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Evaluation of the frequency, risk factors and outcomes of ROP in preterm infants with a BW >1500 g or GA >32 weeks in Türkiye (TR-ROP 2) and medicolegal fears: a Turkish Neonatal Society multicentre study

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ABSTRACT

Background This study aimed to evaluate the prevalence and risk factors of retinopathy of prematurity (ROP) in preterm infants with a birth weight (BW) >1500 g or gestational age (GA) >32 weeks in Türkiye.

Methods A prospective cohort study (TR-ROP 2) was conducted in 80 neonatal intensive care units between 30 September 2023 and 1 November 2024. Infants with a BW >1500 g or GA >32 weeks who had an unstable clinical course or were deemed at risk for ROP were included. The effect of medicolegal concerns on the decision to screen was also evaluated.

Results The study included 4140 infants at risk for ROP development; 242 (5.8%) developed any stage of ROP, and 17 (0.4%) developed severe ROP requiring treatment. Risk factors independently associated with ROP included lower GA and BW, being small for GA, red blood cell transfusion, oxygen therapy >5 days, mechanical ventilation >1 day, early neonatal sepsis (ENS) with comorbidities or presence of ≥3 comorbidities (excluding ENS). Of those with BW ≥2000 g, 31.4% were screened for medicolegal reasons; 2.2% developed ROP, but none had severe ROP.

Conclusions ROP in mature infants is rare but can occur in the presence of multiple risk factors. Medicolegal concerns may contribute to overscreening. Developing evidence-based, risk-adapted screening guidelines is essential to ensure appropriate care without unnecessary interventions.

INTRODUCTION

Retinopathy of prematurity (ROP) is a leading cause of preventable vision loss and blindness in children worldwide.¹ The global prevalence of ROP varies, with lower rates observed in high-income countries where strict oxygen monitoring and advanced neonatal care are implemented.²

The TR-ROP study, published in 2018, reported that the incidence of treatment-requiring ROP in Türkiye was 26% among extremely low birth weight (BW) and 11% among very low BW infants (VLBW), comparable to those from other middle-income countries.³ Subsequently, the national guideline was revised to offer ROP screening for

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Severe retinopathy of prematurity (ROP) can occasionally occur in more mature and larger preterm infants.

WHAT THIS STUDY ADDS

⇒ Being small for gestational age and the presence of multiple systemic comorbidities play an important role in ROP development in infants with greater gestational age.
⇒ Medicolegal concerns drive expanded screening beyond evidence-based indications.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Revisiting and refining existing ROP screening guidelines to incorporate population specific systemic risk factor stratification could reduce unnecessary screening, improve resource utilisation and maintain patient safety.

preterm infants born before 34 weeks of gestation or with a BW under 1700 g, as well as for any preterm infants with existing risk factors. As gestational age (GA) remains the strongest risk factor for ROP, both our earlier cohort and international data confirm that ROP predominantly affects extremely preterm infants. However, larger preterm infants have also been reported to develop ROP requiring treatment.^{4–6} Still, specific risk factors for ROP in this more mature population remain undefined. As an upper-middle-income country, Türkiye continues to enhance ROP screening criteria while addressing the specific needs of its healthcare system.

In this multicentre study, we aimed to assess the prevalence and risk factors associated with the development of ROP in preterm infants with a BW >1500 g or a GA >32 weeks. Additionally, we investigated the effect of medicolegal concerns on the decision to screen. By providing context-specific data, we hope this study will support the refinement of screening guidelines in



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middle-income settings while contributing to the global discussion on ROP prevention.

METHODS

The TR-ROP 2 study was initiated by the Turkish Neonatal Society and included preterm infants screened for ROP between 1 September 2023 and 1 November 2024, across 80 level 3 neonatal intensive care units (NICUs).

Study population

This prospective cohort study examined ROP incidence, risk factors, severity and treatment in preterm infants >1500 g BW or >32 weeks gestation. At-risk infants identified by clinicians were included, excluding those with major congenital anomalies, chromosomal abnormalities or early death before the first eye exam.

Then the medical records of retinal examinations of preterm infants who met the screening criteria were evaluated. Examinations took place in the NICU or outpatient facility (for discharged infants). Eligible infants who were discharged before the first screening and missed or did not complete all screening sessions were excluded from the study. The data are restricted to all babies who underwent all the screening sessions.

