

# Ophthalmological follow-up of prematurely born children in preschool age: prospective study of visual acuity, refractive errors and strabismus

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**Background.** Preterm birth is a very relevant problem. Retinopathy of prematurity in its severe forms causes visual impairment or can lead to blindness. The aim of the present study was to describe the visual outcome in prematurely born and full-term children at the preschool age and to evaluate the effects of prematurity per se, ROP, and treatment on visual acuity and refractive errors.

**Materials and methods.** A prospective study on the incidence of ROP during 2006–2008 included 103 preterm infants. 81 had ROP and 22 had no history of ROP; 40 were age-matched healthy children. All underwent a complete ophthalmic examination.

**Results.** Significant myopia ( $\leq -0.50D$ ) in prematurely born children differed from full-term ones. The ROP treated group had the highest prevalence of myopia ( $P < 0.001$ ). Astigmatism ( $>2D$ ) was dominant in the premature group (39%) as compared with the control group (0%) ( $P < 0.05$ ). 65% had significant anisometropia and 35% had high anisometropia in the preterm group and only 5% had significant anisometropia in the full-term group ( $P = 0.014$ ). Within the preterm group, the ROP treated children had the highest frequency of anisometropia and strabismus ( $P = 0.001$ ). Visual acuity was significantly better in the full-term than in prematurely born children ( $P < 0.001$ ). Three children (7.7%) of the premature ROP treated group were visually impaired.

**Conclusions.** Refractive errors, astigmatism, anisometropia and strabismus were more common in prematurely born children than in those born at term, especially the ROP treated group. ROP outcome and prematurity per se remain risk factors for visual impairment to prematurely born children at preschool age.

**Key words:** preterm birth, retinopathy of prematurity, treatment, visual impairment

Preterm birth is still a very relevant problem around the world. The World Health Organization (WHO) describes prematurity as babies born before 37 completed weeks of gestation or fewer than 259 days since the first day of a woman's last menstrual period (1). It is well known that prematurely born children have an increased risk of ophthalmologic problems. The preterm neonate may develop ophthalmic sequelae, which can be due to prematurity per se, due to retinopathy of prematurity (ROP) or due to neurological damage (2).

Retinopathy of prematurity (ROP) is a leading cause of childhood blindness in some regions around the world. ROP is characterized by abnormal vascular development of retina in premature infants (Committee for the Classification of Retinopathy of Prematurity 1984) (3). In its severe forms, it causes severe visual impairment or even can lead to blindness. This brings a high financial cost for the community and huge individual costs by affecting the normal motor, language, conceptual, and social development of the child. In the United States, ROP remains the second most common cause of childhood blindness (4). In the past years, in Lithuania the incidence of ROP is decreasing. It is essential for every country to know the prevalence and major causes of childhood blindness in order to control and monitor the changing patterns over time. Because of socioeconomic status the cause of childhood visual impairment and blindness differs between and within countries.

Few studies have shown that children born prematurely have an increased risk of visual impairment, higher incidences of low vision, strabismus, visual field defects and contrast sensitivity (5–18). Those studies have shown outcome and development of the visual functions of children at different ages. Hence, ophthalmologic follow-up is necessary. But still there is no agreement on a follow-up in these children.

The aim of the present follow-up study is to describe the visual outcome in prematurely born and full-term children at the preschool age (5–7 years) and to evaluate the effects of prematurity per se, ROP, and treatment on visual acuity and refractive errors.

## MATERIALS AND METHODS

Our follow-up study on the incidence of ROP during 2006–2008 in Vilnius, Lithuania, included 103 prematurely born infants with a mean birth weight

of 1 343 g and a mean gestation age of 29.4 gestation weeks. From 103 prematurely born 81(78.6%) had ROP and 22(21.4%) had no history of ROP. From the ROP group 39(48.1%) had been treated and 42(51.9%) did not receive any treatment, because ROP regressed. From the ROP treated group 24(61.5%) had been cryotreated, 14(35.9%) had been treated using laser therapy and cryotherapy, and 1(2.6%) had been treated using only laser therapy. There were no treated patients with intravitreal bevacizumab (Avastin, Genentech, USA), a vascular endothelial growth factor (VEGF) antibody injection (19). The criterion for treatment was ROP stage 3 in at least 5 contiguous clock hours in zone II, even in the absence of plus disease. All eyes fulfilling our criterion for treatment were treated.

