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Original Article

Frequency of ROP Diagnosis and Treatment in Very Low Birth Weight Preterm Infants by Gestational Week and Birth Weight: A Single-Center Experience

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Abstract

Objectives: The objective of the study was to evaluate the prevalence and potential risk factors associated with retinopathy of prematurity (ROP) in very low birth weight (BW) ROP patients stratified by different BW categories.

Methods: This retrospective cohort study examined very low BW patients (≤1500 g) treated at a neonatal intensive care unit and subsequently assessed for ROP at the outpatient clinic. Data on gestational age (GA), BW, ROP severity, treatments, and outcomes were collected following international ROP classification criteria. Patients with type 1 ROP and aggressive ROP received treatment. Patients were categorized based on 250 g BW intervals, and ROP frequency and treatment rates were assessed by GA.

Results: In this study, 116 patients, comprising 60.3% of females and 39.7% of males, were analyzed. The GA ranged from 23 to 34 weeks, with a mean of 30.03±2.64 weeks, while the mean BW was 1108±275 g, ranging from 370 g to 1490 g. ROP was present in 49.1% of patients and 19.8% required treatment. Lower BW and GA were significantly associated with ROP ($p<0.05$). ROP incidence and treatment rates varied across BW groups.

Conclusion: ROP diagnosis and treatment rates have risen over time, reflecting improvements in intensive care. Categorizing premature infants based on BW facilitates the development of screening criteria tailored to neonatal intensive care units and aids in predicting ROP diagnosis and treatment rates.

Keywords: Follow-up criteria, gestational age, low birth weight, retinopathy of prematurity

Introduction

Retinopathy of prematurity (ROP) remains a major clinical problem in neonatal care, affecting the visual development and quality of life of premature infants worldwide. Although there are many risk factors that cause this pathology, ROP is closely associated with birth weight (BW) and gestational age (GA), as highlighted in studies (1-3). Low BW, a common feature of premature infants, has been identified as an important predictor of susceptibility to ROP (2). In addition, the critical role of GA in determining the stage of retinal development at birth plays an important role in our understanding of this condition (3).

With advances in neonatal care, the number of extremely premature infants surviving has increased. Identifying risk factors for the development of ROP is critical, especially for

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eyecare practitioners performing ROP screening in very low BW infants. When determining ROP screening criteria, the relevant country's neonatal intensive care standards and the highest BW and GA that would require ROP diagnosis and treatment are taken into consideration. Studies have shown varying rates of ROP diagnosis and treatment among different clinics within the same country (4,5). To the best of our knowledge, there is no study in the literature evaluating the diagnosis and treatment of ROP in Türkiye by classifying BWs in detail and proposing the development of ROP screening criteria. In most cases of ROP, timely treatment can be successful, potentially avoiding unnecessary surgical intervention. The aim of this study is to carefully analyze the prevalence and potential risk factors associated with ROP in very low BW infants followed up at an ROP diagnostic and treatment center in Istanbul, stratified by different BW categories.

Methods

This retrospective cohort study included premature infants with BW ≤1500 g who were treated in the neonatal intensive care unit of Başakşehir Çam and Sakura City Hospital and who were consulted and followed up in the outpatient clinic for ROP between January 1, 2023, and January 1, 2024. This study adhered to the principles outlined in the Declaration of Helsinki, and Ethical Approval for the study was obtained from the Ethics Committee of Başakşehir Çam and Sakura City Hospital (February 05, 2024, Approval number E-96327027-514.10-235695968). Data were collected on GA, BW, the most severe stages of ROP, treatments administered, and treatment outcomes for all infants. ROP findings were recorded according to international ROP classification criteria (6). Infants with Type 1 ROP and aggressive ROP were treated. The infants were classified according to their 250 g range (e.g., 1000–1250 g, 1250–1500 g, etc.), and the frequency of ROP and the rate of ROP treatment were determined according to their GA.

Criteria for discontinuation of follow-up included complete retinal vascularization and patients who did not develop subthreshold disease or more severe ROP by postmenstrual week 45. Infants who did not meet these follow-up criteria and those who died were excluded from the study.

Statistical Analysis

In the study, statistics for continuous variables were presented as mean±standard deviation or median with minimum and maximum (min-max), while descriptive statistics for categorical variables were presented as counts and percentages. The Kolmogorov–Smirnov test was used to assess the normal distribution of numerical data. Differences between groups were analyzed using either the independent samples t-test or the Mann–Whitney U test, depending on distribution characteristics. Associations between categorical variables were examined using Fisher's exact and Chi-squared test. Statistical analyses were performed using IBM SPSS Statistics software version 28 (SPSS Inc., Chicago, IL). The significance level for all analyses was set at 95%, and results were considered statistically significant if P values were <0.05.