Data collection

Neonatologists participating in the study submitted data on ROP cases in their NICUs. For each patient, a case report form was completed using an online system via the 'Trials-Network'. All questions had to be answered; the system blocked submission if any were left blank. Data were entered anonymously into a password-protected database. To ensure data completeness and consistency, the coordinating investigators maintained regular communication with local investigators and randomly verified the submitted data against NICU admission and ophthalmology screening records before analysis. In total, records from 80 NICUs were collected and analysed at the conclusion of the study to ensure comprehensive results.

CLINICAL CHARACTERISTICS

Antenatal, perinatal and postnatal characteristics of included infants were evaluated, including:

- ▶ Antenatal characteristics: Corticosteroid administration (complete; two doses), pre-eclampsia/eclampsia, oligohydramnios, chorioamnionitis and maternal diabetes.
- ▶ Perinatal characteristics: Assisted reproduction, multiple births, mode of delivery, GA, BW and sex.
- ▶ Postnatal characteristics: Small for GA (SGA, <10th percentile),⁷ delivery room resuscitation, respiratory distress syndrome, red blood cell (RBC) transfusions, delayed weight regain (> 14 days to regain weight), and early morbidities and respiratory treatment characteristics both were evaluated within the first month of life. The early morbidities included intraventricular haemorrhage (Papile's classification),^{8,9} patent ductus arteriosus required treatment for ductal closure, clinical or culture positive early neonatal sepsis (ENS) and late neonatal sepsis, necrotising enterocolitis (≥stage II, per Bell's criteria).¹⁰ Respiratory treatment characteristics were recorded; initial respiratory support, duration of oxygen, mechanical ventilation (MV) and positive pressure ventilation (PPV; last day of positive pressure), any oxygen or PPV treatment and fractional inspired oxygen requirement on 28th postnatal day.

To assess medicolegal influences on ROP screening, participants were asked the reason to perform ROP screening if the infant with a BW ≥2000 g underwent retinal examination. The multiple-choice options were: (a) clinical indication, (b) medicolegal indication or (c) both.

Retinal examinations

The International Classification of Retinopathy of Prematurity, Third Edition, was used to classify ROP based on disease location (zone), stage (appearance at the avascular-vascular junction) and the presence of plus disease.¹¹ Screening continued until full or near-complete retinal vascularisation was achieved, and the maximum stage of ROP was documented. Severe ROP was defined as requiring treatment per the Early Treatment for Retinopathy of Prematurity guidelines.¹² Treatment modalities, including laser photocoagulation and intravitreal bevacizumab, were also recorded.

Statistical analysis

Statistical analyses were conducted using SPSS statistical software for Windows, V.25.0 (SPSS). The results are presented as numbers (n), frequencies (%), means with the respective SDs, and medians with their IQRs. Parametric or non-parametric tests were used to analyse variables based on the normality of their distribution. The χ^2 test was used to compare categorical variables. A two-tailed value of $p \leq 0.05$ was considered statistically significant. Two consecutive multivariate logistic regression analyses were performed. In the initial model, all variables that were significantly different between infants with and without ROP in the univariate analysis were entered to identify independent predictors of any ROP. In the final model, variables were recategorised based on their clinical relevance and collinearity assessment to refine the analysis and better represent the combined effects of early morbidities and respiratory support characteristics. The Hosmer-Lemeshow goodness-of-fit statistic was used to assess model fit. A $p \leq 0.05$ was considered statistically significant. The ORs and 95% CIs for each risk factor were determined.

Table 1 Incidence of any ROP and severe ROP in relation to gestational age and birth weight

Included infants n=4140	Any ROP n=242 (5.8%)	Severe ROP n=17 (0.4%)
Gestational age; weeks		
≤ 32 weeks (n=632)	66 (10.4)	8 (1.3)
28 ^{0/7-6/7} weeks (n=2)	0 (-)	0 (-)
29 ^{0/7-6/7} weeks (n=7)	3 (42.9)	1 (14.3)
30 ^{0/7-6/7} weeks (n=81)	17 (21.0)	2 (2.5)
31 ^{0/7-6/7} weeks (n=142)	17 (12.0)	3 (2.1)
32 ^{0/7-6/7} weeks (n=400)	29 (7.2)	2 (0.5)
33–36 weeks (3508)	176 (5.0)	9 (0.3)
33 ^{0/7-6/7} weeks (n=1002)	75 (7.5)	6 (0.6)
34 ^{0/7-6/7} weeks (n=1210)	65 (5.4)	2 (0.2)
35 ^{0/7-6/7} weeks (n=798)	28 (3.5)	1 (0.1)
36 ^{0/7-6/7} weeks (n=498)	8 (1.6)	0 (0.0)
Birth weight; grams		
<1500 g (n=176)	26 (14.8)	3 (1.7)
1500–1999 g (n=1578)	106 (6.7)	10 (0.6)
≥2000 g (n=2386)	110 (4.6)	4 (0.2)
Data are presented as n (%). ROP, retinopathy of prematurity.		