There were 51(49.5%) boys and 52(50.5%) girls in the premature group. According to the stage of ROP, all children (between 5–7 years of age) were divided into 4 groups: group I was children, who had ROP and had been treated ( $n = 39$ ); group II was children with regressed ROP, who had not received any treatment ( $n = 42$ ); group III was children who were born prematurely but who had no history of ROP ( $n = 22$ ); group IV was the age-matched group of healthy children who had been born at full term (gestation age [GA] 39–41 weeks, birth weight [BW] 3 000–4 000 g, control subjects,  $n = 40$ ). The full-term children had been born in exactly the same period and in the same geographical area as the prematurely born children, and were recruited from our clinic.

Patients were selected from the records of our hospital, and a telephone call was made to the families to take part in the study. During 2006–2008, in the Children's Hospital, Affiliate of Vilnius University Hospital Santariškių Clinics, there were 150 preterm infants who were diagnosed with ROP. Of the 150 children, 4 emigrated, 2 died, 27 declined to participate in the study, 5 were excluded because of general diseases unrelated to prematurity, 6 were excluded from the study, because they had a history of cerebral damage or severe congenital defects that prevented their cooperation in the test, and 25 were not reachable. As well, we included 22 patients, who were born prematurely in 2006–2008, were treated in our hospital, but had no history of ROP. Hence, 103 children were examined at 5–7 years of age.

A written informed consent was taken from the parents or guardians of each child.

The present study conformed to the tenets of the Declaration of Helsinki and the approval for this study was obtained from the Institutional Ethics Committee of our center.

We reviewed the birth histories of 103 patients and perinatal data were abstracted from the medical records regarding their birth history – gestational age (GA), birth weight (BW), stage of ROP, maximal severity in acute disease, presence of neurologic deficits or events (as an intraventricular hemorrhage in the neonatal period and obvious neurologic sequelae – epilepsy, cerebral palsy, mental retardation), and significant complications that developed in the neonatal stage. The ophthalmological status – the type of peripheral ablative procedure, such as laser therapy or cryotherapy, was recorded. The stage and severity of ROP were classified according to the International Classification of ROP (20).

All children underwent a complete ophthalmic examination by the same physician, including the best-corrected distance and near visual acuity (VA), automatic cycloplegic refraction followed by manual cycloplegic retinoscopy (spherical equivalent and astigmatism were determined) and indirect fundus examination. The best-corrected visual acuity (BCVA) of each eye was separately evaluated according to the Monoyer system at a distance of 5 meters with a Snellen E chart, and near BCVA at a distance of 0.4 m. The Snellen VA was converted to the logarithm of the minimum angle of resolution VA (logMAR) for statistical analysis. BCVA was divided into three groups in the Decimal notation: group I – when visual acuity was lower than 0.3; group II – visual acuity ranged between 0.3 – <0.7; group III – visual acuity was 0.7–1.2. The visual acuity of <0.3 was considered as low vision (21).

An examination of ocular movement and a cover test for distance and near vision were performed. Stereopsis was assessed by using the Stereo 'Fly' test (standard stereo testing) and the 'Lang' Stereo test 'I and II'. Stereoscopic vision and depth perception testing was important in identifying a defect in binocular vision and higher risk of amblyopia, strabismus, severe anisometropia, or extremely poor vision caused by retinal or optic disease. Cover and cover-uncover tests for distance and near vision were performed to detect strabismus. Strabismus was defined as all types of intermittent and manifest strabismus, and microtropia was determined as well. All patients were tested for ocular motility.

