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Incidence and risk factors of retinopathy of prematurity in Palestine: a retrospective cohort study, 2024

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Abstract

Background Retinopathy of prematurity (ROP) is a major, yet preventable, cause of childhood blindness. This study aimed to determine the incidence in Palestine and the risk factors for ROP development.

Methods We conducted a retrospective cohort study involving 520 preterm infants born between January 2020 and December 2023 in 7 major Palestinian Neonatal Intensive Care Units (NICUs) who were screened for ROP. We examined a range of clinical variables from medical records to explore their relationship with the development of the disease.

Results The incidence of ROP and severe type 1 ROP was 42.9% and 8.8%, respectively. Many risk factors were significant in univariate analysis, such as respiratory distress syndrome (RDS), the duration of mechanical ventilation, the number of blood transfusions needed, and the need for supplemental oxygen at 28 days. However, only lower gestational age (OR, 10.4; 95% CI, 3.66–29.9; $p < 0.001$), lower birth weight (OR, 2.5; 95% CI, 1.3–4.7; $p = 0.006$), lower postmenstrual age at the time of diagnosis, and multiple gestations were significant in multivariate analysis.

Conclusion ROP is a significant problem in Palestine, with a relatively higher incidence than in neighboring countries. Considering the statistically significant variables in the clinical practice will prevent missing severe cases that may progress to blindness.

Keywords Retinopathy of prematurity, Palestine, Risk factors, Incidence

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Introduction

Retinopathy of prematurity (ROP) is one of the most severe preterm birth complications. It is the leading cause of blindness in children under five, accounting for an estimated 50,000 blind children worldwide. Furthermore, it is the second most common cause of preventable blindness in children worldwide [1, 2].

ROP is a disease of premature infants whose retinal vascularization is immature and underdeveloped. Retinal development and vascularization progress normally in the relatively hypoxic intrauterine environment, becoming fully vascularized by term. However, preterm delivery



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exposes the retina to a relatively hyperoxic environment, suppressing pro-angiogenic factors like vascular endothelial growth factor (VEGF). The incompletely vascularized retina grows with limited oxygen to meet the increased metabolic demand, causing localized hypoxia and inducing non-physiological neovascularization [3].

In the last decades, the prevalence rates of ROP in all its stages and the incidence of ROP necessitating treatment have exhibited fluctuations worldwide [4]. The prevalence of ROP in Arab countries shows considerable variation, largely influenced by disparities in neonatal care quality and screening protocols. In Saudi Arabia, ROP is reported in 20–32% of preterm infants, with severe forms occurring in 5–12% of cases [5, 6]. In Egypt, the incidence has been reported as high as 45%, with 5.6% of affected infants classified as having high-risk disease [7].

The occurrence of ROP arises from multiple contributing factors, with low gestational age (GA) and low birth weight (BW) being the most strongly associated risk elements. Newborns delivered before 28 weeks of gestation or weighing less than 1,000 g are at the highest risk [8–11]. Additional significant risk factors include prolonged oxygen therapy, mechanical ventilation, low Apgar scores, multiple births, and assisted conception [9, 11]. Comorbidities such as apnea, respiratory distress syndrome (RDS), patent ductus arteriosus (PDA), intra-ventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), and the need for transfusions or erythropoietin therapy further increase susceptibility [9–11]. Maternal comorbidities may also contribute to ROP risk [10]. Understanding these risk factors is essential for improving screening and interventions, especially in resource-limited settings like Palestine.

The establishment of neonatal intensive care units (NICUs) has significantly improved survival rates among premature infants while also increasing the identification of ROP cases through screening. Modern advancements in ROP screening and treatment not only benefit affected children and their families but also influence the financial burden on healthcare facilities and government budgets [1].

In Palestine, a developing nation facing ongoing occupation-related challenges, effective ROP prevention could encounter multiple challenges. These include resource limitations, restricted intercity healthcare access, inconsistent screening adherence, and insufficient healthcare provider awareness [12]. Abutrabi et al. found that 48% of Palestinian NICU nurses demonstrated limited ROP knowledge, with 78% exhibiting neutral attitudes toward prevention efforts [13]. Similarly, Akkawi et al. reported that most Palestinian pediatricians lacked familiarity with ROP screening guidelines and service delivery protocols [14].

The current Palestinian screening guidelines for ROP target infants with a $GA \leq 32$ weeks or a $BW < 1,500$ g, with the possibility of including older or heavier infants if a neonatologist determines clinical instability [15]. In contrast, many other countries, including China, adopt broader screening criteria [8, 16]. A 2019 Palestinian study reported an ROP incidence of 23.5%, with 11.3% of cases requiring treatment, highlighting the substantial disease burden [15]. However, comprehensive epidemiological data remain limited, particularly from major neonatal intensive care units (NICUs) in the region. This study aims to provide a more representative evaluation of ROP incidence in Palestine, identify key risk factors, and address critical gaps to guide targeted interventions.