RESULTS

During the study period, 20943 preterm infants with a BW >1500g or a GA >32 weeks were admitted to 80 centres. Of these, 369 were excluded due to major congenital anomalies or death before the first retinal examination. The study population included 4140 patients (20.1% of total), who were considered at risk for ROP by their attending clinicians. Among the screened infants, the incidence of any ROP was 5.8%, while severe

ROP was diagnosed in 17 infants (0.4%). The study included 46 university hospitals (2208 infants), 28 state hospitals (1521 infants) and 6 private hospitals (411 infants). The incidence of any ROP was 5.7%, 6.0% and 6.1% ($p=0.918$) and severe ROP was 0.4%, 0.3% and 1.0% ($p=0.169$) across these hospital types, with no significant differences.

The mean BW and GA for the total cohort were 2141 ± 465 g (range: 850–4300g) and 34 ± 1 weeks (range: 28–36 weeks, respectively). Of the cohort, 632 infants (15.3%) had a GA ≤ 32 weeks. Most were late preterm infants ($n=2490$; 60.1%) and had a BW ≥ 2000 g ($n=2386$; 57.6%). Table 1 presents the incidences of any ROP and severe ROP in relation to GA and BW. The mean postnatal day and postmenstrual age at initial ROP diagnosis were 34 ± 12 days and 38 ± 3 weeks, respectively. At the time of maximum ROP severity, these were 38 ± 16 days and 38 ± 3 weeks.

Infants who developed ROP were more frequently SGA, required delivery room resuscitation and had higher rates of RBC transfusion, delayed postnatal weight gain and early neonatal morbidities. They were also more likely to receive initial MV and had prolonged durations of respiratory support. A detailed comparison of clinical characteristics between infants with and without ROP is presented in table 2.

Variables that were significantly different between infants without ROP and with any ROP in the univariate analysis were included in the multivariate regression model. Higher GA and BW, and antenatal steroid exposure were associated with a decreased risk of ROP development. In contrast, being SGA (OR 2.055, 95% CI 1.095 to 3.854, $p=0.025$), any RBC transfusion (OR 1.923, 95% CI 1.248 to 2.964, $p=0.003$), MV as initial respiratory support (OR 2.360, 95% CI 1.236 to 4.507, $p=0.009$), prolonged oxygen therapy (OR 1.045, 95% CI 1.015 to 1.075, $p=0.003$) and ENS (OR 1.699, 95% CI 1.231 to 2.346, $p=0.001$) were identified as independent predictors for ROP.