Cycloplegic refraction was carried out by manual streak retinoscopy after dilating the pupil with cyclopentolate 1%, twice at an interval of 10 min, 30 min before examination. Refractive values were converted to the spherical equivalent (= spherical refractive value + half of cylindrical refractive value) as well astigmatism was documented. Astigmatism was recorded as a negative cylinder and defined as significant when  $\geq 1.0$  diopters (D) and high when  $\geq 2.0$  D. Children were considered to have a significant refractive error if they had hypermetropia  $\geq 2.0$  diopters (D), myopia  $\leq -0.50$  D. Anisometropia was defined as significant when the difference in the spherical equivalent between the eyes was  $\geq 1$ D, and high if  $\geq 2$ D. Amblyopia was defined as a 2-line logMAR difference between the two eyes in the presence of an amblyogenic factor such as anisometropia, strabismus, high ametropia, or form deprivation. An anterior segment examination with a slit lamp and indirect funduscopy were performed in all children. Ophthalmoscopy was performed through dilated pupils. The peripheral fundus was examined with an indirect ophthalmoscope and a type of a peripheral ablative procedure, such as laser therapy or cryotherapy, was recorded.

A statistical analysis was performed using the standard statistical program (SPSS 23, EXCEL for Windows). Categorical data were presented as frequency (%) and continuous variables were presented as a mean  $\pm$  standard deviation (SD). Normal distribution of the continuous data was tested by a Shapiro-Wilk test. Comparing several groups a 1-way analysis (ANOVA) was used, and the Fisher's exact test was used to compare the differences in the categorical variables between the two groups. Finally, a stepwise multiple regression analysis was used to evaluate the effects of GA at birth, BW, stage of ROP, treatment, and refraction on VA and astigmatism.

$P < 0.05$  was considered significant.

## RESULTS

A total of 143 patients met our screening criteria and completed the examinations. There were 39 in group I, 42 in group II, 22 in group III, and 40 in group IV. Data on demographic features – GA, BW and gender are given in Table 1.

The distribution of ROP stages and treatment among prematurely born children are given

**Table 1.** Demographic data of prematurely born and full-term children

	Participants, n	Gender, M/F, n	GA at birth, wk *	Birth weight, g *
Control group (IV)	40	23/17	39–41	3 000–4 000
Preterm without ROP (III)	22	12/10	31.1	1 698
Preterm with regressed ROP (not treated) (II)	42	19/23	29.8	1 332
Preterm with ROP (treated) (I)	39	20/19	27.9	1 155

\*Data are given as mean GA, BW for preterm children. The full-term children had GA at birth of 39–41 weeks and BW of 3 000–4 000 g.

in Table 2 (all eyes fulfilling the criterion for treatment were treated).

**Table 2.** ROP stages and treatment among prematurely born children

	ROP treated (39)		ROP untreated (42)	
	n	%	n	%
ROP stage I	0	0.0	19	45.2
ROP stage II	0	0.0	22	52.4
ROP stages III–V	39	100.0	1	2.4
	39	100.0	42	100.0

There was no statistically significant difference between the right and left eyes in the analyses of spherical equivalence (SE) or astigmatism ( $P > 0.05$ ). Therefore, we decided to present our results of the right eyes only.

The mean GA and BW for group I were significantly lower than those of the other groups ( $P = 0.0004$  and  $P = 0.002$ ). The mean age of children at the time of examination was  $6.55 \pm 0.70$  years (range, 5–7 years) ( $P < 0.05$ ). There was no difference in gender distribution among the groups.

The mean SE's in the control and premature groups were similar, even when we compared the right and left eyes separately. In the group of premature born children, treated eyes (group I) differed from the not treated ROP group (group II) and had a lower SE mean value (0.35D) ( $P = 0.04$ ). But we did not find any significant difference when we compared the control group (IV) with the premature group (III) ( $P > 0.05$ ).