Methodology

Study design, setting, and population

This multicenter retrospective cohort study evaluated all preterm infants who underwent ROP screening between January 2020 and December 2023 across seven major NICUs in Palestine, representing governmental and non-governmental healthcare sectors. Participating centers included tertiary referral hospitals such as Specialized Arab Hospital (Nablus), Al-Makassed Hospital (Jerusalem), and Palestinian Medical Complex (Ramallah), ensuring broad geographical representation.

Inclusion criteria consisted of: (1) premature infants with a gestational age (GA) of ≤ 32 weeks or a birth weight (BW) of < 1500 g; and (2) infants with a $GA > 32$ weeks and a BW of 1500–2000 g who required supplemental oxygen for > 72 h or were clinically unstable as assessed by a neonatologist, including but not limited to those with apnea, neonatal acidosis, twin death, intra-ventricular hemorrhage, patent ductus arteriosus (PDA), sepsis, necrotizing enterocolitis (NEC), or requiring surgical intervention [17]. Exclusion criteria were: (1) infants with incomplete medical records; (2) those who died before eye examination and lacked sufficient medical documentation; and (3) infants with ocular conditions that hindered proper ROP screening, such as congenital cataracts or corneal opacity [18].

Sample size and sampling technique

The estimated incidence of retinopathy of prematurity (ROP) in Palestine is approximately 40%, as reported in previous studies conducted both locally and in neighboring countries such as Saudi Arabia and Egypt [5, 6, 15, 19, 20]. To determine the appropriate sample size for estimating ROP incidence, we utilized the OpenEpi Info software [21]. Gestational age ($GA \leq 30$ weeks vs. > 30 weeks) was designated as the exposure variable for the calculation. The sample size estimation was based on a two-sided confidence level of 95%, a statistical power of 80%, and an assumed outcome rate of 45% in the exposed

group and 33% in the unexposed group. This yielded a minimum required sample size of 510 participants. All premature infants who met the inclusion criteria were enrolled during the study period. Of 652 eligible neonates, 520 met the inclusion criteria and constituted the final study sample.

Data collection

In Palestinian NICUs, screening for ROP typically begins between 4 and 6 weeks after birth or at a corrected GA of 31 weeks for infants born before 27 weeks of gestation [18]. If no signs of ROP are observed, follow-up examinations are scheduled biweekly until complete retinal vascularization is achieved [16]. When ROP-related abnormalities are identified, they are classified using the Revisited International Classification of Retinopathy of Prematurity, which assesses the disease based on five stages of retinal vascularization and three anatomical zones within the eye [22]. According to the Early Treatment for Retinopathy of Prematurity (ETROP) guidelines, findings are further categorized into two types: Type 1 and Type 2 ROP [23]. Type 1 ROP includes Zone 1 with plus disease (tortuosity of retinal vessels), Zone 1 Stage 3 ROP without plus disease, or Zone 2 Stage 2 or 3 with plus disease. Type 2 ROP encompasses Zone 1 Stage 1 or 2 without plus disease, and Zone 2 Stage 3 without plus disease. Infants diagnosed with Type 1 ROP are referred immediately for treatment [24], whereas those with Type 2 ROP are monitored weekly until either complete vascularization is achieved up to the ora serrata or until the infant reaches 42 weeks of gestational age [23].

The eye examination process begins approximately one hour before evaluation. Pupil dilation is achieved by administering topical tropicamide 0.5% and phenylephrine 2.5% every 15 min for four doses. After achieving adequate dilation, topical anesthesia is applied, and a sterile pediatric speculum is used to open the eye gently [25]. The examination is conducted using an indirect ophthalmoscope equipped with a +20, +25, or +28 diopter lens. A sterile scleral depressor is used to rotate the eyeball, allowing visualization of the peripheral retina up to the ora serrata, which is essential for a thorough evaluation of retinal vascularization [26].

Study variables and measurement tool

The study's primary outcome (dependent) variables were ROP and its severity. Diagnosis was established through indirect ophthalmoscopy with posterior pole visualization. Classification followed the guidelines of the International Committee for the Classification of Retinopathy of Prematurity (ICROP), considering disease severity, location, and vascular features in the posterior pole [22].

The independent variables were categorized into six groups. The first group included neonatal characteristics:

gender, GA, BW, and Apgar score [2]. GA was recorded based on the last menstrual period or, when unavailable, from an ultrasound. BW was measured at birth in grams. The five-minute Apgar score, used as an indicator of neonatal status after initial resuscitation, assessed heart rate, respiratory effort, color, activity, and response to stimulation.

