

Evaluation of refractive errors in retinopathy of prematurity screening

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ABSTRACT

Aim To evaluate the frequency of refractive errors in premature children in retinopathy of prematurity (ROP) screening to find mutual connection of the prematurity level, disease activity and refractive errors.

Methods A retrospective study was conducted in the Eye Clinic of the University Clinical Centre Sarajevo, between December 2013 and January 2017. A total of 126 patients of gestational age ≤ 34 weeks and birth weight ≤ 2000 g underwent ROP screening program. The patients were divided into three groups: patients without ROP ($n=15$), patients with spontaneous regression ($n=106$) and those with active form of ROP ($n=5$).

Results There were 68 (54.0%) patients with refractive errors: 45 (35.7%) had hyperopia, 17 (13.5%) myopia and six (4.8%) astigmatism. There were three (60.0%) patients with an active form of ROP who had refractive errors: two (40.0%) had myopia and one (20.0%) hyperopia. The group without active ROP had hyperopia as most frequent refractive error, with 10 (66.7%) patients. The average birth weight of the patients without refractive errors was 1403.9 ± 43.4 g compared to 1390.3 ± 104.2 g of the patients with refractive errors ($p=0.498$). The average gestational age was 29.7 ± 0.3 weeks in patients without and 29.0 ± 0.3 weeks in patients with refractive errors ($p=0.126$).

Conclusion The birth weight and the gestational age were significantly lower in patients with the active form of ROP. Lower gestational age and birth weight of premature children increase the chance for the development of refractive errors such as hyperopia in all premature children and myopia in patients with active form of ROP.

Key words: hyperopia, myopia, astigmatism, preterm birth

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INTRODUCTION

Prematurely born infants have an increased probability for developing eye disorders, especially of retinopathy of prematurity (ROP). The ROP is a disease of the eye that affects immature retinal blood vessels during their development. Retinal vascularization begins at the 16th week of gestation starting from the optic nerve and proceeds anteriorly being fully developed by the 36-40th week of gestation (1). Due to preterm birth, the process of vascularization remains incomplete and avascular retina releases vasoactive factors, especially vascular endothelial growth factor (VEGF), which then leads to the formation of new blood vessels (2).

The first case of ROP was described in Boston in 1942 by doctor TL Terry (3) as fibroblastic overgrowth of vascular sheath not recognizing retina as the source of the problem, but noticing that the disease was common in prematurely born infants. Dr Harry K Messenger introduced a term "retrolental fibroplasia", which was used in the next 40 years (3). The term retinopathy of prematurity was introduced by Heath in 1951 (1). Afterwards, many studies have confirmed that the degree of prematurity (gestation age and birth weight) is the main risk factor for the development of ROP (1,4).

After these findings many studies were published supporting ROP evidence. It was found that ROP was one of the most common causes of blindness among children (1). There was a need to develop the screening program that would diagnose ROP in an early stage of life, which provides enough time for the treatment and prevention of the most serious complications. The first guideline with the recommendations for screening was published in 1998 as a Canadian Pediatric Society (CPS) Clinical Practice Guideline (5). The most recent guidelines are published in 2006 by American Academy of Pediatrics (AAP), and in 2008 by the Royal College of Ophthalmologists and the Royal College of Paediatrics and Child Health, UK, both providing recommendations for the detection and treatment of ROP (1,6).

Even though ROP is the main problem during neonatal period, there are other ophthalmological complications that can occur even up to 30 years after the birth as the result of ROP (8). The most severe but rare complications are retinal detachment and blindness. All complications of

ROP can be divided into structural (late retinal detachment, macular dragging, retinal folds, lattice like degeneration, retinal tears) and functional (strabismus, refractive errors, nistagmus, amblyopia, decreased visual acuity, visual field changes, secondary glaucoma) (1).

There were no studies in Bosnia and Herzegovina investigating ROP and its association with refractive anomalies. The results will provide better insight in the problem of prematurity, current treatment options and importance of early screening since many complications may be detected and even prevented with regular check-ups and early treatment.

