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Original Article

Retinopathy of Prematurity Screening Criteria in Turkey's South Marmara Region

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Abstract

Objectives: Retinopathy of prematurity (ROP) is the leading cause of preventable blindness in premature infants and a growing problem in the middle- and low-income countries. To prevent ROP, effective screening, prevention, and treatment programs are essential; they should be modified according to each country's requirements. In this study, we offered modified screening criteria for Turkish children.

Methods: The medical records of the patients who had ROP screening between January 2015 and May 2018 were retrospectively reviewed. Five different criteria were applied to all 1720 babies, as follows: ≤35 weeks and/or 2600 g, ≤34 weeks and/or 2400 g, ≤33 weeks and/or 2100 g, ≤32 weeks and/or 2000 g, and ≤31 weeks and/or 1800 g. The sensitivities and specificities were found for all the strategies.

Results: In this study, a total of 1720 babies screened for ROP (774 girls and 946 boys) were evaluated retrospectively. The mean gestational age (GA) of the babies examined was 32.1±2.9 weeks (range 24–36 weeks), and the mean birth weight (BW) of the babies screened was 1817±594 g (range 510–3360 g). ROP was diagnosed in 430 (25%) of the patients, and of these, 165 (9% of all patients) required treatment. Overall, the screening protocols of ≤33 weeks of GA and ≤2100 g of BW had 100% sensitivity to detect treatment-requiring babies.

Conclusion: The screening protocols used in highly developed countries are not suitable for all countries, especially for low- and middle-income countries. Thus, the criteria may miss a high number of ROP treatment-requiring patients. Neonatal intensive care unit should coordinate system and continuously updates the ROP screening guidelines so that these data could form a basis for the national ROP standards. We recommend screening premature patients of ≤33 weeks of GA or ≤2100 g of BW for our region.

Keywords: Criteria, retinopathy of prematurity, screening, Turkey.

Introduction

Retinopathy of prematurity (ROP) is the leading cause of preventable blindness in premature infants (1), and it is a growing problem in low- and middle-income countries (2). To prevent ROP, effective screening, prevention, and treatment programs are essential. ROP screening programs differ from country to country, and they should be modified according to each country's requirements. Individual, organized, and timely detection and treatment are critical to preventing unfavorable outcomes (3).

In low- and middle-income countries, ROP occurs more often in heavier babies and those of an older gestational age (GA) than their equivalents in developed nations. Therefore, different states should establish specific screening criteria modified for their requirements (3). In 2013, the American Academy of Pediatrics recommended screening infants having birth weights (BWs) of ≤1500 g or GAs of ≤30 weeks, as well as screening selected infants having BWs between 1500 g and 2000 g or GAs >30 weeks with unstable clinical courses believed to be at a high risk for ROP (4). However,

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one size does not seem to fit all in ROP screening, and numerous reports have already been published suggesting that this screening protocol is ineffective for many low- and middle-income countries (5).

In this study, we described our observations of 1720 babies screened for ROP at our center, and we offered modified screening criteria for Turkish children.

Methods

The medical records of the patients who underwent ROP screenings between January 2015 and May 2018 in the Bursa province were retrospectively reviewed. The ROP classifications and treatment decisions were made according to the International Classification of ROP and early treatment for ROP (ETROP) study results (6, 7). This research was conducted according to the principles of the declaration of Helsinki, and the parents were kept informed about any possible complications. Before the procedure, written informed consent was obtained from the parents.

First, the pupil was dilated with 1.25% phenylephrine (Mydfrin Ophthalmic Solution, Alcon Laboratories Inc., Fort Worth, TX, USA) and 1% tropicamide (Tropamid, Bilim Drug, Istanbul, Turkey). All of the examinations were carried out using indirect ophthalmoscopy (Omega 500, HEINE Optotechnik, Herrsching am Ammersee, Germany), with the scleral indentations performed by the same ophthalmologist. Those infants born at GAs ≤36 weeks and BWs ≤3000 g were initially screened at the 31st week of GA or 4 weeks after birth, whichever was later. Further examinations were performed depending on the disease status, and they continued until the retina was fully vascularized. In the ROP infants, the examinations continued until disease regression. The treatment criteria followed the ETROP recommendations. To determine the best screening strategy, while ensuring that those babies who needed treatment received it and to scan the minimum number of babies, five different criteria were applied to all 1720 babies, as follows (GA and BW, respectively): ≤35 weeks and/or 2600 g, ≤34 weeks and/or 2400 g, ≤33 weeks and/or 2100 g, ≤32 weeks and/or 2000 g, and ≤31 weeks and/or 1800 g. The sensitivities and specificities were found for all the strategies (criteria sets), and a receiver operating characteristic (ROC) curve was created.

