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RESEARCH ARTICLE

Outcomes of Screening for Retinopathy of Prematurity Using United Kingdom and United States Criteria at a Tertiary Referral Center in Türkiye

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ABSTRACT

Objective: To investigate the impact of using United Kingdom (UK) or United States (US) criteria instead of Turkish criteria for retinopathy of prematurity (ROP) screening on infants who require ROP treatment.

Materials and Methods: Four hundred and twenty-two infants underwent ROP screening. ROP screening was performed in all infants with a gestational age of less than 34 weeks or a birth weight of less than 1,700 g. Gestational age, birth weight, stages of ROP, treatments administered, and treatment outcomes were documented.

Results: ROP was diagnosed in 136 (32.2%) of 422 infants. Of these, 60 (14.2%) required treatment due to either type 1 ROP or aggressive ROP (A-ROP). If the UK screening criteria had been used, only 245 infants would have been screened, resulting in a 41.9% reduction compared to the screening criteria used in Türkiye. Thirteen (9.5%) cases of ROP developed in the 167 infants who were excluded from screening. Of these cases, five (8.3%) required treatment. If the screening criteria used in the US had been applied, the number of screened infants would have been reduced by 49.3% compared to the screening criteria used in Türkiye. Of the 208 infants who were not screened, 20 (14.7%) developed ROP, with 8 (13.3%) requiring treatment.

Conclusion: The use of the US or UK screening criteria for ROP in our center has led to the underdiagnosis and undertreatment of ROP. Increased awareness of ROP in intensive care units may lead to further standardization of screening criteria in the future.

Keywords: Birth weight, gestational age, retinopathy of prematurity, screening criteria

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INTRODUCTION

The establishment of clear criteria for the screening of ROP, a condition that can potentially result in blindness among preterm infants, is crucial for ensuring its early detection and effective management. The guidelines consider various risk factors, including the infant's gestational age (GA) and birth weight (BW), as well as the specific environment within NICUs. To reduce the likelihood of severe visual impairment or blindness in newborns, each country has developed tailored screening protocols that emphasize early identification and timely intervention. The primary determinants of these screening guidelines are GA and BW (Table 1).

An extensive and comprehensive study conducted across 69 NICUs in Türkiye revealed that newborns with a BW of up to 1,700 grams and a GA of up to 34 weeks are particularly vulnerable to developing more severe forms of ROP—conditions that, in many cases, necessitate urgent and targeted medical intervention.[1] In alignment with the 2021 guidelines set forth by the Turkish Neonatology Society ROP Study Group and the Turkish Ophthalmology Society ROP Commission, it is strongly recommended that all infants with a GA below 34 weeks and a BW of 1,700 g or less should undergo ROP screening.

On the other hand, the 2008 United Kingdom (UK) guidelines recommend ROP screening for all infants born at or before 31 weeks and 6 days, or with a BW below 1,501 g.[2] Similarly, the 2018 guidelines provided by the American Academy of Pediatrics and the American Academy of Ophthalmology recommend ROP screening for all newborns in the United

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States (US) who weigh 1,500 g or less at birth, or are born at 30 weeks of gestation or earlier.[3] However, research has shown that these screening criteria, as utilized in the US and the UK, may not be universally applicable across different populations and settings.[4–9] It is imperative to ascertain the underlying causes of this situation to achieve the more optimal developed-country screening criteria.

According to the "Early Treatment of Retinopathy of Prematurity" (ETROP) and International Classification of Retinopathy of Prematurity (ICROP) criteria, ROP requiring treatment consists of two main conditions: type 1 ROP and aggressive ROP (A-ROP).[10,11] The aim of this study was to compare cases of ROP requiring treatment using the screening criteria of the UK or the US, as opposed to those of our country, among patients admitted to our ROP diagnosis and treatment center. Furthermore, the underlying reasons for any observed disparities were sought to be identified.

MATERIALS and METHODS

This retrospective study aimed to evaluate preterm infants monitored at the ROP clinic of Basaksehir Cam and Sakura Hospital, with the study period spanning from January 1, 2023, to January 1, 2024. The study was approved by the institutional review board and the local ethics committee (E-96317027-514.10-238025866). Informed consent, both verbal and written, was obtained from the parents or legal guardians of all participating infants, in full compliance with the ethical principles outlined in the Declaration of Helsinki.