The aim of this research was to evaluate the frequency of refractive errors in premature children diagnosed during the process of ROP screening, and also to establish an association between the stage of prematurity, disease activity and refractive errors.

PATIENTS AND METHODS

Patients and study design

A clinical, descriptive, retrospective study was conducted at the Ophthalmology-Pediatric and Strabismus Department, Eye Clinic University Clinic Centre Sarajevo. The study included a total of 126 patients, male and females with premature birth and subsequent screening for ROP during the period of December 2013 until January 2017.

All patients had a regular follow up during the six-month period after the screening.

The data were collected using medical histories and the protocol archives of screening for ROP: demographic and clinical data, gestation age, birth weight, medical information from the first exam and all the follow-ups, the copy of medical report of the screening exam, the data about the stage of ROP, conducted eye exams in order to diagnose refractive errors and other ophthalmological complications associated with ROP.

Eligibility criteria were: birth weight (BW) \leq 2000 g, gestation age (GA) \leq 34 weeks. Exclusion criteria were: gestation age $>$ 34 weeks, birth weight $>$ 2000 g, irregular follow-ups, other congenital anomalies in term born babies.

The patients were divided into three groups: Group A - premature born infants who did not develop ROP, Group B - premature born infants who

had less severe form of ROP which spontaneously regressed over time and Group C - premature born infants who had active form of ROP and needed therapy.

The study was approved and supported by the Ethical Committee of the Clinical Centre of the University of Sarajevo. Patient records/information was anonymous and de-identified prior to the analysis.

Methods

Each exam included the eye fundus examination using indirect ophthalmoscopy. The development of retinal vascularization was followed starting from the first exam indicated by neonatologists following the periodic follow-ups. The frequency of follow-ups was determined by the ophthalmologist educated for the screening of ROP.

Refractive errors were determined using retinoscopy and sciascopy in cycloplegia.

The results of screening determined the frequency of follow-ups according to the guidelines of the International Classification of Retinopathy of Prematurity (ICROP) (9).

Statistical analysis

Gathered data were presented through tables and graphs using percentage, mean value, standard deviation, standard error, maximum and minimum values. The χ^2 test and Spearman correlation test were used to test the association. The results were considered statistically significant at $\alpha < 0.05$ with the two-sided confidence interval of 95%.

RESULTS

Of 126 premature infants included in this study, 53 (42.1%) were males and 73 (57.9%) were females. The average gestation age (Figure 1) was 29.6 weeks (range: 24-34 weeks). The average birth weight was 1456.3 g (range: 640 -2000 g) (Figure 2).

The patients were divided in 3 groups. There were 15 (11.9%) patients in group A, 106 (84.1%) in group B and five (4.0%) patients in group C. Refractive errors were diagnosed in 68 (54.0%) patients, of which 45 (35.7%) had hyperopia, 17 (13.5%) myopia and six (4.8%) astigmatism. In Group A five (33.3%) patients had refractive error and all patients had hyperopia, in Group B 60 (56.6%) patients were with refractive error, hyperopia being the most frequent, with