Table 2 Characteristic of infants without ROP and with any ROP

	No ROP (n=3898)	Any ROP (n=242)	P value
Infant and maternal characteristics			
Gestational age (weeks), mean $\pm$ SD,	34 $\pm$ 1	33 $\pm$ 2	<0.001
≤ 32 weeks, n (%)	566 (14.4)	66 (27.3)	<0.001
33 ^{0/7} –36 ^{6/7} weeks, n (%)	3332 (85.5)	176 (72.2)	
Birth weight (g), mean $\pm$ SD,	2154 $\pm$ 463	1900 $\pm$ 447	<0.001
<1500 g, n (%)	150 (3.8)	26 (10.7)	<0.001
1500–1999 g, n (%)	1472 (37.8)	106 (43.8)	
≥ 2000 g, n (%)	2276 (58.4)	110 (45.5)	
Maternal age (years), mean $\pm$ SD	30 $\pm$ 6	30 $\pm$ 6	0.314
In vitro fertilisation, n (%)	448 (11.5)	28 (11.6)	0.971
Multiple births, n (%)	1009 (25.9)	61 (25.2)	0.441
Antenatal steroid, two doses, n (%)	1186 (33.7)	60 (29.6)	0.024
Chorioamnionitis, n (%)	70 (1.8)	2 (0.8)	0.263
Oligohydramnios, n (%)	268 (6.9)	21 (8.7)	0.286
Pre-eclampsia, n (%)	530 (14.2)	30 (13.1)	0.653
Gestational diabetes, n (%)	373 (10.2)	21 (9.4)	0.679
Small for gestational age, n (%)	285 (7.3)	28 (11.6)	0.047
Male gender, n (%)	2088 (53.6)	135 (55.8)	0.502
Caesarean section, n (%)	3370 (86.5)	209 (86.4)	0.968
Resuscitation at birth, n (%)	1141 (29.3)	113 (46.7)	<0.001
Any RBC transfusion, n (%)	306 (7.9)	61 (25.2)	<0.001
Delayed time to regain birth weight, n (%)	710 (18.2)	70 (28.9)	<0.001
Early morbidities**			
Respiratory distress syndrome, n (%)	1104 (28.3)	119 (49.2)	<0.001
Patent ductus arteriosus treatment, n (%)	139 (3.6)	24 (9.9)	<0.001
Intracranial haemorrhage (>grade II), n (%)	194 (5.0)	34 (14.0)	<0.001
Early neonatal sepsis, n (%)	843 (21.6)	102 (42.1)	<0.001
Culture-proven sepsis, n (%)	42 (1.1)	4 (1.7)	<0.001
Late neonatal sepsis, n (%)	538 (13.8)	63 (26.0)	<0.001
Culture-proven sepsis, n (%)	172 (4.4)	28 (11.6)	<0.001
Necrotising enterocolitis ($\geq$ stage II), n (%)	44 (1.1)	12 (5.0)	<0.001
Respiratory treatment characteristics			
Initial respiratory support			<0.001
None/oxygen, n (%)	928 (23.8)	21 (8.7)	
Non-invasive ventilation, n (%)	1795 (46.0)	89 (36.8)	
Mechanical ventilation, n (%)	1175 (30.2)	132 (54.5)	
Duration of oxygen;* (days), median (25p–75p)	5 (1–9)	10 (4–19)	<0.001†
Duration of positive pressure;* ‡ (days), median (25p–75p)	4 (1–6)	6 (3–11)	<0.001†
Duration of mechanical ventilation;* (days), median (25p–75p)	0 (0–1)	1 (0–6)	<0.001†
Any positive pressure on day 28, n (%)	77 (2)	12 (5.0)	0.002
Any oxygen treatment on day 28, n (%)	168 (4.3)	32 (13.2)	<0.001
FiO2 on day 28, all infants	21 (21–21)	21 (21–21)	0.164†

The values are presented as mean $\pm$ SD, median (25p–75p) and n (%) where appropriate.

*All infants, until first examination.

†Mann-Whitney U test.

‡ The last postnatal day on which the infant received any positive pressure support, either via mechanical or non-invasive ventilation.

FiO2, fractional inspired oxygen; RBC, red blood cell; ROP, retinopathy of prematurity.

Table 3 Multivariate regression analysis for development of any retinopathy of prematurity in study infants

Covariates	OR	95% CI	P value
Gestational age; week	0.795	0.694 to 0.910	<0.001
Birth weight; 100 g	0.591	0.352 to 0.992	0.047
Small for gestational age	2.043	1.092 to 3.827	0.025
Resuscitation at birth	1.021	0.739 to 1.410	0.902
Antenatal steroid	0.602	0.431 to 0.841	0.003
Any RBC transfusion	1.914	1.278 to 2.866	0.002
Delayed weight regain	1.169	0.825 to 1.656	0.380
Early morbidities (Reference: No morbidity)			0.028
ENS	1.633	0.939 to 2.839	0.082
ENS + 1 morbidity	1.939	1.150 to 3.270	0.013
ENS + ≥ 2 morbidities	2.263	1.215 to 4.214	0.010
≤ 2 morbidities, no ENS	1.230	0.800 to 1.891	0.345
≥ 3 morbidities, no ENS	2.684	1.074 to 6.461	0.034
Mechanical ventilation > 1 day	1.590	1.024 to 2.467	0.039
Positive pressure > 4 days	0.824	0.493 to 1.376	0.459
Oxygen > 5 days	2.285	1.443 to 3.369	<0.001
Positive pressure on day 28	0.507	0.217 to 1.184	0.117
Oxygen on day 28	1.535	0.844 to 2.792	0.161

$p<0.05$ represents statistical significance.