Results

A total of 116 patients were enrolled in the study, including 60.3% (70) females and 39.7% (46) males. GA ranged from 23 to 34 weeks with a mean of 30.03±2.64 weeks. The mean BW was 1108±275 g, with values ranging from a minimum of 370 g to a maximum of 1490 g among the included patients. Table 1 shows the demographic and clinical characteristics of the patients in the study. Figure 1 shows the distribution of patients by GA at delivery. The most common GA range was 30–32 weeks, accounting for 29.3% of cases. In addition, 5.2% of babies were born at <25-week gestation.

Table 2 shows the mean GA and BW of patients with and without ROP. In patients with ROP, the mean GA ranged from 23 to 34 weeks with a mean of 28.33±2.37 weeks. The mean BW in this group ranged from 370 to 1490 g, with a mean of 1006±296 g. Both BW and GA were significantly lower in patients with ROP compared to those without ROP ($p<0.05$).

Table 1. Demographic and clinical characteristics of patients

Sex	
Female	70 (60.3)
Male	46 (39.7)
Gestational Age	30.03±2.64/30.5 (23–34)
Birth Weight (g)	1108±275/1155 (370–1490)
Development of ROP	
With ROP	57 (49.1)
Without ROP	59 (50.9)
ROP Treatment Requirement	
Treated	23 (19.8)
Not Treated	93 (80.2)
Birth Weight (g)	
<750 g	15 (12.9)
750–1000 g	22 (19.0)
1000–1250 g	37 (31.9)
1250–1500 g	42 (36.2)

Continuous data are reported as Mean±Standard deviation/Median (Min-Max) values, and categorical variables are reported as Number (Percentage) values.

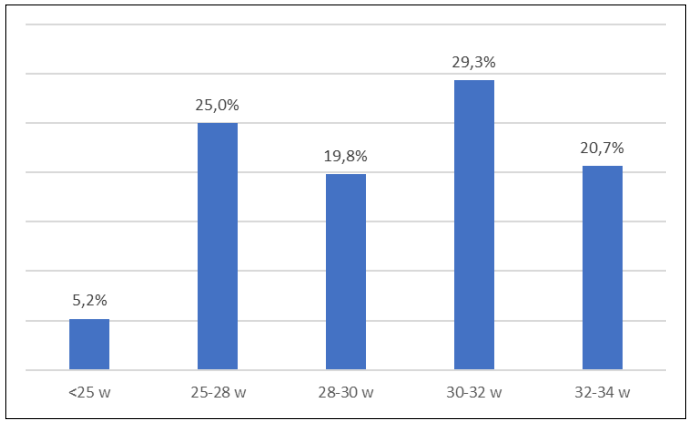

Figure 1. Distribution of babies according to weeks of birth.

Table 3 shows the mean GA and BW of patients treated for ROP. Among the treated patients, the mean GA ranged from 23 to 30 weeks, with a mean of 26.78±1.83 weeks. BW ranged from 370 to 1400 g, with a mean of 860±257 g. Both the mean GA and BW of treated patients were significantly lower than those of untreated patients ($p<0.05$).

Table 4 shows ROP incidence and treatment rates categorized by BW groups (<750 g, 750–1000 g, 1000–1250 g, and 1250–1500 g). In addition, ROP incidence and treatment rates are presented by week of birth. Figures 2 and 3 display the diagnosis and treatment status of ROP based on BW and GA.

Discussion

This study describes the differences between cases of ROP and those requiring treatment among infants of different BWs. Infants weighing <750 g are typically born before 28 weeks of gestation. Conversely, infants weighing more than 1250 g are usually born after 28 weeks of gestation. A direct correlation between BW and gestational week in these two groups may not be appropriate. Significantly increased rates of ROP diagnosis and treatment were observed in infants with BWs between 750 and 1000 g and GAs <28 weeks. However, no significant change in ROP diagnosis and treatment by GA was observed in infants with BWs between 1000 and 1250 g.