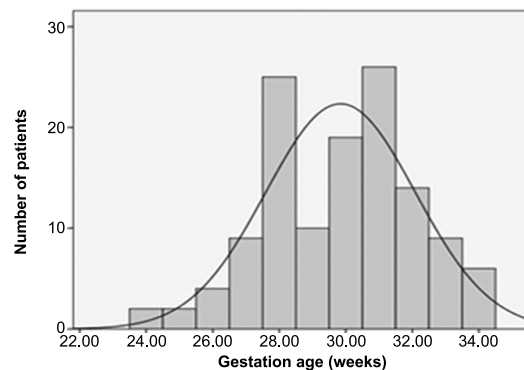


Figure 1. Distribution of patients according to gestation age

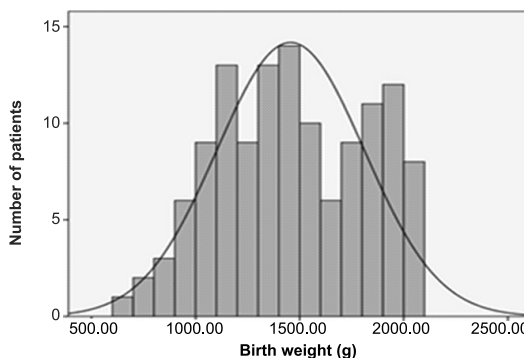


Figure 2. Distribution of patients according to birth weight

39 (36.8%) patients, myopia with 15 (14.2%) and astigmatism with 6 (5.7%) patients. Group C had three (60.0%) patients with refractive error, two (40.0%) with myopia and one (20.0%) patient with hyperopia. There was negative, statistically not significant, correlation between the stage of ROP and the appearance of refractive errors ($\rho = -0.079$; $p = 0.082$) (Table 1).

Table 1. The correlation between the stage of retinopathy of prematurity (ROP) and refractive errors*

Refractive error	Number (%) of patients in the group			
	A	B	C	Total
Absent	10 (66.7)	46 (43.4)	2 (40.6)	58 (46.0)
Myopia	0	15 (14.2)	2 (40.0)	17 (13.5)
Hyperopia	5 (33.3)	39 (36.8)	1 (20.0)	45 (35.7)
Astigmatism	0 (0.0)	6 (5.7)	0	6 (4.8)
Total	15 (100.0)	106 (100.0)	5 (100.0)	126 (100.0)

* $\chi^2 = 7.785$; $p = 0.254$; $\rho = -0.079$; $p = 0.082$

The average birth weight (BW) in patients who did not develop any form of refractive error was 1403.9 ± 43.4 g (range: 820 – 2000 g). There was a small difference in patients who had a refractive error. The average BW of patients who had myopia was 1390.3 ± 104.2 g (range: 740 – 2000 g). Patients with hyperopia had average BW of 1545.8 ± 53.6 g (range: 640 - 2000 g), astigmatism had average BW 1478.3 ± 91.6 g (range 1200 g - 1750 g) (Figure 3).

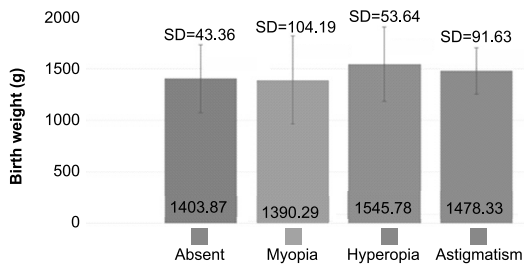


Figure 3. Refractive errors compared to birth weight

The average gestation age (GA) in patients who did not develop a refractive error was 29.7 ± 0.3 weeks (range: 25-34 weeks). The average GA in children with myopia was 29.0 ± 0.6 weeks (range: 24 – 32 weeks), in hyperopia 30.3 ± 0.3 weeks (range 26- 32 weeks) and in astigmatism 30.7 ± 0.8 weeks (range: 28 – 34 weeks) (Figure 4).

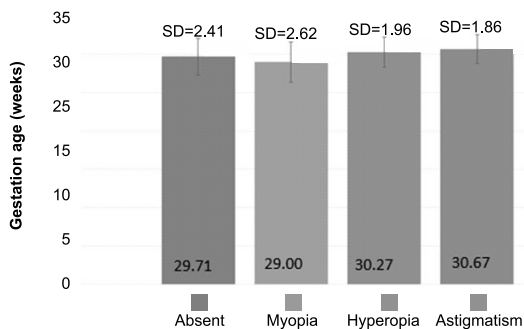


Figure 4. Refractive errors compared to gestation age

DISCUSSION

A total of 126 premature infants met the inclusion criteria for the study. There was a small difference in sex distribution of patients, with females being more frequent compared to male patients.