Early morbidities include: ENS, RDS, PDA, IVH, LNS, NEC

ENS, early neonatal sepsis; IVH, intraventricular haemorrhage; MV, mechanical ventilation; RBC, red blood cell; SGA, small for gestational age.

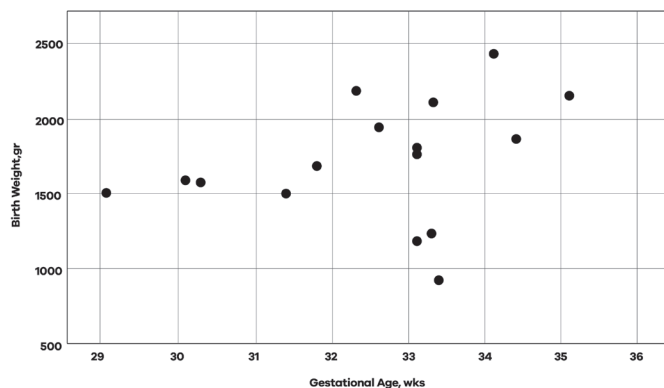


Figure 1 Plot graph of infants with severe ROP in relation to BW and GA. BW, birth weight; GA, gestational age; ROP, retinopathy of prematurity.

Final multivariate regression analysis for the development of any ROP in study infants is shown in [table 3](#). Since only ENS remained statistically significant among early morbidities, the final regression model categorised early morbidities according to the presence of ENS and its coexistence with other morbidities. Variables were categorised for regression model as follows: early morbidities; (1) ENS only, (2) ENS+1 morbidity, (3) ENS + ≥ 2 morbidities (4) ≤ 2 morbidities without ENS and (5) ≥ 3 morbidities without ENS. The distribution of these morbidities significantly differed between groups. (Any ROP vs no ROP; %: (1): 12.8 vs 9.6; (2): 15.3 vs 8.4; (3): 14.0 vs 3.6; (4): 28.5 vs 26.7 and (5): 4.1 vs 0.9; $p < 0.001$). The duration of respiratory treatments was categorised based on the median duration for infants without ROP (any ROP vs no ROP; %: (1) MV > 1 day (76.5 vs 23.5), (2) PPV > 4 days (67.3 vs 32.7) and (3) oxygen > 5 days (62.6 vs 37.4) ($p < 0.001$ for all comparisons). ENS combined with any comorbidity or the presence of at least three comorbidities (excluding ENS), prolonged oxygen therapy for more than