Routine ROP screenings were performed on all infants born with a BW below 1,700 g or a GA under 34 weeks. The follow-up period ended when the infants either achieved complete retinal vascularization or showed no signs of subthreshold or more severe stages of ROP by 45 weeks postmenstrual age. For those who achieved full retinal vascularization before reaching 45 weeks postmenstrual age, follow-up was concluded earlier. Infants who failed to meet these follow-up criteria or who passed away during the study were excluded from the analysis.

The infants were stratified into two cohorts: those monitored in our hospital's NICU and followed up at the ROP clinic constituted the internal NICU group, while those monitored in other hospitals' NICUs and referred to our ROP clinic comprised the external NICU group. The data collected included BW, GA, the most advanced stages of ROP observed, the treatments administered, and their corresponding outcomes. The documentation of ROP findings followed the international classification criteria for ROP.[11] Infants diagnosed with A-ROP or type 1 ROP were treated.

Table 1. Key differences in ROP screening criteria

Country	Gestational age (GA) threshold	Birth weight (BW) threshold
Türkiye	≤34 weeks	≤1700 g
United Kingdom (UK)	≤31 weeks 6 days	≤1500 g
United States (US)	≤30 weeks	≤1500 g

ROP: Retinopathy of Prematurity

This research explores the discrepancies between ROP cases detected or missed based on the screening criteria used in the UK and those identified or missed under the screening guidelines in the US. The study assessed the number of cases requiring treatment under each set of criteria and compared the effectiveness of these screening approaches. The present study also examined the association of differences in ROP diagnosis and treatment between screening criteria and NICU type.

Statistical Analysis

Data analysis was conducted using IBM SPSS Version 20 (IBM Corparate, USA) software. The normality of the data was assessed using the Shapiro–Wilk test. Descriptive statistics of the data are presented as median and interquartile range (IQR). For data with a normal distribution, intergroup comparisons were performed using the independent sample t-test, while the Mann–Whitney U test was applied for data that did not follow a normal distribution. The relationship and differences between categorical variables were analyzed using the chi-square test. A p-value of less than 0.05 was considered statistically significant. The statistical analyses aimed to thoroughly examine the characteristics of the groups, their distributions, and potential relationships between variables within the dataset.

RESULTS

Throughout the course of the study, a total of 422 premature infants were systematically evaluated in accordance with the current screening criteria established by Türkiye. Among these infants, 224 (53.1%) were identified as male, while 198 (46.9%) were female. The median GA of the participants was found to be 32 weeks, with the observed range spanning from 22 weeks and 6 days to 33 weeks and 6 days. In terms of BW, the median value was recorded at 1,540 g, with a broad range extending from 370 g to 3,140 g. It was ascertained that all infants included in the study successfully completed their final ROP screening as part of the follow-up procedures. This comprehensive screening process ensured that all relevant data were collected, facilitating the thorough examination of the infants' ROP findings during the study period.

Table 2. Demographics and clinical characteristics of the infants

	All		Internal NICU		External NICU		p
	n	%	n	%	n	%	
n, %	422		245	58.1	177	41.9	
Female	198	46.9	131	53.5	67	37.9	0.001
Gestational age (week), median (range)	32 (22.6–33.6)		32 (22.6–33.6)		31.3 (23–33.6)		0.008
Birth weight (gram), median (range)	1540 (370–3140)		1530 (370–3000)		1550 (500–3140)		0.401
With any stage ROP	136	32.2	61	24.9	75	42.4	0.001
Gestational age (week), median (range)	28.1 (22.6–33.6)		27.5 (22.6–33.6)		29 (23–33.6)		0.182
Birth weight (gram), median (range)	1040 (370–2400)		1040 (370–1860)		1020 (500–2400)		0.204
With Type 1 ROP/A-ROP	60	14.2	23	9.4	37	20.9	0.001
Gestational age (week), median (range)	26.4 (22.6–33.6)		26 (22.6–29.6)		28 (23–33.6)		0.029
Birth weight (gram), median (range)	930 (370–2400)		800 (370–1400)		980 (500–2400)		0.022

NICU: Neonatal Intensive Care Unit; ROP: Retinopathy of Prematurity

Out of a total of 136 infants (32.2%) diagnosed with ROP, 14.2% (60 infants) exhibited either type 1 ROP or A-ROP and were subsequently treated. The median GA of infants diagnosed with ROP was 28 weeks and 1 day, with a range between 22 weeks and 6 days to 33 weeks and 6 days. The median BW for these infants was 1,040 g, with the lowest being 370 g and the highest reaching 2,400 g. The median GA of infants with ROP requiring treatment was 26 weeks and 4 days. The GA for this group spanned from 22 weeks and 6 days to 33 weeks and 6 days. Regarding BW for this specific group, the median was found to be 930 g, with a range that spanned from 370 g to 2,400 g (Table 2).