In our study, we included all very low BW infants (<1501 g) who were born in the same hospital, treated in the same intensive care unit, and were subsequently followed up in the regular ROP outpatient clinic after discharge. The prevalence of ROP in these infants was 49.1%, while the prevalence of severe ROP requiring treatment was 19.8%. Several studies conducted worldwide have reported contrasting results. A study conducted in the United Kingdom documented a prevalence of ROP in infants born <1501 g as 1.28% in 1990 and 12.55% in 2011, with cases requiring treatment reported as 1.48% in 2011 compared to 0.17% in 1990 (7). Similarly, a study in India in 2023 reported an ROP incidence of 59.9% in infants <1500 g, with 11.8% cases

Table 2. The mean gestational age and birth weight of patients with and without ROP

	Patient without ROP (n=59)		Patient with ROP (n=57)		p
	Avg.±SD	Median (Min-Max)	Avg.±S.D	Median (Min-Max)	
Gestational Age	31.68±1.68	32 (28–34)	28.33±2.37	28 (23–34)	<0.001†,*
Birth Weight (g)	1206±213	1200 (500–1485)	1006±296	1040 (370–1490)	<0.001††,*

†Mann–Whitney U test; ††The Independent Groups t-test, *p<0.05.

Table 3. Ages of gestation and birth weight by treatment status

	Not treated (n=93)		Treated (n=23)		p
	Avg.±S.D	Median (Min-Max)	Avg.±S.D	Median (Min-Max)	
Gestational Age	30.84±2.15	31 (26–34)	26.78±1.83	27 (23–30)	<0.001†,*
Birth Weight (g)	1169±244	1200 (500–1490)	860±257	800 (370–1400)	<0.001†,*

†Mann–Whitney U test; *P<0.05.

Table 4. The relationship between gestational age and the occurrence and treatment of ROP according to birth weight

Birth weight (g)	ROP and treatment status	Gestational age		p†
		≤28 weeks	>28 weeks	
	ROP status			
<750 g	Without ROP	0 (0)	1 (50)	0.133
	With ROP	13 (100)	1 (50)	
	Treatment status			
	Not treated	5 (38.5)	2 (100)	0.200
	Treated	8 (61.5)	0 (0)	
	ROP Status			
750–1000 g	Without ROP	0 (0)	8 (80)	<0.001*
	With ROP	12 (100)	2 (20)	
	Treatment status			
	Not treated	3 (25)	9 (90)	0.004*
	Treated	9 (75)	1 (10)	
	ROP Status			
1000–1250 g	Without ROP	4 (44.4)	19 (67.9)	0.255
	With ROP	5 (55.6)	9 (32.1)	
	Treatment status			
	Not Treated	8 (88.9)	26 (92.9)	1.000
	Treated	1 (11.1)	2 (7.1)	
	ROP Status			
1250–1500 g	Without ROP	0 (0)	27 (65.9)	0.357
	With ROP	1 (100)	14 (34.1)	
	Treatment status			
	Not treated	0 (0)	40 (97.6)	0.048*
	Treated	1 (100)	1 (2.4)	

†Fisher's exact test, *p<0.05.

requiring treatment (8). In Hong Kong in 2013, the prevalence of ROP in infants born <1500 g was 19.7%, with 4.2% of cases requiring treatment (4). Studies from the Netherlands in 2009 and Brazil between 2009 and 2011 reported different prevalence rates of ROP and treatment requirements among infants with similar BW criteria (9,10). These divergent findings between studies may be due to several factors. Differences in the level of development of countries and variations in intensive care standards may contribute to the observed disparities. In addition, advances in intensive care practices may have led to the survival of more immature infants, thereby increasing the prevalence of ROP. In our study, the high prevalence of ROP and the rate of cases requiring treatment may be attributed to the recent nature of the study and the exclusive focus on infants <1501 g. It is plausible that if we had included infants <32 weeks GA and/or <1501 g, the rates of ROP and cases requiring treatment may have been lower.

The International Classification of ROP (ICROP) provides a standardized framework for diagnosing and categorizing ROP, which has been instrumental in harmonizing ROP screening and treatment practices worldwide (11). According to the ICROP guidelines, the staging of ROP is based on the extent and location of retinal vascularization and the presence of plus disease, which denotes vascular dilation and tortuosity in the posterior retinal vessels. Our study adhered to these international classification criteria, ensuring that our diagnostic and treatment approaches are aligned with global standards. The American Academy of Pediatrics recommends initiating ROP screening at 31-week postmenstrual age or 4-week postnatal age, whichever comes later, for infants with a BW of < 1500 g or a GA of 30 weeks or