The second group encompassed neonatal comorbidities such as RDS, apnea, neonatal sepsis, Intraventricular hemorrhage, patent ductus arteriosus, and NEC [15, 27]. RDS was diagnosed based on clinical signs—such as tachypnea, nasal flaring, and cyanosis in room air, radiological findings, and the requirement for surfactant administration [28, 29]. Apnea was defined as a pause in breathing lasting at least 20 s or less if accompanied by cyanosis or bradycardia [30]. Neonatal sepsis was confirmed by a positive blood culture for bacteria or fungi within the first 90 days of life [31]. NEC was diagnosed through clinical symptoms and radiographic evidence of pneumatosis intestinalis [32]. Diagnoses of IVH and PDA were confirmed via trans-fontanelle ultrasound and echocardiography, respectively [33, 34].

The third group included therapeutic interventions such as the number of blood transfusions, types of respiratory support (invasive vs. non-invasive), days on mechanical ventilation, highest recorded FiO₂ percentage (as a continuous variable), the need for supplemental oxygen at 28 days of life, and total length of stay in the NICU. Invasive ventilation involved intubation and mechanical support, whereas non-invasive approaches included nasal cannula and CPAP. The requirement for oxygen at 28 days was used as a proxy for prolonged oxygen dependency and increased risk of oxygen-related complications [35, 36].

The fourth group focused on metabolic factors, specifically hyperglycemia and hyperbilirubinemia. Hyperglycemia was defined as either three or more random blood glucose measurements above 150 mg/dL or a single measurement above 250 mg/dL requiring treatment [37]. Hyperbilirubinemia was identified based on the need for phototherapy, determined according to age- and gestation-specific serum bilirubin thresholds defined by the national protocol, which is adapted from the NICE guidelines [18, 38]. The administration of phototherapy served as an indicator of clinically significant hyperbilirubinemia.

The fifth group addressed obstetric-related risk factors, including pregnancy type (singleton, twin, or triplet), delivery mode (vaginal vs. cesarean), and method of conception (natural vs. in vitro fertilization) [16]. The final group included neonatal characteristics at the time of ROP screening, such as postmenstrual age (the sum of GA and chronological age) [39], and weight at the time of examination. All variables were recorded using

a standardized data abstraction tool designed to ensure consistent and accurate data collection across the participating NICUs.

Ethical approval

All study procedures were conducted per the principles outlined in the Declaration of Helsinki and were approved by the Institutional Review Board (IRB) of An-Najah National University (Reference #: Med. Dec.2023/57). Since the study utilized secondary data, the IRB granted a waiver for obtaining informed consent from participants. Prior authorization was secured from the Palestinian Ministry of Health to access and use patients' personal information and medical records. The data were stored securely, with access restricted solely to the research team. Additionally, to ensure participant confidentiality, all identifying details of premature infants were anonymized before data analysis.

Statistical analysis

The data was initially entered into Microsoft Excel for organization and quality assurance. It was then imported into SPSS software (version 26, IBM Corp., Armonk, NY, USA) for comprehensive statistical analysis. Categorical variables were presented as frequencies and percentages, while numerical variables were represented as means \pm standard deviations. All hypothesis tests were conducted with a two-tailed approach, and the significance level (P-value) was set at less than 0.05. The enrolled premature infants were categorized into two groups: those who developed ROP and those who did not. Initial univariate analysis was conducted to assess potential risk factors and compare variables between the two cohorts. Categorical data were evaluated using the Chi-square test, while continuous variables were analyzed via independent t-tests, as appropriate. A binary logistic regression model was employed to determine independent predictors of ROP. Variable selection for the model was guided by clinical relevance and existing evidence, rather than relying solely on statistical significance. We also checked the variance inflation factor (VIF) of the model to adjust for multicollinearity, and the values were within the acceptable range ($VIF < 2$), showing that multicollinearity did not seem to have any effect on the estimates.

Results

The study cohort comprised 520 neonates [256 males (49.6%), 260 females (50.4%)], with a mean GA of 30.4 ± 2.2 weeks and mean BW of 1386.1 ± 351.6 g. ROP was diagnosed in 223 neonates (42.9%; 95% CI: 38.6–47.3), with no significant gender-based difference in incidence (males: 43.0% vs. females: 43.1%, $p = 0.98$) (Table 1; Fig. 1).

Stratified analysis revealed the highest ROP incidence in neonates with $GA \leq 30$ weeks (58.0%) and $BW < 1250$ g (59.1%), both $p < 0.001$. Type 1 ROP occurred in 8.8% of cases, predominantly in neonates with $GA \leq 30$ weeks (14.9%) and $BW < 1250$ g (14.5%) (Fig. 2).