The median GA of infants undergoing ROP screening in the internal NICU is 32 weeks, with a range spanning from 22 weeks and 6 days to 33 weeks and 6 days. In contrast, the median GA for infants screened in external NICUs is 31 weeks and 3 days, with a range from 23 weeks to 33 weeks and 6 days (p=0.008). The average BW of infants screened in the internal NICU is 1,530 g, ranging from 370 g to 3,000 g, while the average BW for those screened in external NICUs is 1,550 g (range: 500 g to 3,140 g) (p=0.401) (Table 2).

In our study, the group of infants who developed ROP in the internal NICU had a median GA of 27 weeks and 5 days, with the range spanning from 22 weeks and 6 days to 33 weeks and 6 days. The median BW for this cohort was 1,040 g, while the range of weights varied from 370 g to 1,860 g. In infants from external NICUs who also developed ROP, the median GA was 29 weeks, with a range extending from 23 weeks to 33 weeks and 6 days. The median BW for this group was 1,020 g, and their weight distribution ranged from 500 g to 2,400 g. No statistically significant differences were found between the groups in terms of GA (p=0.182) or BW (p=0.204) (Table 2).

Table 3. Comparison of United Kingdom and United States screening criteria with Türkiye criteria

	Türkiye (a)	UK (b)	US (c)	b/a (%)	c/a (%)
Total number of infants screened	422	245	214	58.1	50.7
ROP detected	136	123	116	90.4	85.3
Type 1 ROP detected	60	55	52	91.7	86.7

The infants in the internal NICU with ROP requiring treatment had a median BW of 800 g, with the observed range between 370 g and 1,400 g. The median GA for this cohort was 26 weeks, and the range of GA varied from 22 weeks and 6 days to 29 weeks and 6 days. In contrast, infants in external NICUs with ROP requiring treatment had a median BW of 980 g, with the range extending from 500 g to 2,400 g. The median GA in this group was 28 weeks, ranging from 23 weeks to 33 weeks and 6 days. The differences in GA (p=0.029) and BW (p=0.022) between the two groups were statistically significant (Table 2).

Had the screening criteria applied in the UK been adopted, 245 infants would have undergone screening, reflecting a 41.9% reduction when compared to the criteria used in Türkiye. Of the 167 infants excluded from screening, 13 cases of ROP developed, with 5 of these cases progressing to type 1 ROP or A-ROP, necessitating treatment (Table 3).

Had the US screening criteria been applied, 214 infants would have been screened, resulting in a 49.3% decrease compared to the screening criteria followed in Türkiye. Among the 208 infants excluded from screening, 20 cases of ROP developed, with eight of these cases progressing to type 1 ROP or A-ROP, which required treatment (Table 3).

DISCUSSION

The findings of this study indicate that the ROP screening guidelines applied in the US and UK are unsuitable for the premature infant population examined. The analysis demonstrates that 8.3% of infants requiring ROP treatment would be overlooked under the UK screening criteria, while the rate would increase to 13.3% under the US criteria. The primary rationale for this predicament is that more mature infants treated in external NICUs, who are not subject to screening according to the criteria established by developed countries, nevertheless require treatment for ROP.

In the multicenter TR-ROP study carried out in our country, 27% of the infants screened were diagnosed with some stage of ROP, and 6.7% required treatment for severe ROP.[1] In our study, 32.4% of the infants were diagnosed with some stage of ROP, and 14.2% of them required treatment. The TR-ROP study divided hospitals into private and public and found that severe ROP cases occurred more frequently in infants who were more mature in private hospitals. In our patient population under study, infants treated in external NICUs and referred to our center were from private hospital NICUs. In our study, all infants requiring treatment but non-compliant with the US criteria were monitored in the NICUs of private hospitals. The rates of ROP diagnosis and treatment in our study were notably higher than those documented in the TR-ROP study. This inconsistency may have arisen due to only specific cases being referred from private hospitals to our hospital, rather than all infants. These selected cases may not fully reflect the general population. These findings indicate a need for increased awareness of ROP development among NICUs in private hospitals in Istanbul.