Table 4 Characteristics of infants with severe ROP

BW; grams GA; weeks	Retinal examination Treatment	Existing risk factors * <i>calculated risk factors</i> - Other infant characteristics
930 g 33 ^{3/7} wks	Zone 1 stage 3, plus, A-ROP LP, IVB	* SGA, RBC transfusion, ENS + ≥ 2 morbidities (LNS, NEC, IVH) - Resuscitation at birth, initial support: NIV
1200 g 33 ^{1/7} wks	Zone 2 stage 3, plus LP	* SGA, MV > 1 day, Oxygen > 5 days, No ANS - Initial support: MV, positive pressure > 4 days, RDS, PDA
1250 g 33 ^{2/7} wks	Zone 2 stage 3, plus LP	* SGA, Oxygen > 5 days, No ANS - Initial support: NIV, positive pressure > 4 days
1505 g 29 ^{1/7} wks	Zone 1 stage 1, plus LP	* MV > 1 day, Oxygen > 5 days, RBC transfusion, ENS + ≥ 2 morbidities (RDS, LNS, NEC), No ANS - Resuscitation at birth, delayed weight regain, initial support: MV, positive pressure > 4 days, oxygen and positive pressure on day 28.
1520 g 31 ^{3/7} wks	Zone 2 stage 2, plus IVB	* Oxygen > 5 days - Delayed weight regain, initial support: NIV, oxygen on day 28.
1585 g 30 ^{2/7} wks	Zone 2 stage 2, plus IVB	* RBC transfusion, ENS + ≥ 2 morbidities (RDS, PDA, IVH, NEC), No ANS, MV > 1 day, Oxygen > 5 days - Delayed weight regain, initial support: MV, positive pressure > 4 days, oxygen on day 28.
1600 g 30 ^{1/7} wks	Zone 1 stage 1, plus IVB	* MV > 1 day, Oxygen > 5 days, ENS + 1 morbidity (RDS), No ANS - Resuscitation at birth, initial support: MV, positive pressure > 4 days, delayed weight regain
1705 g 31 ^{6/7} wks	Zone 2 stage 3, plus LP	* MV > 1 day, Oxygen > 5 days, No ANS - Initial support: MV, positive pressure > 4 days, resuscitation at birth, PDA
1700 g 31 ^{6/7} wks	Zone 2 stage 3, plus LP	* MV > 1 day, Oxygen > 5 days, No ANS - Initial support: MV, positive pressure > 4 days, RDS, PDA
1800 g 33 ^{1/7} wks	Zone 2 stage 2, plus IVB	* MV > 1 day, Oxygen > 5 days - Initial support: MV, positive pressure > 4 days, RDS, PDA
1815 g 33 ^{1/7} wks	Zone 2 stage 3 LP	* Oxygen > 5 days - Initial support: NIV, positive pressure > 4 days
1900 g 34 ^{3/7} wks	Zone 2 stage 3, plus, A-ROP IVB	* Oxygen > 5 days, No ANS - Resuscitation at birth, initial support: NIV
1970 gr 32 ^{4/7} wks	Zone 2 stage 3, plus LP	* MV > 1 day, Oxygen > 5 days, No ANS - Resuscitation at birth, initial support: MV, positive pressure > 4 days, RDS, LNS
2140 g 33 ^{2/7} wks	Zone 2 stage 3, plus, A-ROP IVB	* MV > 1 day, Oxygen > 5 days, RBC transfusion, No ANS - Resuscitation at birth, delayed weight regain, initial support: MV, positive pressure > 4 days, ENS, oxygen on day 28.
2200 g 35 ^{1/7} wks	Zone 2 stage 3, plus LP, IVB	* MV > 1 day, Oxygen > 5 days, No ANS - Initial support: MV, positive pressure > 4 days, RDS, LNS
2210 gr 32 ^{2/7} wks	Zone 3 stage 1, plus IVB	* Oxygen > 5 days, No ANS - Delayed weight regain, initial support: NIV, positive pressure > 4 days, LNS
2400 g 34 ^{1/7} wks	Zone 2 stage 3, plus, A-ROP IVB	* MV > 1 day, Oxygen > 5 days, RBC transfusion, No ANS - Resuscitation at birth, delayed weight regain, initial support: MV, positive pressure > 4 days, PDA, oxygen and positive pressure and on day 28.

* *calculated risk factors*, - Other infant characteristics

A-ROP, aggressive posterior retinopathy of prematurity; ENS, early neonatal sepsis; IVB, intravitreal bevacizumab; IVH, intraventricular haemorrhage; LNS, late neonatal sepsis; LP, laser photocoagulation; MV, mechanical ventilation; NEC, necrotising enterocolitis; NIV, non-invasive ventilation; PDA, patent ductus arteriosus; RBC, red blood cell; RDS, respiratory distress syndrome; SGA, small for gestational age; wks, weeks.

5 days and MV for more than 1 day were found to be associated with an increased risk of ROP.

Among all infants screened for ROP, 17 (0.4%) required treatment. Laser photocoagulation was performed in nine patients, anti-VEGF in ten, and two received both. Sixteen infants received treatment for both eyes; no infants required vitreoretinal surgery. The maximum BW and GA among these infants were 2.400 g and 35 weeks, respectively.

Figure 1 illustrates the plot graph of infants with severe ROP in relation to BW and GA. The mean BW (1731 ± 392 g) and mean GA (32 ± 2 weeks) were significantly lower than those of infants without ROP ($p=0.03$ and $p=0.01$, respectively). Table 4 presents the individual characteristics of infants with severe ROP.

Among infants with a BW ≥ 2000 g, the decision to perform ROP screening was based on medicolegal concerns in 37.8% ($n=901$), clinician discretion in 40.4% ($n=964$), and a combination of both in 21.8% ($n=521$). The incidence of any ROP within these groups was 2.2%, 7.3% and 3.8%, respectively. Notably, four infants developed severe ROP, none of whom were screened solely due to medicolegal concerns.