Differences in the distribution of SE's between four groups are illustrated in Table 3.

**Table 3.** Distribution of SE's between four groups

	Group I (39)	Group II (22)	Group III (22)	Group IV (40)
SE (SD)	0.35(3.51)	1.61(1.43)	1.15(1.92)	1.21(1.15)
Min	-9.63	-0.50	-1.38	-1.63
Max	7.25	5.50	6.38	4.00

In a multiple regression analysis of the premature born children, GA at birth, BW, stage of ROP, and treatment were included as independent risk factors. Only treatment was significantly associated with reduction of SE ( $P < 0.05$ ).

The prevalence of hypermetropia ( $\geq 2D$ ) was higher in the premature group, especially in groups I and II, but there was no significant difference from the control group ( $P = 0.051$ ), and no difference within the preterm group.

Significant myopia was measured from  $\leq -0.50D$ . We found that prematurely born children differed from the full-term group. In the ROP treated group (group I) they had the highest prevalence of myopia ( $P < 0.001$ ) and differed from other subgroups. Especially significant difference was seen when we compared group I and group II, it showed that the ROP treated children had the highest prevalence of myopia ( $P = 0.0001$ ).

The distribution of refractive errors between four groups is illustrated in Table 4.

There was an obvious tendency in the distribution of refractive errors according to GA and BW.

Table 5 represents a statistically significant difference between the myopic and emmetropic children in the analysis of GA and BW ( $P = 0.05$ ).

When we evaluated astigmatism, we found that the control group (IV) had less total astigmatism (mean value) than the preterm group ( $P = 0.03$ ).

Astigmatism more than 2D was more dominant in the premature group (39%) than in the control group (0%) ( $P < 0.05$ ), especially the premature

**Table 4.** Distribution of refractive errors between four groups

	Preterm with ROP (treated) (I) n, %	Preterm with regressed ROP (not treated) (II) n, %	Preterm without ROP (III) n, %	Control group (IV) n, %
Myopia ( $\leq -0.50$ D)	14(35.9%)	6(14.4%)	5(22.7%)	3(7.5%)
Hypermetropia ( $\geq 2$ D)	12(30.8%)	13(31%)	5(22.7%)	6(15%)

**Table 5.** Difference between the myopic and emmetropic children in the analysis of GA and BW

	GA, wk	BW, g
Myopic	27.9	1 118.5
Hyperopic	28.6	1 217.6
Emmetropic	29.4	1 312.1

treated group had the highest prevalence of astigmatism – more than 2D.

The distribution of astigmatism in all four groups is given in Table 6.

In a stepwise logistic multiple regression analysis of astigmatism (total) in the premature born children, GA at birth, BW, stage of ROP, and treatment were included as independent risk factors. Only treatment was significantly associated with increased astigmatism ( $P < 0.05$ ).

Anisometropia was significantly greater in the premature group than in the control group. There were 65% ( $n = 15$ ) significant anisometropia ( $\geq 1$ D

and  $< 2$ D) and 35% ( $n = 8$ ) high anisometropia ( $\geq 2$ D) in the preterm group and only 5% ( $n = 2$ ) significant anisometropia in the full-term group ( $P = 0.014$ ).

Within the preterm group, the ROP treated children (group I) had the highest frequency of significant and high anisometropia. The distribution of anisometropia is given in Table 7.

Amblyopia was found in 2.5% of the control group and 4.5% in the premature group, without ROP. It was significantly greater in the group I (41%) than in the group II (7.1%) children ( $P = 0.0005$ ). Strabismus had significant prevalence in the preterm groups, especially in the ROP treated group ( $P = 0.001$ ) (Table 8).

In our study monocular BCVA was significantly better in the full-term than in the prematurely born children ( $P < 0.001$ ).

Within the preterm group, distance and near BCVA of the group I children was lower than in the other subgroups.