Neonates with ROP exhibited significantly lower GA (29.5 ± 2.1 vs. 31.0 ± 1.9 weeks, $p < 0.001$) and BW (1296.3 ± 358.2 vs. 1453.7 ± 331.3 g, $p < 0.001$) compared to those without ROP. Comorbidities significantly associated with ROP included RDS (48.8% vs. 27.4%, $p < 0.001$), apnea (53.4% vs. 39.0%, $p = 0.004$), neonatal sepsis (50.4% vs. 40.4%, $p = 0.045$), IVH (55.0% vs. 39.2%, $p = 0.002$), and patent ductus arteriosus (59.6% vs. 39.2%, $p < 0.001$). NEC showed no significant association with ROP occurrence ($p = 0.326$) (Table 1).

ROP incidence was significantly higher among neonates receiving mechanical ventilation (48.3% vs. 27.4%, $p < 0.001$) and neonates with longer ventilation duration (8.4 ± 13.5 vs. 4.5 ± 8.9 days, $p < 0.001$). Supplemental oxygen at 28 days significantly increased ROP likelihood (60.6% vs. 38.7%, $p < 0.001$). NICU stays were significantly longer in neonates with ROP (64.7 ± 37.9 vs. 47.0 ± 31.5 days, $p < 0.001$) (Table 2).

Triplet pregnancies had a significantly higher ROP incidence compared to singletons (53.9% vs. 39.8%, $p < 0.001$). Neonates with ROP had significantly lower mean weight at diagnosis (1573.6 ± 392.6 vs. 1711.3 ± 329.5 g, $p = 0.001$) and younger GA at examination (34.9 ± 2.2 vs. 35.5 ± 2.1 weeks, $p = 0.002$). No significant associations were observed for hyperglycemia, delivery mode, or in vitro fertilization (Table 3).

In multivariable analysis, GA was significantly associated with the development of ROP. Neonates with a $GA \leq 30$ weeks demonstrated significantly higher odds of ROP (OR, 10.4; 95% CI, 3.66–29.9; $p < 0.001$). BW categories also remained significant, with neonates in the lower BW category (< 1250 g) having significantly higher odds of ROP (OR, 2.5; 95% CI, 1.3–4.7; $p = 0.006$). Additionally, the type of pregnancy (singleton vs. multiple) was significantly associated with higher odds of ROP, with twins (OR, 1.8; 95% CI, 1.1–3.3; $p = 0.044$) and triplets (OR, 2.4; 95% CI, 1.3–4.1; $p = 0.003$) showing increased odds. Moreover, GA at ROP diagnosis was significantly associated with the condition (OR, 1.2; 95% CI, 1.1–1.4; $p = 0.013$) (Table 4).

Discussion

This multicenter retrospective study found a notably high incidence of ROP among premature infants in Palestine (42.9%), with 8.8% diagnosed with type 1 ROP and 34.0% with type 2. The incidence was significantly associated with lower GA, lower BW, and multiple gestations. Compared to an earlier Palestinian study (23.5% incidence in three NICUs with 115 neonates) and the regional average

Table 1 Neonatal characteristics, demographic features, and comorbidities (n = 520)

Variable	Total n (%)	ROP diagnosis		P-value
		Yes n(%)	No n(%)	
Gender				0.980
Male	256 (49.6%)	110 (43.0%)	146 (57.0%)	
Female	260 (50.4%)	112 (43.1%)	148 (56.9%)	
Missing	4			
Gestational age	30.4 ± 2.2	29.5 ± 2.1	31.0 ± 1.9	< 0.001
≤ 30 wks	269 (51.7%)	156 (58.0%)	113 (42.0%)	
31–32 wks	179 (34.4%)	55 (30.7%)	124 (69.3%)	
> 32 wks	72 (13.8%)	12 (16.7%)	60 (83.3%)	
Birth weight	1386.1 ± 351.6	1296.3 ± 358.2	1453.7 ± 331.3	< 0.001
< 1250 gr	159 (30.6%)	94 (59.1%)	65 (40.9%)	
1250–1500 gr	215 (41.3%)	89 (41.1%)	126 (58.6%)	
> 1500 gr	146 (28.1%)	40 (27.4%)	106 (72.6%)	
Apgar Score at the five minutes	7.7 ± 1.3	7.4 ± 1.2	7.8 ± 1.2	< 0.001
Missing	5			
Respiratory Distress syndrome				< 0.001
Yes	373 (71.9%)	182 (48.8%)	191 (51.2%)	
No	146 (28.1%)	40 (27.4%)	106 (72.6%)	
Missing	1			
Apnea				0.004
Yes	133 (25.8%)	71 (53.4%)	62 (46.6%)	
No	382 (74.2%)	149 (39.0%)	233 (61.0%)	
Missing	5			
Neonatal sepsis				0.045
Yes	131 (25.2%)	66 (50.4%)	65 (49.6%)	
No	389 (74.8%)	157 (40.4%)	232 (59.6%)	
Intraventricular hemorrhage				0.002
Yes	120 (23.1%)	66 (55.0%)	54 (45.0%)	
No	400 (76.9%)	157 (39.25%)	243 (60.75%)	
Patent ductus arteriosus				< 0.001
Yes	94 (18.1%)	56 (59.6%)	38 (40.4%)	
No	426 (81.9%)	167 (39.2%)	259 (60.8%)	
Necrotizing enterocolitis				0.326
Yes	64 (12.4%)	31 (48.4%)	33 (51.6%)	
No	453 (87.6%)	190 (41.9%)	263 (58.1%)	
Missing	3			