Descriptive statistics of the data, including the proportion, standard deviation, frequency, lowest-highest, and median values were used. The data distribution was measured using the Kolmogorov–Smirnov test. The quantitative data were analyzed using the Mann–Whitney U-test and student's t-test, and the cutoff values were determined using an ROC curve. IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA) was used for the analysis.

Results

In this study, a total of 1720 babies screened for ROP (774 girls and 946 boys) were evaluated retrospectively. The mean GA of the babies examined was 32.1±2.9 weeks (range 24–36 weeks), and the mean BW of the babies screened was 1817±594 g (range 510–3360 g). ROP was diagnosed in 430 (25%) of the patients, and of these, 165 (9% of all patients) required treatment. In the ROP+ group, the mean BW was less than that in the ROP group ($p<0.05$). In the treatment+ group, the GA was less than that in the treatment - group ($p<0.05$). For the ROP detection, the area under the curve (AUC) of the ROC curve was 0.821 (95% confidence interval [CI]=0.759–0.883) for the GA, and it was 0.821 (95% CI=0.762–0.880) for the BW. In addition, the AUCs for the ROP cases requiring treatment were 0.838 (95% CI=0.771–0.906) for the GA and 0.828 (95% CI=0.755–0.902) for the BW. Therefore, the GA and BW were statistically effective for detecting the ROP+ and treatment+ babies. Overall, the screening protocols of ≤33 weeks of GA and ≤2100 g of BW had 100% sensitivity to detect treatment-requiring babies and seemed minimum safe values (Figs. 1, 2).

According to our screening strategy (GA ≤36 weeks and BW ≤3000 g), 654 (38%) of the infant screenings based on the GA, and 293 (17%) of the infant screenings based on the BW were unnecessary (compared to minimum safe values).

If the infants <35 weeks of GA or 2600 g of BW were screened instead of the infants born at GAs of ≤36 weeks and BWs of ≤3000 g, 138 BW - based babies (8%), and 499 GA - based babies (29%) would have been unnecessarily