**Table 6.** Astigmatism

	$\geq 1$ D and $< 2$ D	$\leq 2$ D	Total n, %
Control group (IV) ( $n = 40$ )	11(27.5%)	0(0%)	11(27.5%)
Preterm without ROP (III) ( $n = 22$ )	15(68%)	2(5%)	17(73%)
Preterm with regressed ROP (not treated) (II) ( $n = 42$ )	19(45.2%)	4(9.5%)	23(54.7%)
Preterm with ROP (treated) (I) ( $n = 39$ )	12(30.8%)	24(61.5%)	36(92.3%)

**Table 7.** Anisometropia

	$\geq 1$ D and $< 2$ D	$\geq 2$ D	Total n, %
Control group (IV) ( $n = 40$ )	2(5%)	0(0%)	2(5%)
Preterm without ROP (III) ( $n = 22$ )	1(4.5%)	0(0%)	1(4.5%)
Preterm with regressed ROP (not treated) (II) ( $n = 42$ )	3(7.1%)	0(0%)	3(7.1%)
Preterm with ROP (treated) (I) ( $n = 39$ )	11(28.2%)	8(20.5%)	19(48.7%)

**Table 8.** Strabismus (Esotropia/Exotropia)

	Preterm with ROP (treated) (I) n, %	Preterm with regressed ROP (not treated) (II) n, %	Preterm without ROP (III) n, %	Control group (IV) n, %
Esotropia	11(28.2%)	4(9.5%)	2(9.1%)	1(2.5%)
Exotropia	5(12.8%)	0(0%)	0(0%)	0(0%)

The mean value (SD) of distance and near BCVAs are summarized in Table 9.

**Table 9.** The mean value (SD) of BCVAs

	BCVA (logMAR) distance	BCVA (logMAR) near
Control group (IV) (n = 40)	-0.01(0.03)	-0.04(0.03)
Preterm without ROP (III) (n = 22)	0.00(0.00)	0.00(0.00)
Preterm with regressed ROP (not treated) (II) (n = 42)	0.00(0.03)	0.03(0.02)
Preterm with ROP (treated) (I) (n = 39)	+0.11(0.16)	+0.12(0.14)

When distance VA was divided into three groups, we found that 3 children (7.7%) of the premature ROP treated group were visually impaired according to the WHO's criteria, that is, VA below 0.3 in the better eye (21). 15.4% of the group I and 2.4% of the group II children had BCVA between 0.3 – <0.7.

Children who had received treatment differed from all other subgroups; therefore only 76.9% in this group had BCVA in the best vision group ( $P = 0.001$ ).

We have not found any significant difference of hypermetropia ( $\geq 2D$ ) in the control and premature group children, but a significant difference of myopia ( $-0.50D$  or less) and astigmatism ( $\geq 2D$ ) in the premature born children, especially in the ROP treated group than in other subgroups. The ROP treated children had the highest risk of myopia and high astigmatism, but those who were born prematurely, with regressed ROP or without ROP, also tend to develop astigmatism and myopia. Distance and near BCVAs were significantly reduced in the ROP treated children group (group I).

## DISCUSSION

It is well known that ocular structures are continuing to develop and grow even after birth (22). No doubt that children born prematurely, even without clinically significant complications, have an increased incidence of unfavourable ophthalmic outcomes. These risks exist not only for extremely

premature babies but also even for those who did not develop ROP.

In this study, we focused on evaluating the visual outcome of prematurely born children at the pre-school age and their risk factors in comparison with full-term children at the same age.

There is data that low birthweight children have increased difficulties at school and require significantly more educational assistance because they usually have lower intelligence quotients and academic achievement scores (23).

We examined children at 5–7 years of age, who were born prematurely and had or not a history of ROP. This study showed that refractive errors, as myopia and astigmatism, were more common in the prematurely born children than in those born at term.