for Lower-Middle-Income Middle Eastern countries (30%) [15, 40], our findings indicate a growing burden. However, the results align more closely with data from Egypt [7] and Oman [41]. The slightly lower rate of type 1 ROP compared to the earlier local study (11.3%) may be attributed to our larger, more representative sample of neonates from seven NICUs across the West Bank.

These findings emphasize the need to strengthen neonatal care infrastructure and ROP screening protocols across Palestine. The results support the current Palestinian screening guidelines, which include clinically unstable infants regardless of GA and BW. This inclusive approach is crucial, as applying stricter international guidelines (e.g., USA and UK) would have led to missed diagnoses, seven infants in our study with GA > 32 weeks and BW > 1500 g were diagnosed with ROP, including one

with type 1 ROP. International screening recommendations vary. For example, the U.S. and U.K. guidelines recommend screening infants born at ≤ 30 weeks GA or with BW < 1500 g [8, 42], whereas India's criteria are more inclusive, extending to GA < 34 weeks or BW < 1750 g [43]. The Palestinian National Protocol adopts a middle ground, recommending screening for infants with GA ≤ 32 weeks or BW < 1500 g, as well as those deemed clinically unstable [18]. Our findings strongly support retaining this broader national approach.

Our results further confirmed that lower GA and BW are ROP's most consistent risk factors. Infants with ROP had a mean GA of 29.5 ± 2.1 weeks and BW of 1296.3 ± 358.2 g, significantly lower than those without ROP. This is biologically plausible given that critical stages of retinal vascularization occur during this

