DOI:10.14744/bej.2018.32032
Beyoglu Eye J 2018; 3(3): 128-132

Original Article

The Incidence of Retinopathy of Prematurity in a Tertiary Care Center in Turkey

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Abstract

Objectives: The objective of our study was to determine the incidence of retinopathy of prematurity (ROP) in our hospital, which gives tertiary health services.

Methods: In this retrospective study, the medical files of the infants, who were born before the 36th gestational age and applied for the examination of ROP between 2014 and 2017 to Istanbul Kanuni Sultan Suleyman Training and Research Hospital, were investigated. The birth weight, gestational age, type of delivery, and the development of ROP were recorded.

Results: The mean gestational age and mean birth weight of 2913 infants, who were screened for ROP, were 32.3±2.9 (22–36) weeks and 1846±580 g (360–4300), respectively. 48.7% of the patients were females and 51.3% were males. 32.4% of the patients had ROP at any stage. 8.8% of the infants had severe ROP and were treated accordingly. The mean gestational age and the mean gestational weight of the infants in this group were 28.0±2.6 weeks (22–35) and 1171.9±417.5 g (360–2500), respectively. The mean birth weight was lower in the severe ROP group compared to the group with no ROP development. 28 infants (0.9%) with birth weight over 2500 g (2502–3740) had only mild ROP and improved spontaneously.

Conclusion: As it was determined that the mean gestational age and weight were lower in infants with ROP than the infants with no ROP development, so the importance of the low birth weight and the gestational age was confirmed as risk factors for ROP development.

Keywords: Gestational age, low birth weight, retinopathy of prematurity, screening results.

Introduction

Retinopathy of prematurity (ROP) was described by Terry as retrolental fibroplasia in 1942 and defined as a vasoproliferative retina disorder of the premature infants (1). ROP is worldwide the third most common cause of the blindness in childhood (2). In addition, such as cataract and glaucoma, it is also one of the preventable causes of blindness (2). Today, with the help of the screening and monitoring programs, infants under risk can be easily detected, and the blindness can be prevented with proper treatment (3).

In recent years, with the improvement of the neonatal intensive care conditions, infants even with a very early gestational age kept alive (4). However, the increase in the number of the premature infants kept alive, an epidemia of ROP emerged (5). In the developed countries, the rate of blindness related to ROP is less than developing countries thanks to the technological development and presence of sufficient experienced staff (6). In less developed countries, ROP is encountered also in infants with a relatively higher gestational age, and birth weight and the blindness related

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Submitted Date: September 12, 2018 **Accepted Date:** December 18, 2018 **Available Online Date:** December 27, 2018

to ROP is much more common (6–9). In a multicenter study conducted in our country, the investigators reported that the rate of ROP at any stage was 30% and they stated that the ROP incidence was comparable with other developing countries (10).

The objective of our study was to determine the incidence of ROP in premature infants followed up in our hospital, which gives tertiary health-care services in Istanbul, the biggest metropolis of Turkey.

Methods

This study was conducted in the Istanbul Kanuni Sultan Süleyman Training and Research Hospital with the retrospective screening of the premature infants, who were followed up and treated in the Diagnosis and Treatment Center with the diagnosis of ROP between April 2014 and September 2017. In line with the recommendations of the American Academy of Pediatrics and American Academy of Ophthalmology in 2006, we included in the ROP screening program, the premature infants, who were under the gestational age of 32 weeks and under the birth weight of 1500 g and the premature infants with a gestational age of 32 weeks and the birth weight over 1500 g but with risk factors. We obtained informed patient consents from the families of all infants enrolled in the screening program. We recorded the gender, gestational ages, birth weights, types of delivery, and postconceptional ages determined during the examination.

The first ophthalmological examination of the patients was performed between 30th and 31st postmenstrual weeks in infants with a gestational age <27 weeks and in the 4th postnatal week in infants with a higher gestational age (≥27 weeks).

Regarding the examination, after the discontinuation of oral feeding, mydriasis was obtained with the 3 times application of 0.5% tropicamide (Tropamid, Bilim İlaç, Turkey) and 2.5% phenylephrine (Mydfirin, Alcon, USA). 30 min following the installation the infant was referred to the examination room, and topical anesthesia was carried out with 0.5% proparacaine hydrochloride (Alcain, Alcon, USA). Three experienced ophthalmologists examined the infants (DYE, SEB, AV) with a binocular indirect ophthalmoscope and 20 and 28 dioptry lenses (Volk, USA). Following the application of the sterile ophthalmic speculum, the peripheral retina was examined with the scleral depressor. Findings were recorded according to the classification of ROP zone, stage, extent of the disease (11). The examination interval was set according to the presence of the disease, zone, and severity between 2 days and 3 weeks. All patients were followed up until the completion of the retinal vascularization. Infants, who had a high-risk prethreshold disease (Type 1 ROP) and aggressive posterior ROP (APROP) according to the early treatment for ROP criteria, were treated. The treatment was performed with laser photocoagulation or intravitreal anti-vascular endothelial growth factor (VEGF) within 72 h.