Significantly it was notable in the ROP treated children (group I) when we compared them with the ROP children who did not receive the treatment (group II). The ROP treated group had the highest prevalence of myopia, astigmatism ( $\geq 2$ ) and anisometropia. The prematurity per se was found as a risk factor for astigmatism ( $\geq 1$  and  $< 2$ ) and myopia in prematurely born children, without ROP.

The preterm born children had a higher prevalence of hypermetropia ( $\geq 2D$ ), especially in group I and II, but it did not reach a statistically significant difference when we compared with the control group (IV). Significant myopia was measured from  $\leq -0.50D$  and differed in prematurely born children from the full-term group. In the ROP treated group (group I) they had the highest prevalence of myopia and differed from other subgroups. Anisometropia and astigmatism were also more frequent and greater in the premature group than in the control group. Hypermetropia was found equally in the ROP treated (group I) and untreated (group II) children (30.8 and 31%).

High prevalence of various refractive errors was found in the prematurely born ROP treated children, but it does not explain all differences between the control and preterm children, because we also found differences in myopia and astigmatism between the control and prematurely born children without ROP (prematurity per se).

This study has proved that prematurely born children had poorer VAs than children born at term. We found this difference in distance and near BCVA.

ROP treatment and astigmatism were significantly correlated with reduced VA in the preterm ROP groups.

There are few similar studies in the world (24, 8–10, 25–29, 5, 30, 11, 13) that evaluated refraction, vision, optical components and changes of retina in prematurely born children with and without ROP. Those researchers evaluated preterm born children of age different from our study. Because of different age of the study group, different epidemiological features and methods, it is difficult to compare our study to other studies performed worldwide.

There are studies that are hospital based (24, 26–28) while others are population based (8–11, 13, 25). To our knowledge, a Swedish population-based study of prematurely born children at 6.5 years of age is going in Sweden, but still there is no data published on their visual outcome.

Our study was hospital based regarding children born preterm and full-term. The preterm and full-term children groups were born in the same period and in the same geographical area, and were examined in exactly the same way, what warranted exact comparison between the groups. A comparison of the refractive data from our study with those of other studies (11, 7, 28, 14) is quite difficult because those studies differ in their methods and epidemiological features.

Despite differences of those studies, we found that some researches (31, 32, 26–28) had also found a high prevalence of myopia in prematurely born children. This was very similar to our findings, where we noticed that myopia and astigmatism were more common in prematurely born children than in those born at term. In comparison with the Swedish population-based study (11), our findings were quite similar. The difference was that we did not distinguish significant and high myopia as they did, we evaluated significant hypermetropia as  $\geq 2D$ , not as the Swedish study  $\geq 3D$ , either children's age differed at the examination.

The results of both studies showed that in the preterm group, ROP treated children had higher prevalence of myopia (despite different significant myopia evaluation), astigmatism and anisometropia. Both astigmatism and anisometropia were slightly frequent in our study.

Fielder et al. (33) had reported about the association of myopia and premature birth (physiological myopia, myopia without ROP, myopia caused

by ROP). Our study results confirmed 2 types of myopia: without ROP, and myopia caused by ROP. Together with other researchers (27, 28, 34–36) we have found a high prevalence of myopia in ROP treated children. We did not observe similar distribution of myopia in both ROP treated and ROP untreated eyes, as Quinn et al. (27). Unfortunately, we cannot answer the question whether the prevalence of myopia in the ROP treated group of our study was due to the cryotreatment or the severe ROP per se since all eyes fulfilled the criteria for treatment in the neonatal period. Data from other studies (7, 10, 38) have also shown a higher prevalence of myopia in prematurely born children without ROP than in those born at term. In the Swedish population-based study (11) prematurity per se had the greatest effect on myopia of less than  $-3D$ . In the beginning of our study we evaluated myopia as significant from  $\leq -0.50D$  and did not distinguish separate groups. When we decided to reanalyze our results according to the criteria of the Swedish study, it became very similar to it. Finally, in the present study prematurity per se showed to have the greatest effect on myopia of less than  $-3D$ . None of the preterm children without ROP had higher myopia.