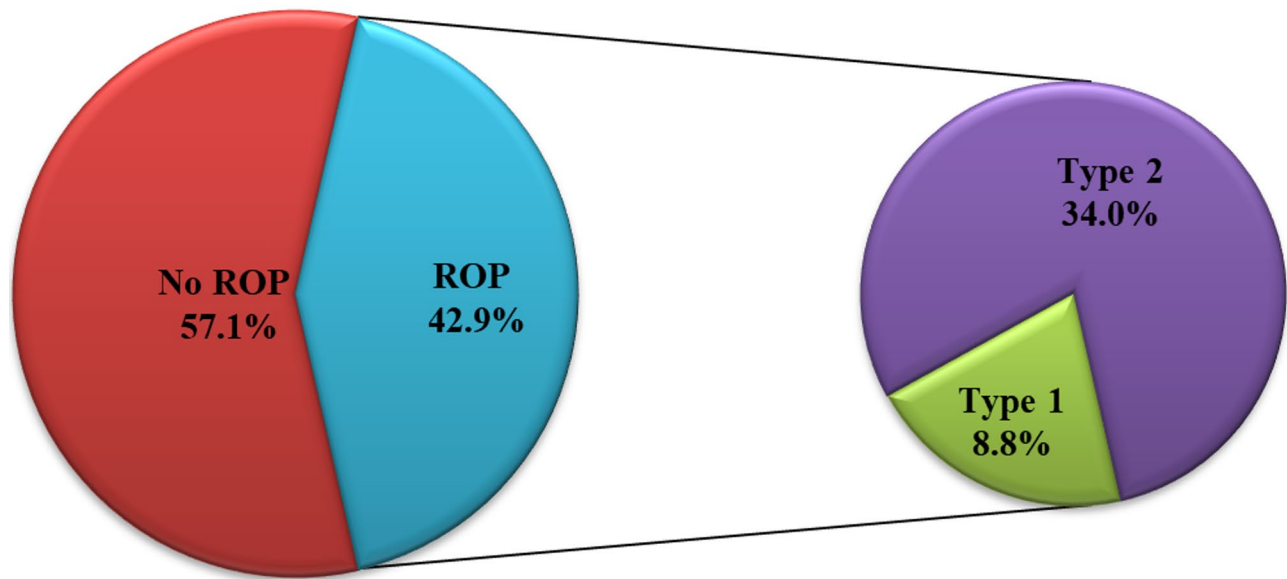


Fig. 1 Incidence of ROP in Palestine

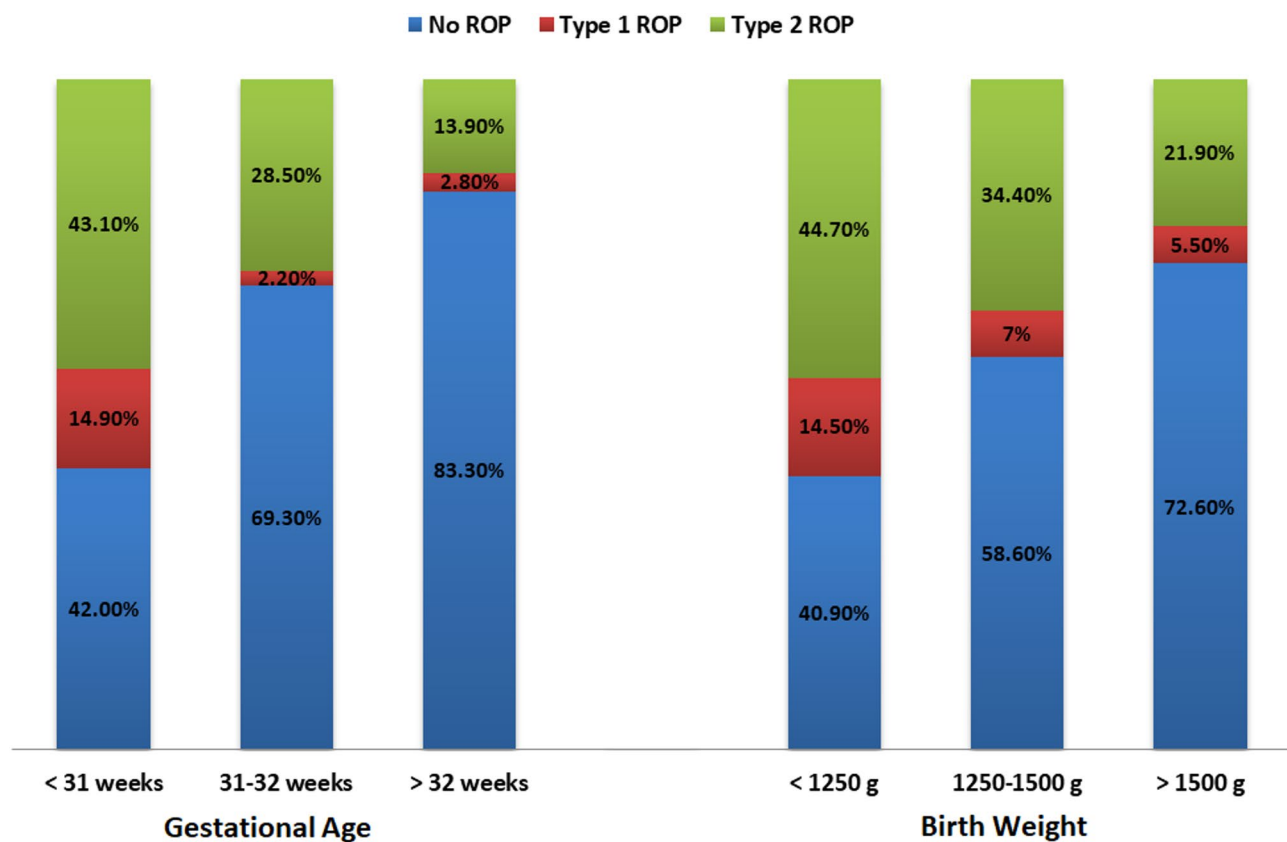


Fig. 2 Incidence of ROP according to different GA and BW subgroups

gestational window. These results align with a Spanish cohort study [17] and reaffirm the importance of timely screening, ideally at 4–6 weeks after birth, since our study’s mean age of ROP diagnosis was 34.9 ± 2.2 weeks.