The establishment of ROP screening criteria is contingent upon the developmental stage of countries.[12] Research carried out in developed countries has demonstrated that infants born at or beyond 32 weeks of GA face a markedly lower likelihood of developing ROP. Furthermore, the majority of infants born at over 28 weeks' gestation who do develop ROP tend to manifest mild forms of the disease that often resolve spontaneously without requiring treatment.[13] Research conducted in developing countries has yielded findings that are consistent with those observed in our study.[14] Research conducted in Hong Kong revealed that if the UK criteria were replaced with the US criteria, no cases of ROP requiring treatment would have been missed.[15] Similarly, had we confined our examination to infants treated in our NICU, no infant outside the US screening criteria would have required treatment. This is comparable to the ROP screening criteria in developed countries. Nevertheless, it is evident that the US and UK screening criteria are not universally applicable across Istanbul. Moreover, the division of ROP centers into two distinct categories—those dedicated solely to diagnosis and those offering both diagnosis and treatment—has created a significant challenge in managing ROP effectively.

A multitude of studies have been conducted on a global scale with the objective of evaluating the suitability of the criteria utilized in the US and the UK.[8,15–18] The primary aim of these studies is twofold: firstly, to evaluate the efficiency of the screening guidelines used in developed countries within their respective regions; and secondly, to explore ways in which these criteria can be made applicable in other contexts.

The application of UK screening criteria to the study conducted in China revealed that 9.4% of ROP cases requiring treatment would have been overlooked if these criteria had been used. The same study revealed that if the US screening criteria were applied, 14.7% of cases would have been overlooked.[8] Research conducted in Iran showed that 25.4% of ROP cases and 8.4% of cases that needed treatment would not have been detected if the US criteria had been used.[16] Studies conducted in Pakistan and Saudi Arabia found no cases of ROP requiring treatment in infants born with a GA higher than 32 weeks and a BW exceeding 1,500 g.[17,18]

A prior study conducted in Türkiye found that 3.8% of infants born at or after 32 weeks and 6.5% of infants born at or after 1,500 g developed severe ROP.[19] In the more recent TR-ROP study, 1.2% of babies born over 1,500 g and over 32 weeks developed severe ROP that required treatment.[1] In our study, the rate was found to be 8.3%. A possible reason for this difference is that a considerable number of infants transferred to our hospital from private hospitals were later referred for treatment.

To establish more optimal ROP screening criteria in Istanbul, it may be necessary to increase the educational levels of NICUs in private hospitals regarding ROP. In our country, a neonatologist is typically the head of the NICU in public hospitals. However, in private hospitals, the responsibility for NICUs can also fall upon general pediatricians. Ensuring the presence of a neonatologist in all NICUs could potentially lead to a decline in the rate of ROP treatment.

This study has certain limitations. Firstly, its retrospective design limited the evaluation of other potential factors that may play a role in the development of ROP. Secondly, the study did not include all public and private hospitals in Istanbul. Consequently, it is not possible to extrapolate the current results to all private and public hospitals. Thirdly, the conditions of care and the nurse-to-patient ratio for infants treated in external NICUs are not available for analysis. Furthermore, there were instances where information was missing for infants who had recently passed away or were treated at other facilities without recorded ROP outcomes.

CONCLUSION

In conclusion, applying ROP screening criteria in Istanbul based on those developed in the US or UK led to underdiagnosis and insufficient treatment of ROP cases. By enhancing the educational standards and intensive care practices regarding ROP in private hospitals, it may be feasible to implement screening criteria derived from developed countries. Furthermore, the strategic transformation of hospitals from mere diagnosis centers to comprehensive diagnosis and treatment facilities has the potential to enhance awareness regarding ROP. This approach may prevent the performance of unnecessary examinations and treatments.

Disclosures

Ethics Committee Approval: The study was approved by the Basaksehir Cam and Sakura Hospital Ethics Committee (No: E-96317027-514.10-238025866, Date: 06/03/2024).

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