Most patients had a mild form of the disease, which spontaneously regressed during the period of follow-up. Only several patients developed the active form of ROP, which required the treatment. The treatment options included anti-VEGF, laser treatment or vitrectomy. All of these patients were regularly controlled due to the possibility of developing ophthalmological changes even 30 years after the diagnosis (8). In the study from the Netherlands, Schalijs-Delfos et al. showed a higher percentage of children with the active form of ROP (25.9%) compared to our study (10). This difference can be due to improved care for premature children in the last two decades.

More than a half of patients in our study (54.0%) developed a refractive error. Hyperopia was most frequent followed by myopia and astigmatism. These results were similar to findings in healthy newborns, where hyperopia was more frequent

and more common than other refractive errors. However, other studies showed myopia as more frequent in premature infants (11-13).

Quinn GE et al. also showed that myopia was the most frequent refractive error among premature infants, which was explained with the structural changes happening in the eye due to ROP, but also with the laser or anti-VEGF treatment that leads to eye elongation thus causing myopia (7,11,12). The low number of children with active ROP and therefore the low number of children treated with laser or anti-VEGF can be the reason for low percentage of myopic patients in our research.

The prevalence of hyperopia in our study could be explained with the high number of patients with a mild form of ROP which spontaneously regressed, or patients who did not have any form of ROP, which was consistent with term-born children (8,13). Astigmatism in our study was the least frequent refractive error, with lower frequency than in other studies (8,12). According to the study the prevalence of astigmatism was increased in those patients who were treated with laser due to the structural changes caused by laser scars (12). Low prevalence of astigmatism could again be explained with the low number of performed laser treatments.

In group A 66.3% of infants in our study were emmetropic at the end of the follow-up period. Natural course of these patients is a shift during the development of the eye (14). Group B had 49% of emmetropic patients. When already myopic patients from this group are taken into account, it is expected that the number of myopic patients gets as high as 63.2%. In group C 80% of patients are expected to be myopic at the end of the development stage. These results are now even more consistent with other studies worldwide that indicate that children with active ROP are most likely to develop myopia (7,12). A limitation to our study was the fact that hyperopia was not defined in charts available to the study, and low hyperopia (as high as +3.25) is found in 95% of all normal infants (14). If it had been defined, these patients would probably become myopic in the future.

The average birth weight in the patients without refractive errors was higher than in the patients with refractive errors, where hyperopia had the highest average BW. The lowest BW was in patients with myopia. This showed that there was a negative correlation between the appearance

of refractive errors and birth weight. As the birth weight was lower, the higher was the opportunity for developing a refractive error, especially myopia. These results were consistent to the other studies (11,13).

The highest gestation age was found in patients who had astigmatism followed by hyperopia; the lowest one was in emmetropic patients and in myopia. Taking into account myopic shift, it can be argued that there was a difference in average GA and the appearance of refractive errors. As the GA was lower, the higher was the chance of developing myopia, which was again consistent with the other studies (7, 11, 13). However, these results were not statistically significant, which could be explained with the fact that structural changes occur during the active phase of ROP, and thus lead to the change of refractive power of the eye, more than the level of prematurity does (13).

The limitation of this study was primarily a relatively small number of patients in active form of ROP group. Additionally, long term follow up of

18 years would be more accurate, because of natural changes in refraction and eye function occur in this period of life. Also different ophthalmological conditions could occur as a result of ROP through life, of which refractive errors are most common. A higher level of significance would be accomplished if the number of patients treated with laser photocoagulation were higher. If these limitations would be corrected, more statistically significant results would be achieved.

The results of this study are beneficial to give more insight into changes of premature babies and their refractive errors in everyday practice of paediatric ophthalmologists and paediatricians and to encourage similar screening programs in all major medical centres in Bosnia and Herzegovina.

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TRANSPARENCY DECLARATION

Competing interests: none to declare.

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