Results

A total of 2913 infants, who were enrolled in the study, were gestational age lower than 32 weeks and had a birth weight lower than 1500 g or were gestational age higher than 32 weeks and had a birth weight over 1500 g birth weight but had risk factors. These infants were hospitalized, screened and followed up for ROP between April 2014 and September 2017. 1419 of the patients (48.7%) were females and 1494 (51.3%) were males. The mean gestational age was 32.3±2.9 weeks (22–36) and the mean birth weight was 1846±580 g (360–4300) (Table 1). 18.6% of the infants were born with normal spontaneous vaginal and 81.4% with cesarean delivery.

Nearly 67.6% of the patients (n=1963) did not develop ROP. 14.6% of the infants had Stage 1 ROP, 9.3% Stage 2, 4% Stage 3, and 4.5% had APROP. We did not encounter Stage 4 or 5 ROP at the time of the first diagnosis (Table 2). The mean gestational age and birth weight of infants, who developed ROP, were 30.0±2.9 weeks and 1462.2±515.1 g. The mean gestational age and mean birth weight of infants, who did not develop ROP, were 33.4±2.1 weeks and 2034.0±514.6 g. According to these results, the mean gestational age and birth weight of infants with ROP were significantly lower than the infants without ROP ($p<0.000$). The mean gestational age of the ROP diagnosis was 37.0±2.4 weeks (30–46). In patients with mild-to-moderate ROP, who did not need treatment, the disease regressed on average at the 43.8±5.0 (35–65) premenstrual weeks (PMW). Besides the treated infants, the retinal vascularization was completed at 44.3±4.4 (40–73) PMW. There were no unfavorable outcomes such as retinal detachment, macular ectopia, and optic disc dragging among the followed up patients (Table 3).

Severe ROP diagnosed in 8.8% of the patients (n=257) and all of these patients eyes were treated. In 42.2% of the 257 patients, who were diagnosed with severe ROP and treated accordingly, the disease was in Zone 1 and 57.8% in Zone 2. Laser photocoagulation or intravitreal anti-VEGF treatment was carried out within 24 h in infants, who were diagnosed with Type 1 ROP or APROP. We did not encounter any complication related to the administered treatments.

Nearly 77.1% of the infants with a gestational age below 28 had ROP at any stage. This rate was 13.1% in infants with gestational weeks (GW) over 32. The rate of the infants, who were below 28 GW and treated due to the severe ROP, was 38 % and the rate of the infants, who were higher than 32 GW and treated, was 0.9 % (n=14). There were only 9 infants (0.3%) with a birth weight between 2000 g and 2500 g, who underwent treatment. We detected mild ROP in 28

Table 1. The average gestational age and birth weight

	n	Minimum	Maximum	Mean±SD
Gestational age	2913	22.00	36.00	32.3134±2.92117
Birth weight	2913	360.00	4300.00	1846.9949±580.42741

SD: Standard deviation.

Table 2. The distribution of ROP in the eyes

ROP	Frequency (%)	Valid percent	Cumulative percent
Valid			
Stage 0	3935 (67.5)	67.5	67.5
Stage 1	851 (14.6)	14.6	82.1
Stage 2	544 (9.3)	9.3	91.5
Stage 3	234 (4.0)	4.0	95.5
APROP	262 (4.5)	4.5	100.0
Total	5826 (100.0)	100.0	

ROP: Retinopathy of prematurity.

Table 3. The distribution of treated and untreated eyes

	Frequency (%)	Valid percent	Cumulative percent
Valid			
Untreated eyes	5312 (91.2)	91.2	91.2
Treated eyes	514 (8.8)	8.8	100.0
Total	5826 (100.0)	100.0	

infants (0.9%) with birth weight over 2500 g (2502–3740). The disease regressed spontaneously in all these infants during the follow-up.

Statistical Analysis

SPSS (SPSS Inc, PASW Statistics for Windows, Version, 18.0, Chicago, USA) software package was used for the statistical analysis. The normal distribution of the data was evaluated with the Kolmogorov–Smirnov test. Normally, distributed parameters were compared with the "ındependent t-test." For the comparison of the parameters, which did not show a normal distribution, we used "Mann–Whitney U-test".

Discussion

Although most of the risk factors of ROP are known today, it is still not a preventable disease. The blindness rate related to ROP is under 10% in the developed countries but can increase up to 40% in the developing countries, where it affects also infants with relatively higher birth weight and GW (3, 8, 9). American Academies of Pediatrics and Ophthalmology recommended that infants with a birth weight of ≤1500 g or gestational age of 30 weeks or less and infants with birth weight between 1500 g and 2000 g or gestational age of >30 weeks with an unstable clinical course, should be screened for ROP (12). However, studies have shown that these screening criteria might be insufficient for the prevention of blindness related to ROP in developing countries (10, 13, 14).