We evaluated significant hypermetropia ( $\geq 2D$ ) and found no significant difference in the control and premature group children, unlike the Swedish population-based study (11), but equal to some other reports (39, 40). In their study Swedish researchers asserted that prematurity per se seemed to be of importance for significant hypermetropia (11). As Darlow et al. (9) and Larsson (11), we found no difference in the prevalence of hypermetropia within the premature group. When we used the analysis of Swedish criteria in the present study, the results showed that cryotreated children had very similar prevalence of hypermetropia as children without ROP, in accordance with the study by Ricci (41) and Larsson (11).

Astigmatism was significantly more common in the preterm group than in the control children group in the present study, similar results confirmed by Larsson (11) and Fledelius (7). The degree of astigmatism in prematurely born children increases with severity of ROP (42). The present study revealed that the prevalence of astigmatism more than  $2D$  was dominant in the premature group compared with that in the control

group, especially the premature treated group had the highest prevalence of astigmatism more than 2D. The Swedish population-based study (11, 13, 14, 16) had confirmed that the stage of ROP and cryotreatment per se were identified as risk factors for astigmatism of 1D. In the Quinn et al. (27) study the results showed a tendency for a higher frequency of astigmatism of 1D or more in treated than untreated eyes. Our study was unable to evaluate the influence of treatment on ROP treated eyes, because all eyes fulfilling the criteria for treatment underwent laser or cryotherapy.

In accordance with Larsson (11, 13, 15) and Fledelius (7), in our study we found the prevalence of significant and high anisometropia in the prematurely born children than in full-term children. Within the preterm group, ROP treated children (group I) had the highest frequency of anisometropia, as noted by other researches (40, 34).

In the studies by Fledelius (6) and Holmstrom et al. (17) the incidence of strabismus was frequent in the prematurely born group than in the full-term group. Our findings coincide with latter studies, and agree that particularly strabismus was expressed in those given treatment children. Esotropia was the dominant type of strabismus as noted by our and other studies (17, 18).

This study showed that group I (ROP treated children) had the highest risk of reduced VA. The reduction in BCVA showed a gradual progression from group IV to group I. Nevertheless, we did not find any difference in distance and near BCVA between the children with regressed ROP (group II) and the children without ROP (group III). Our VA findings are very similar with the Swedish population-based study in prematurely born children at 10 years of age (13) where they noted that children who had received cryotherapy had the highest risk of a reduced VA. In the present study, in the ROP treated group 24(61.5%) were cryotreated, 14(35.9%) got both laser and cryotherapy, and 1(2.6%) were treated using only laser therapy. Therefore we could not exclude cryotherapy as a separate treatment from other options, and cannot compare results of different treatment groups.

Fledelius (7) and Darlow et al. (9) in their population-based studies analyzed premature born children and noted that children with ROP in the neonatal period had the highest risk of re-

duced VA. This was also observed in the O'Connor et al. (10) study, concerning children with severe ROP, but in the mild ROP group they have found VAs similar to those without ROP. In our study as well as in the Swedish population-based study (11, 13, 14, 16), it could not be determined whether the reduced VA in the treated eyes was due to the treatment or the severe ROP per se. Therefore all eyes corresponding to the criteria for ROP treatment had been treated.

The American multicenter trial of CRYO-ROP (37) and the study by Ng et al. (30) showed that VA outcome of children who received cryotherapy was worse than that in our study. The idea was that ROP might change the function of photoreceptors (43, 44).

But this hypothesis whether the treatment prevented progression to a more severe ROP, saved the retinal function and conducted to better outcome of VA cannot be clarified. Though, in the multicenter study of the Early Treatment for Retinopathy of Prematurity (ETROP) better visual outcome was found in 9-month-old children treated at high risk prethreshold ROP than in those children who were treated with threshold ROP (45).