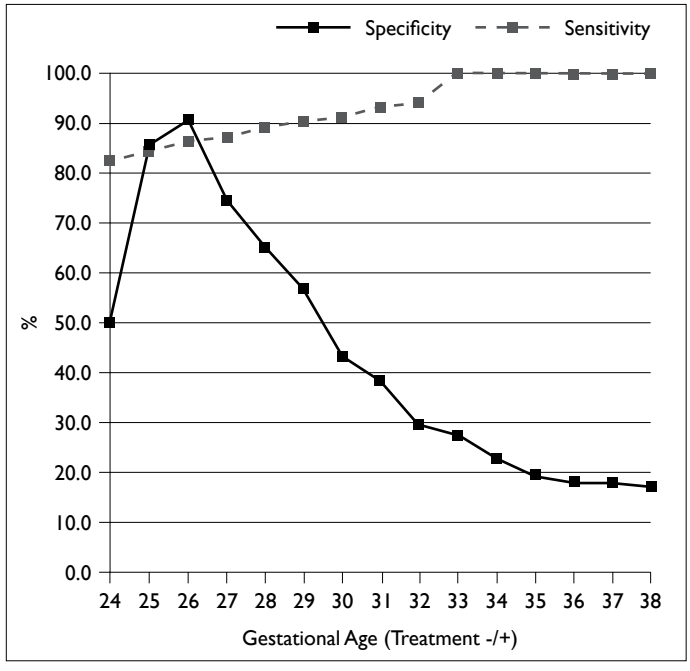

Figure 1. Specificity and sensitivity for gestational age

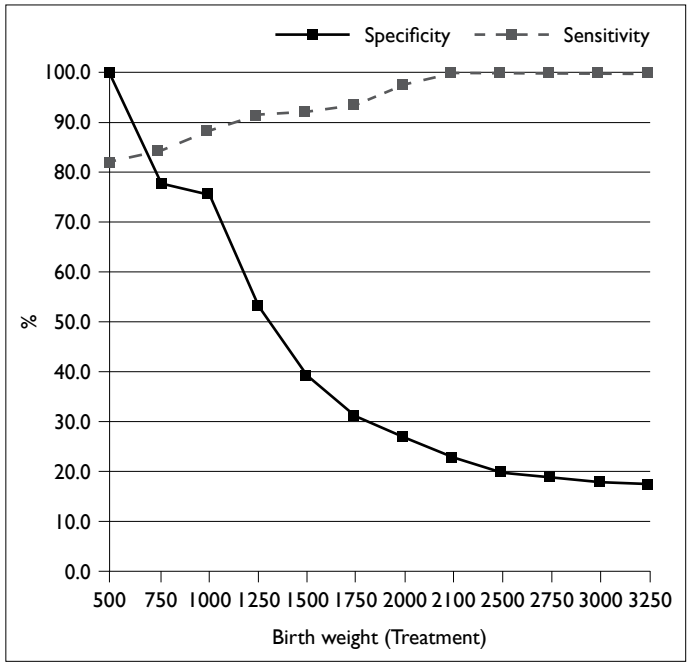

Figure 2. Specificity and sensitivity for birth weight

scanned (compared to minimum safe values), and infants requiring ROP treatment would not have been left untreated. If the limit was set to 34 weeks of GA or 2400 g of BW, 258 (15%) babies and 52 (3%) babies, respectively, would be screened unnecessarily (compared to minimum safe values), without any ROP treatment-requiring babies left. Moreover, if the limits were set to 33 weeks of GA or 2100 g of BW, the treatment-requiring babies could still be safely screened. However, 32 weeks seemed to be critical because, when using this limit of 32 weeks of GA or younger, 25 (15%) treatment-requiring babies would be missed. In addition, the 2000 g of BW limit would result in 10 (6%) missed treatment-requiring babies. When using 31 weeks of GA as the screening strategy 1118 (65%) fewer babies would be screened (compared to 36 weeks-1720 babies); however, 35 (21%) ROP treatment-requiring patients would be missed. In the same way, when using 1800 g of BW as the limit, 35 (21%) patients would be missed, although 826 (48%) fewer babies would be screened (compared to 3000 gr - 1720 babies) with 30 weeks of GA and below as the screening strategy, 1255 (73%) fewer babies would be examined (compared to 36 weeks - 1720 babies); however, 60 (36%) ROP treatment-requiring patients would be missed. With 1500 g of BW as the limit, 1169 (68%) fewer babies would be screened (compared to 3000 gr, 1720 babies), but 50 (30.3%) babies who needed treatment would be missed (Tables 1, 2).

Discussion

In this study, we attempted to determine a better screening strategy specifically for a Turkish population. ROP was diagnosed in 430 infants (25%) and 165 (9.5%) of them required treatment. When compared to the results from other low- and middle-income countries, our results were better. However, the ROP incidence rates were different, such that the reported ROP incidences were 34.3% (152 babies) in Egypt (8), 30% in Iran, and 47% in India (9, 10). A study in Sweden focusing on 1744 infants <32 weeks of GA, ROP was found in 24% of the babies, and 4.2% of these required treatment. The mean GA was 28.4 weeks (range 22–31 weeks), and the mean BW was 1239 g (range 382–2615 g) (11). Our infants were heavier and older (1817±594 g of BW and 32.1±2.9 weeks of GA). In addition, the treatment rate (9.5%) was higher than those in Sweden, the USA, and Canada (12, 13), but it was comparable to that from Egypt (9.8%) (8).