DISCUSSION

In middle-income countries, ROP can be diagnosed among more mature preterm infants born at 32 weeks of gestation and beyond.^{6,13,14} We found that ROP in these more mature infants was rare, with an incidence of 5.8% for any ROP and 0.4% for severe ROP, which occurred only in the presence of multiple risk factors. It is noteworthy that if the current Turkish national guideline thresholds (<34 weeks or <1700 g) were applied without consideration of additional risk factors, three infants with severe ROP would have been missed, reflecting the appropriateness of the Turkish national guideline recommending screening above these thresholds when risk factors are present. This observation reinforces the importance of integrating risk assessment into screening decisions and supports the view that selected larger or more mature preterm infants who manifest such risk factors benefit from ophthalmologic screening. Nevertheless, our findings also indicate that screening has often been extended beyond these evidence-based limits, mainly driven by medicolegal concerns, which may contribute to an increased clinical workload.

Our results align with previous evidence identifying low GA and low BW as the strongest predictors of ROP. Prematurity-related morbidities, including neonatal sepsis, being SGA, prolonged oxygen exposure, MV and RBC transfusions, were also associated with increased ROP risk, consistent with prior studies.^{15–19} Moreover, oxygen therapy beyond 5 days and MV for over 1 day emerged as independent risk factors in our study, reflecting the well-established association between prolonged hyperoxia and ROP development.¹⁷ It was also shown in our results that antenatal steroid administration was protective against ROP, supporting findings from meta-analyses and likely attributable to a proposed retinal protective effect in addition to established respiratory benefits.^{20,21} The regression model highlights the cumulative impact of these factors.

The finding on the significance of a composite measure of morbidities and the progressive increase in OR with a higher number of morbidities emphasises the multifactorial nature of ROP. The central role of sepsis among these morbidities highlights the relevance of inflammation-induced oxidative stress, VEGF expression, microglial activation and retinal ganglion cell death in the early postnatal period.¹⁵ Based on these insights, we propose a more individualised, risk-based approach for infants exceeding standard GA and BW thresholds; recommending screening only in the presence of

risk factors such as MV >1 day, oxygen therapy >5 days, being SGA transfusions, ENS accompanied by any morbidity, or any three prematurity-related morbidities. Further prospective, multicentre studies are warranted to validate this approach and to support optimal resource utilisation without compromising patient safety.

Several risk-based algorithms have been developed to optimise ROP screening practices while ensuring patient safety. Among these, WINROP, G-ROP, CO-ROP, Alex-ROP, ROPScore, CHOP-ROP, DIGIROP and the PINT model use postnatal weight gain as a central predictor of treatment-requiring ROP and also incorporate clinical parameters such as hydrocephalus, ventilation and/or oxygen exposure, blood transfusions and sepsis. Although these algorithms have demonstrated high sensitivity for detecting treatment-requiring ROP, their relatively low specificity in middle-income countries limits their generalisability.^{22–24}

A striking finding was that nearly one-third of infants with a BW ≥ 2000 g underwent retinal examinations due to medicolegal concerns, yet none had severe ROP. This suggests that medicolegal fears may lead to overscreening. In our country, significant legal fines are imposed on paediatricians or neonatologists who fail to perform ROP screening resulting in blindness, with compensation to the patient's family ranging from 300 000 to 500 000 dollars. This threat of substantial legal penalties has driven defensive medical practices, contributing to unnecessary examinations. While the national guideline recommends screening for all infants with BW ≤ 1700 g or GA <34 weeks and selected more mature or heavier preterm infants requiring cardiorespiratory support, our findings support that infants above these thresholds without additional risk factors are at extremely low risk for severe ROP.³

The strength of the TR-ROP 2 study lies in its large-scale, multicentre, prospective design, allowing the collection of robust, real-world data across 80 NICUs. This comprehensive methodology provides valuable insight into actual ROP screening practices in more mature preterm infants and highlights individual risk factors. However, the lack of data on nutritional status and growth outcomes is a notable limitation.

In conclusion, while prematurity and inappropriate oxygen therapy remain key risk factors for ROP, numerous additional factors have been reported. Notably, the exact impact of various risk factors in more mature preterm infants remains unclear, leading to increased medicolegal concerns and, in some cases, potentially excessive screening practices. Developing risk factor assessment tools and determining the relative contribution of each risk factor would be valuable in refining screening criteria and ensuring that infants at genuine risk receive appropriate evaluation. Given that these more mature infants differ from VLBW infants in how clinical factors influence ROP development, tailored screening strategies specific to this population are essential.

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