of Environmental Research and Public Health, 18(7), 3530. https://doi.org/10.3390/ijerph18073530

[8] Almeida, A. C., Silva, G. A., Santini, G., Brízido, M., Correia, M., Coelho, C., & Borrego, L. M. (2021). Correlation between hyperglycemia and glycated albumin with retinopathy of prematurity. Scientific Reports, 11(1), Article 21469. https://doi.org/10.1038/s41598-021-00976-9

[9] Afaratu, J. A. (2023). Risk factors of retinopathy of prematurity among very preterm and very low birth weight infants [Unpublished bachelor's thesis]. Universitas Airlangga.

[10] Hellström, A., Smith, L. E., & Dammann, O. (2013). Retinopathy of prematurity. The Lancet, 382(9902), 1445–1457. https://doi.org/10.1016/S0140-6736(13)60178-6

[11] Wang, J., Li, M., Geng, Z., Khattak, S., Ji, X., Wu, D., & Dang, Y. (2022). Role of oxidative stress in retinal disease and the early intervention strategies: A review. Oxidative Medicine and Cellular Longevity, 2022, Article 7836828. https://doi.org/10.1155/2022/7836828

[12] Zhu, Z., Hua, X., Yu, Y., Zhu, P., Hong, K., & Ke, Y. (2020). Effect of red blood cell transfusion on the development of retinopathy of prematurity: A systematic review and meta-analysis. PLOS ONE, 15(6), Article e0234142. https://doi.org/10.1371/journal.pone.0234142

[13] Rivera, J. C., Sapieha, P., Joyal, J. S., Duhamel, F., Shao, Z., Sitaras, N., Picard, E., Zhou, E., Lachapelle, P., & Chemtob, S. (2011). Understanding retinopathy of prematurity: Update on pathogenesis. Neonatology, 100(4), 343–353. https://doi.org/10.1159/000330174

[14] Blazon, M. N., Rezar-Dreindl, S., Wassermann, L., Neumayer, T., Berger, A., & Stifter, E. (2024). Retinopathy of prematurity: Incidence, risk factors, and treatment outcomes in a tertiary care center. Journal of Clinical Medicine, 13(22), 6926. https://doi.org/10.3390/jcm13226926

[15] Hakeem, A. H. A., Mohamed, G. B., & Othman, M. F. (2012). Retinopathy of prematurity: A study of prevalence and risk factors. Middle East African Journal of Ophthalmology, 19(3), 289–294. https://doi.org/10.4103/0974-9233.97924

[16] Lin, W. C., Jordan, B. K., Scottoline, B., Ostmo, S. R., Coyner, A. S., Singh, P., Kalpathy-Cramer, J., Erdogmus, D., Chan, R. V. P., Chiang, M. F., & Campbell, J. P. (2024). Oxygenation fluctuations associated with severe retinopathy of prematurity: Insights from a multimodal deep learning approach. Ophthalmology Science, 4(2), Article 100417. https://doi.org/10.1016/j.ogla.2023.100417

[17] Strauss, R. G. (2010). Anaemia of prematurity: Pathophysiology and treatment. Blood Reviews, 24(6), 221–225. https://doi.org/10.1016/j.blre.2010.08.001

[18] Banerjee, J., Asamoah, F. K., Singhvi, D., Kwan, A. W., Morris, J. K., & Aladangady, N. (2015). Haemoglobin level at birth is associated with short term outcomes and mortality in preterm infants. BMC Medicine, 13, Article 230. https://doi.org/10.1186/s12916-015-0470-4

[19] Tandon, M., Ranjan, R., Muralidharan, U., & Kannan, A. (2022). Influence of anaemia on multifactorial disease retinopathy of prematurity: A prospective observational study. Cureus, 14(11), Article e31533. https://doi.org/10.7759/cureus.31533

[20] Prasad, M., Dombrovsky, D., Christiansen, S. P., & Ingolfsland, E. C. (2025). Anemia and retinopathy of prematurity: A narrative review. Pediatric Investigation. Advance online publication. https://doi.org/10.1002/ped4.12450

[21] Rasoulinejad, S. A., Maroufi, F., & Alizadeh, A. (2022). Clinical parameters in different stages, zones, and remission/progression statuses of retinopathy of prematurity. Caspian Journal of Internal Medicine, 13(2), 438–446. https://doi.org/10.22088/cjim.13.2.438

[22] Ashki, N., Chan, A. M., Qin, Y., Wang, W., Kiyohara, M., Lin, L., Braun, J., Wadehra, M., & Gordon, L. K. (2014). Peroxynitrite upregulates angiogenic factors VEGF-A, bFGF, and HIF-1α in human corneal limbal epithelial cells. Investigative Ophthalmology & Visual Science, 55(3), 1213–1220. https://doi.org/10.1167/iovs.13-12822

[23] Pheng, E., Lim, Z. D., Tai Li Min, E., Van Rostenberghe, H., & Shatriah, I. (2021). Haemoglobin levels in early life among infants with and without retinopathy of prematurity. International Journal of Environmental Research and Public Health, 18(13), 6982. https://doi.org/10.3390/ijerph18136982

[24] Jiang, J., Zhang, Z., Xin, Q., Wang, L., Ma, J., & Jiang, H. (2021). Association between platelet parameters and retinopathy of prematurity: A systematic review and meta-analysis. PLOS ONE, 16(2), Article e0245078. https://doi.org/10.1371/journal.pone.0245078

[25] Özkaya, D. (2022). The role of thrombocyte parameters in retinopathy of prematurity development. International Journal of Clinical Practice, 2022, Article 4629479. https://doi.org/10.1155/2022/4629479

[26] Italiano, J. E., Richardson, J. L., Patel-Hett, S., Battinelli, E., Zaslavsky, A., Short, S., Ryeom, S., Folkman, J., & Klement, G. L. (2008). Angiogenesis is regulated by a novel mechanism: Pro- and antiangiogenic proteins are organized into separate platelet α granules and differentially released. Blood, 111(3), 1227–1233. https://doi.org/10.1182/blood-2007-09-113837

[27] Lei, C., Duan, J., Ge, G., & Zhang, M. (2021). Association between neonatal hyperglycemia and retinopathy of prematurity: A meta-analysis. European Journal of Pediatrics, 180(12), 3445–3454. https://doi.org/10.1007/s00431-021-04149-6

[28] Hays, S. P., Smith, E. O., & Sunehag, A. L. (2006). Hyperglycemia is a risk factor for early death and morbidity in extremely low birth-weight infants. Pediatrics, 118(5), 1811–1818. https://doi.org/10.1542/peds.2005-3051

[29] Cakir, B., Hellström, W., Smith, L. E. H., Fu, Z., Liegl, R., Winberg, A., Hansen-Pupp, I., Ley, D., Hellström, A., & Löfqvist, C. (2020). IGF1, serum glucose, and retinopathy of prematurity in extremely preterm infants. JCI Insight, 5(19), Article e140363. https://doi.org/10.1172/jci.insight.140363