Multiple pregnancies were another important risk factor. Twins and triplets were 1.8 and 2.4 times more likely to develop ROP than singletons. This increased risk may be due to complications such as preeclampsia, intrauterine growth restriction, and increased rates of prematurity,

Table 2 Neonatal therapeutic interventions after birth (n = 520)

Variable	Total n(%)	ROP diagnosis		P-value
		Yes n(%)	No n(%)	
Blood transfusion				0.091
Yes	379 (72.9%)	171 (45.1%)	208 (54.9%)	
No	141 (27.1%)	52 (36.9%)	89 (63.1%)	
A number of blood transfusions	2.6 ± 3.2	3.5 ± 3.7	2.0 ± 2.6	< 0.001
Mechanical ventilation				< 0.001
Yes	385 (74%)	186 (48.3%)	199 (51.7%)	
No	135 (26%)	37 (27.4%)	98 (72.6%)	
Mechanical ventilation time	6.2 ± 11.3	8.408 ± 13.481	4.508 ± 8.901	< 0.001
Non-invasive ventilation use				0.020
Yes	358 (69%)	166 (46.4%)	192 (53.6%)	
NO	161 (31%)	57 (35.4%)	104 (64.6%)	
Missing	1			
Highest FIO₂%	49.2 ± 26.5	49.3 ± 26.1	48.9 ± 26.7	0.858
Missing	88			
Supplemental O₂ at 28 days				< 0.001
Yes	99 (19.1%)	60 (60.6%)	39 (39.4%)	
No	419 (80.9%)	162 (38.7%)	257 (61.3%)	
Missing	2			
Length of stay in the NICU	54.6 ± 35.5	64.7 ± 37.91	47.0 ± 31.5	< 0.001
Missing	3			

Table 3 Neonatal metabolic, Obstetric-related risk factors, and neonatal characteristics at the time of diagnosis and/or examination (n = 520)

Variable	Total n(%)	ROP diagnosis		P-value
		Yes n(%)	No n(%)	
Hyperbilirubinemia that required phototherapy				0.382
Yes	463 (89.2%)	202 (43.6%)	261 (56.4%)	
No	56 (10.8%)	21 (37.5%)	35 (62.5%)	
Missing	1			
Hyperglycemia				0.342
Yes	111 (21.6%)	43(38.7%)	68(61.3%)	
No	402 (78.4%)	176(43.8%)	226(56.2%)	
Missing	7			
Type of pregnancy				< 0.001
Singleton	244 (46.9%)	97(39.8%)	147(60.2%)	
Twin	161 (31%)	64(39.8%)	97(60.2%)	
Triplet	115 (22.1%)	62(53.9%)	53(46.1%)	
Route of delivery				0.534
Vaginal	85 (16.4%)	34(40.0%)	51(60.0%)	
Cesarean section	433 (83.6%)	189(43.6%)	244 (56.4%)	
Missing	2			
In Vitro Fertilization (IVF)				0.065
Yes	143 (27.5%)	75(52.4%)	68(47.6%)	
No	377 (72.5%)	178(49.3%)	229(60.7%)	
GA at ROP diagnosis or exam	35.2 ± 2.2	34.9 ± 2.2	35.5 ± 2.1	0.002
Missing	14			
Weight at ROP diagnosis or exam	1650.1 ± 365.0	1573.6 ± 392.6	1711.3 ± 329.5	0.001
Missing	21			

Table 4 Multivariable analysis of variables associated with ROP

	SE	P Value	Adjusted OR (95%CI)
Gestational age (Ref= > 32 wks)			1
≤ 30 wks	0.541	< 0.001	10.4 (3.66–29.9)
31–32 wks	0.479	0.012	3.3 (1.3–8.3)
Birth weight (Ref= > 1500 gr)			1
< 1250 gr	0.329	0.006	2.5 (1.3–4.7)
1250–1500 gr	0.275	0.067	1.7 (0.9–2.8)
Type of pregnancy (Ref= Singleton)			1
Twin	0.298	0.044	1.8 (1.1–3.3)
Triplet	0.285	0.003	2.4 (1.3–4.1)
Apgar score at 5 min	0.090	0.272	1.1 (0.9–1.3)
Respiratory Distress Syndrome (Ref= Singleton)	0.386	0.700	1.2 (0.6–2.5)
Apnea (Ref= No)	0.259	0.825	1.1 (0.6–1.8)
Neonatal sepsis (Ref= No)	0.250	0.643	1.1 (0.7–1.8)
Intraventricular hemorrhage (Ref= No)	0.258	0.535	1.2 (0.7–1.9)
Patent ductus arteriosus (Ref= No)	0.292	0.347	1.3 (0.7–2.3)
Number of blood transfusions (Ref= No)	0.046	0.128	1.1 (0.9–1.2)
Mechanical ventilation (Ref= No)	0.387	0.446	1.3 (0.6–2.9)
Mechanical ventilation time	0.015	0.915	1.0 (0.9–1.0)
Non-invasive ventilation use (Ref= No)	0.253	0.738	1.1 (0.7–1.8)
Length of stay in the NICU	0.004	0.120	1.0 (0.9–1.0)
Supplemental O2 at 28 days	0.346	0.713	1.1 (0.6–2.2)
GA at ROP diagnosis or exam	0.071	0.013	1.2 (1.1–1.4)
Weight at ROP diagnosis or exam	0.011	0.704	1.0 (0.9–1.0)

Ref: Reference group, OR = Odds Ratio, CI = confidence interval

all more common in multiple gestations. These findings are consistent with studies from Iran and Taiwan [44, 45], although other research has reported conflicting results [46, 47], suggesting that the influence of multiple births may depend on local healthcare contexts.