ROP screening protocols are critical to avoid blindness in children. In this study, we employed different strategies to determine all the treatment-needing patients and avoid unnecessary screening. The suggested screening criterion in the USA (<1500 g), Australia (<1250 g), and Canada (<1250

Table 1. Different birth weight usage to detect ROP

Birth weight (gr)	Total number of baby (%)	Total number of ROP and treatment (%)	Total number of unnecessary screening (%)	Total number of missed baby-% (Treatment needed)
* ≤3000	1720 (100)	430 (100)-165 (100)	293 (17)	0
≤2600	1565 (90)	415 (96)-165 (100)	138 (8)	0
≤2400	1479 (85)	390 (90)-165 (100)	52 (3)	0
** ≤2100	1427 (82)	341 (79)-165 (100)	0	0
≤2000	1066 (61)	301 (70)-155 (93)	0	10 (6)
≤1800	894 (51)	225 (52)-130 (78)	0	35 (21)
≤1500	550 (31)	184 (42)-115 (69)	0	50 (30)

* All patients; ** minimum safe birth weight to detect all treatment requiring babies; ROP: Retinopathy of prematurity.

Table 2. Different gestational age usage to detect ROP

Gestational age (Week)	Total number of baby (%)	Total number of ROP and treatment (%)	Total number of unnecessary screening (%)	Total number of missed baby % (Treatment needed)
* ≤36	1720 (100)	430 (100)-165 (100)	654 (38)	0
≤35	1565 (90)	415 (96)-165 (100)	499 (29)	0
≤34	1324 (76)	402 (93)-165 (100)	258 (15)	0
** ≤33	1066 (61)	391 (90)-165 (100)	0	0
≤32	860 (50)	311(72)-140 (84)	0	25 (15)
≤31	602 (35)	248 (57)-130 (78)	0	35 (21)
≤30	464 (26)	198 (46)-105 (63)	0	60 (36)

* All patients; ** Minimum safe birth weight to detect all treatment requiring babies; ROP: Retinopathy of prematurity.

g) is <30 weeks of GA (4, 14, 15). If we used this criterion, 60 type 1 ROP (week-based) infants would remain untreated. If we applied the Saudi Arabia criteria (<32 weeks of GA or <1501 g of BW) 25 babies (week-based) or 50 babies (weight-based) would remain untreated (3). For Turkey, it seems that the Indian screening criterion of <34 weeks of GA could be better for detecting the patients requiring ROP treatment so that none would be missed, but more mature infants would also be screened (10).

In Turkey, the study by Basmak et al. suggested a screening protocol of ≤34 weeks of GA or ≤2000 g of BW. They concluded that the screening protocols should include more mature infants when the ROP screening is done in populations from low- and middle-income countries (16). We recommend screening protocols of ≤33 weeks of GA and ≤2100 g of BW. The change in the screening criteria from 2010 to 2017 was approximately 1 week (≤34–≤33 weeks), but the BW criteria increased from 2000 to 2100 g. This change may have been the result of a better neonatal intensive care unit (NICU).

In the study by Bas et al., (17) 6115 babies were screened, and the recommended screening criteria were ≤34 weeks of GA and <1700 g of BW. It was a large study, and it included multiple centers in Turkey. Our study had fewer patients, but it represented a good national blend of babies.

Many risk factors have been reported for the development of ROP, including neonatal sepsis, blood transfusions, poor postnatal weight gain, sepsis, and necrotizing enterocolitis (18, 19–27). In our study, we did not evaluate the other risk factors because we required more accurate and straightforward criteria for the screening. We believe that, in practical terms, the GA and BW are the most straightforward factors for doctors and nurses to consider when taking action.

The BW is an essential factor for ROP screening, and our study's criterion was ≤2100 g; however, Bas et al.'s criterion was <1700 g, the USA's criterion was <1500 g, and the Canadian criterion was <1250 g. In our study, we understood that for over 33 weeks of GA and below 2000 g of BW, 60 babies did not have ROP. We believe that the GA is the best predictive factor for ROP screening and that the BW can be used secondarily, especially when the GA is not predictable.

Conclusion

The screening protocols used in highly developed countries are not suitable for all countries, especially for low- and middle-income countries. Thus, the criteria may miss a high number of ROP treatment-requiring patients. NICUs should coordinate system and continuously update the ROP screening guidelines so that these data could form a basis for the national ROP standards. We recommend screening premature patients of ≤33 weeks of GA or ≤2100 g of BW based on our experiences in Turkey's South Marmara Region, which contains a diverse genetic population of migrants from all over the country.

Disclosures

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Involved in design and conduct of the study (SGC); preparation and review of the study (IP); data collection (SGC, IP); and statistical analysis (SGC, IP).

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