In our study, we detected ROP at any stage in 32.4% of the screened infants. In a multicenter study conducted in our country, it was found out that the incidence of ROP was 30% (10). The incidence of ROP is 17.9% in the USA, between 19% and 46% in India and 31.3% in Portugal (15–18). According to our results, ROP is a serious problem that may cause potentially blindness for premature babies unless the neonatal intensive care services would be eligible conditions. However, in spite of the high incidence of ROP, the absence of Stage 4 or 5 ROP, which have a poor prognosis at the time of the first diagnosis, shows that an intensive ROP screening program is implemented in our country to reduce the number of blindness related to ROP.

The incidence of severe ROP is 8.31% in the USA, 5%

in Turkey and between 4% and 9% in India (10, 15–17). We considered treatment in 8.8% of the screened infants due to the severe ROP. In light of these data, we noticed that our incidence of severe ROP was comparable with the USA, although the overall incidence of ROP is relatively higher. The finding of the increased incidence of ROP, which should be treated, compared to the data from 2013, may be explained with that our hospital which gives service to the most crowded region of Turkey; the cases, who need treatment, are referred to our hospital from other ROP diagnosis centers in our region, and the ROP incidence increased especially due to the reduced mortality in infants with a lower gestational age.

The incidence of ROP was 77.1% among the infants with a gestational age lower than 28 weeks and 38% of them had severe ROP. In a Swedish study, the incidences of ROP and severe ROP were 72.7% and 34.8%, respectively (19). The same incidences were 64.7 % and 11.6 % in the study of Isaza and Arora; 60.7% and 16.2% in a Chinese study, respectively (20, 21). According to our findings, the incidences of ROP and severe ROP in the patient group with a gestational age lower than 28 are higher than in other countries. Although the mortality rate of the infants with a very low gestational age is gradually declining, the incidence of ROP, which causes severe ocular morbidity, continues to be still at a high level.

The evaluation of infants with a gestational age higher than 32 showed that the incidences of ROP and severe ROP were 13.1% and 0.9%, respectively. Only 4 infants with a gestational age over 34 weeks had ROP, which needed treatment. The incidence of severe ROP was 0.3% in infants with birth weight over 2000 g. In the USA, it was demonstrated that the incidence of ROP was 1.9% in infants with a gestational age higher than 32 weeks and 2.4% in infants with birthweight over 2500 g. Two separate studies in Turkey, one conducted in the Western Black Sea region and the other in a health center with one of the biggest neonatal intensive care unit, it was shown that no ROP requiring treatment was detected in infants with a gestational age higher than 32 weeks, and it was recommended that the ROP screening should be focused on infants with a gestational age lower than 32 weeks and a birth weight under 1500 g (22, 23). In our study, we detected severe ROP in infants with higher birth weight and gestational age compared to these studies conducted in two separate intensive care units in our country. Our ROP diagnosis treatment center provides screening and treatment service to the intensive care units of other private and state hospitals, besides our intensive care unit. Conflicting results in the same country shows that the neonatal care is still not standardized in our country and ROP will be encountered only in smaller premature infants like in developed countries if the conditions of the intensive care units will be improved. In addition, our findings show the importance of the improvement of the neonatal intensive care regarding staff and technological equipment, supervision of the service quality and development of intensive health strategies against ROP, which causes serious rates of mortality.

All infants with a gestational age lower than 36 weeks, who were hospitalized in intensive care units due to various reasons (asphyxia, meconium aspiration, and sepsis ...), should be considered as high-risk infants by neonatologists regardless of the birth weight and should be referred for a ROP examination. ROP was detected in 28 infants with birth weight over 2500 g, and some of them had a birth weight over 3000 g. The presence of the ROP - even mild - in infants with very high birth weight may indicate that these infants received uncontrolled oxygen treatment and received insufficient care. However, as the epicirisis of these patients were not available, the related risk factors could not be evaluated. In our study, the presence of the ROP in infants with birth weight over 2500 g indicates that all infants, who were referred by neonatologists for the ROP examination, should be examined regardless of the birth weight.

In our study, we were not able to access the detailed epicrisis fulfilled during the hospitalization in intensive care units. Therefore, we were not able to evaluate the infants regarding the risk of ROP development. This is the most important limitation of our study. The lower mean gestational age and birth weight in infants with ROP compared to the infants without ROP confirm that low birth weight and gestational age are important risk factors for ROP development. The detected incidence of ROP and severe ROP was high like in other developing countries. In addition, the presence of ROP in infants with higher gestational age and birth weight emphasizes once again the importance of the necessity of the improvement in the neonatal intensive care unit conditions in our country.

Disclosures

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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

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