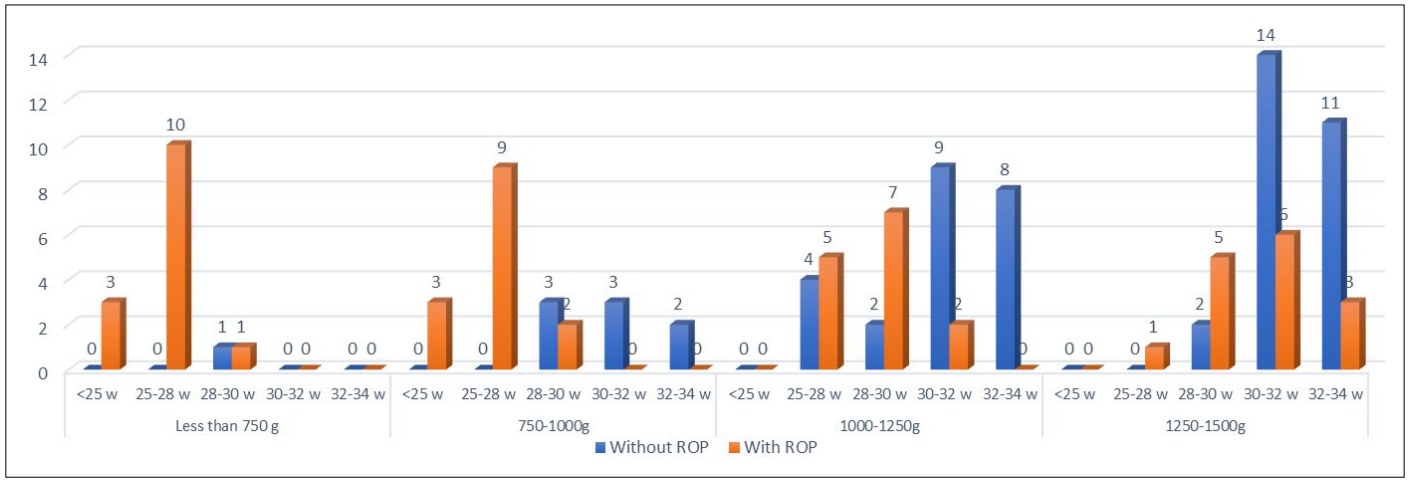

Figure 2. ROP development status by birth weight and gestational age.

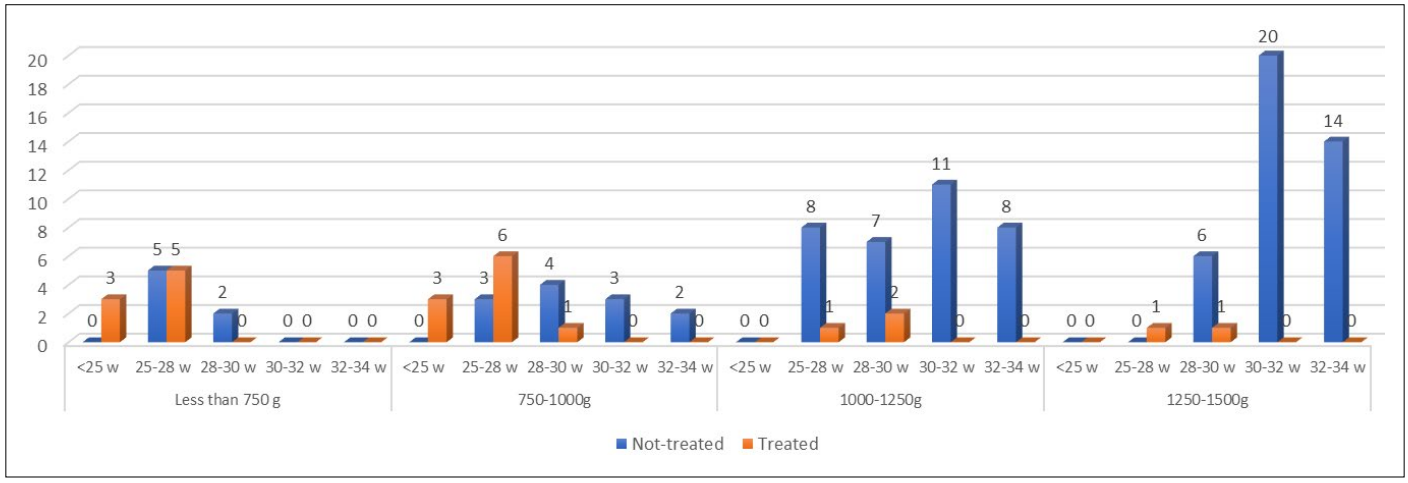

Figure 3. Treatment status by birth weight and weeks of birth.

less (12). In our study, the high prevalence of ROP and the rate of cases requiring treatment highlight the necessity of adhering to these stringent screening protocols.