While several prematurity-related conditions (e.g., PDA, IVH, anemia, neonatal sepsis, RDS) were associated with ROP in univariate analysis, none remained significant in the multivariate model. This implies that these factors may act more as comorbidities than as independent predictors. Similarly, blood transfusions and NICU stay duration, often considered risk factors, were not independently associated with ROP in our adjusted analysis. Literature on these factors remains mixed [6, 20, 48], reinforcing the need for more standardized research approaches.

Ventilation-related variables, including mechanical ventilation, duration, and supplemental oxygen use, were also insignificant predictors in our study. Despite oxygen's well-established role in ROP pathogenesis, our findings align with prior studies in Brazil, and Saudi Arabia [6, 46], though they contrast with other reports highlighting these factors as critical [20, 48, 49]. This discrepancy may be due to differences in oxygen monitoring and delivery protocols, suggesting the need for uniform ventilation guidelines and improved monitoring across NICUs.

This study has several strengths. It includes data from all major NICUs in the West Bank, offering a comprehensive and representative assessment of ROP in Palestine. The large sample size enhances generalizability, and the inclusion of diverse clinical variables strengthens the validity of the findings. Multivariate analysis helped control for confounders, allowing for a clearer understanding of independent risk factors. However, limitations must be acknowledged. The retrospective design introduces potential selection bias. Due to political constraints, NICUs in Gaza were not included, reducing national representativeness. Differences in documentation and clinical practices across centers may have led to minor inconsistencies or underreporting. Missing data and unrecorded cases, including those referred to private clinics, may have affected data completeness. Lastly, the diagnosis of ROP was operator-dependent, potentially introducing variability in assessment.

Conclusion

This study underscores a high burden of ROP in Palestine, with 42.9% of premature neonates affected and 8.8% developing type 1 ROP. Lower GA, lower BW, and multiple gestations were identified as key risk factors. Our findings validate the Palestinian screening guidelines, particularly the inclusion of clinically unstable infants beyond conventional GA and BW thresholds. Policy-makers should consider expanding neonatal screening

infrastructure, mandating pre-discharge eye exams, and standardizing clinical documentation. Moreover, investments in NICU staffing, oxygen monitoring, and infection control are essential to reduce the incidence and severity of ROP. Future prospective studies are recommended to explore additional risk factors and evaluate the impact of standardized care protocols. Strengthening neonatal care and ROP prevention is critical to safeguarding infant vision and reducing avoidable childhood blindness in resource-constrained settings.

Abbreviations

BW	Birth weight
GA	Gestational age
IRB	Institutional Review Board
IVF	In vitro fertilization
IVH	Intraventricular Hemorrhage
MV	Mechanical Ventilation
NEC	Necrotizing Enterocolitis
NICUs	Neonatal Intensive Care Units
PDA	Patent Ductus Arteriosus
RDS	Respiratory Distress Syndrome
ROP	Retinopathy of Prematurity
VEGF	Vascular Endothelial Growth Factor

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Author contributions

Z.N. and S.S. conceived the study idea, contributed to the study design, and supervised the research implementation. W.S., F.M., O.H., and M.A. developed the methodology, collected data, and drafted the initial manuscript. W.S. conducted the data analysis under the guidance of Z.N., with input from O.H. and F.M. Z.E. and A.A., and contributed to the first draft. A.Z. and J.H. were involved in data collection. All authors participated in interpreting the results, provided feedback on earlier drafts, reviewed and approved the final manuscript, and agreed to its submission to the journal.

Data availability

The data provided in the article were collected from patient files. The data sets used and analyzed during the study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

All study procedures were conducted in accordance with the principles outlined in the Declaration of Helsinki and were approved by the Institutional Review Board (IRB) of An-Najah National University (Reference #: Med. Dec.2023/57). Since the study utilized secondary data, the IRB granted a waiver for obtaining informed consent from participants. Prior authorization was secured from the Palestinian Ministry of Health to access and use patients' personal information and medical records. The data were stored securely, with access restricted solely to the research team. Additionally, to ensure participant confidentiality, all identifying details of premature infants were anonymized before data analysis.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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