It is well documented that rates of diagnosis and treatment for ROP increase as BW decreases. However, the specific threshold of BW at which this effect becomes pronounced and the degree of its impact remains uncertain. This situation is related to the level of development and intensive care standards in different countries. The cryotherapy for ROP (CRYO-ROP) cohort study found that for infants with a BW of <1251 g, each 100-g increase in BW decreased the odds of reaching the ROP threshold by 27% (13). In addition, each week increase in GA decreased the odds by 19% (13). The incidence of any stage of ROP in infants weighing <1251 g was reported as 68% in the early treatment of ROP study conducted in the United States (14). A study conducted in Hong Kong found that 53.4% of infants born weighing <1000 g had ROP, with a severe ROP rate of 14.5% requiring treatment (5). In Singapore, the rates were 55.4% and 13.7%, respectively, for infants weighing <1000 g (15). In Southern Taiwan, the rates were 70.9% and 29.3%, respectively, while in Northern Taiwan, the rates were 61.3% and 28.4%, respectively (16,17). Another study conducted in Türkiye reported rates of 55.9% and 19.4%, respectively (18). In this study, it was found that ROP developed in 93.3% of babies born weighing <750 g, while 53.3% of them required treatment for severe ROP. The rates were 63.6% and 45.5% in the 750–1000 g group; 37.8% and 8.1% in the 1000–1250 g group; and 35.7% and 4.8% in the 1250–1500 g group, respectively. These findings demonstrate significant variations in diagnosis and treatment rates across different countries. To ensure consistency in intensive care units, we recommend evaluating annual diagnosis and treatment rates based on BWs, as done in our study. This approach can provide valuable insights into changes in intensive care standards over time and facilitate the identification of areas for improvement.

Our study revealed that ROP cases requiring treatment had an average GA of 26.78 weeks and an average BW of 860 g. In contrast, a study conducted in Hong Kong reported values of 25 + 1 week and 708 g, respectively (4). Similarly, a

study conducted in Türkiye between 2005 and 2008 reported these values to be 28 weeks and 1122 g, respectively (19). In North America between 2011 and 2016, these values for aggressive posterior ROP were found to be 24.3 weeks and 617 g, respectively, while cases requiring treatment other than aggressive posterior ROP had values of 25 weeks and 679 g, respectively (20). In the study conducted in South India between 2018 and 2021, these values were found to be 27.8 weeks and 940.6 g, respectively (21). According to the data from our study, it appears that intensive care standards in our setting are lower than those in developed countries but higher than those in less developed countries. Furthermore, previous studies conducted in your country suggest that intensive care standards have improved over time.

To reduce the need for unnecessary examinations, researchers have developed novel screening algorithms that incorporate various clinical parameters, such as postpartum weight gain and hydrocephalus status. Examples of these algorithms include WINROP, PINT-ROP, CHOP-ROP, ROPScore, CO-ROP, OMA-ROP, G-ROP, STEP-ROP, and DIGIROP (22,23). Despite the availability of these models, screening algorithms based on GA and BW remain essential. Although overscreening for ROP may be acceptable due to the severe consequences of missing it, new screening protocols with high sensitivity and specificity across diverse populations are necessary (24,25). In this study, we evaluated the diagnosis and treatment rates of ROP based on BW. This method can reduce the number of examinations performed on infants above a certain BW and week of birth. Establishing screening criteria tailored to the neonatal intensive care unit can help reduce unnecessary examinations.

This study has several limitations. First, the sample size was small, which may limit the generalizability of the findings. Second, due to the retrospective design, other potential risk factors that could contribute to the risk of developing ROP were not comprehensively evaluated. Finally, only infants who received screening or treatment for ROP were included in the analysis, potentially introducing selection bias, as infants who died before screening were not assessed. These limitations should be considered when interpreting the study's results.

Conclusion

The diagnosis and treatment rates of ROP have shown an upward trend over the years, coinciding with improvements in intensive care standards. However, classifying premature babies by BW can create screening criteria specific to the neonatal intensive care unit and predict ROP diagnosis and treatment rates. This can also provide insight into changes in the standards and self-control of the neonatal intensive care unit over time.

Disclosures

Ethics Committee Approval: This study adhered to the principles outlined in the Declaration of Helsinki, and Ethical Approval for the study was obtained from the Ethics Committee of Başakşehir Çam and Sakura City Hospital (February 05, 2024, Approval number E-96327027-514.10-235695968).

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Conflict of Interest: None declared.

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