Fledelius (7) in his study has noted that children with neurologic complications had poorer VA than those without such complications. In accordance with Darlow et al. (9) and O'Connor et al. (10) we did not associate VA results with neurologic findings.

Though distance and near VAs were poorer in preterm children than in children born at term, we think that the whole visual outcome in our study of preterm children was good. In accordance with the three VA groups, in the present study we summarized that 3 children (7.7%), who had received ROP treatment, were visually impaired according to the WHO's criterion ( $VA < 0.3$ ) (21). 15.4% of group I (ROP treated) and 2.4% of group II (ROP untreated) children had VA between  $0.3 - <0.7$ .

The prematurely born ROP treated group differed from all other subgroups; therefore only 76.9% of this group had VA between 0.7–1.2. All prematurely born children without ROP (III) and the control group children (IV) had VA between 0.7 and 1.2. There were no children from preterm without the ROP group (III) and the control group (IV) in the "low vision" group. According to Larsson et al. (13) in their study, visual



impairment was found in 4(1.8%) of prematurely born children of whom 1(0.4%) was blind. This prevalence was lower than in other population-based studies (7, 9, 10).

In the studies by Fledelius (7), Darlow et al. (9) and O'Connor et al. (10) there were various prevalences of visual impairment; most of those children were blind because of ROP. Whereas none of these children were cryotreated because they had been born prior to recommendations of "threshold disease" treatment were proposed (37).

In the multiple regression analysis of the Swedish study (11, 13, 15), they showed that astigmatism had a negative effect on good VA. According to Fledelius (7) in his study he concluded that children with high and moderate myopia had a reduced VA, but a spherical equivalent was not a significant risk factor in the multiple regression analysis. In the multiple regression analysis of our study myopia and astigmatism were risk factors for the poor VA.

## CONCLUSIONS

In conclusion, refractive errors were more common in prematurely born children than in those born at term. The mean spherical equivalents were similar in both groups, but the distribution of refractive errors differed. The prematurely born children had a higher prevalence of significant myopia. Astigmatism and anisometropia were more common and more severe in premature children, especially in the ROP treated group. Also, prematurely born children without ROP (prematurity per se) had the greatest effect on myopia of less than -3D.

We agree with Holmstrom and Larsson's suggestion, concluded from the Swedish population-based study, that prematurely born children not only treated or with previous ROP, but also those without ROP history in the neonatal period, should be followed up further (11, 13, 15). The results of our present study showed that ROP outcome and prematurity per se remain risk factors for visual impairment to prematurely born children at preschool age.

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Received 7 December 2015

Accepted 14 December 2015

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#### **GIMUSIŲ NEIŠNEŠIOTŲ IKIMOKYKLINIO AMŽIAUS VAIKŲ OFTALMOLOGINĖS SISTEMOS IŠTYRIMAS: REGĖJIMO AŠTRUMO, REFRACINIŲ YDŲ IR ŽVAIRUMO ĮVERTINIMAS PROSPEKTYVINĖJE STUDIJOJE**

##### *Santrauka*

**Tikslas.** Nustatyti gimusių neišnešiotų ir išnešiotų ikimokyklinio amžiaus vaikų regėjimo sistemos būklę ir įvertinti neišnešiotumo, retinopatijos bei jos gydymo pasekmes regėjimo aštrumui ir refrakcinių ydų vystymuisi.

**Medžiaga ir metodai.** Į stebėjimo tyrimą buvo įtraukti 103 neišnešioti vaikai, gimę 2006–2008 m.: 81 buvo diagnozuota neišnešiotų naujagimių retinopatija (NNR), 22 ši liga nepasireiškė, 40 buvo laiku gimusių sveikų vaikų. Visiems jiems buvo atliktas išsamus oftalmologinis ištyrimas.

**Rezultatai.** Neišnešiotų vaikų grupėje trumparegystė ( $\leq -0,50D$ ) reikšmingai skyrėsi nuo išnešiotų vaikų. Nuo NNR gydytų vaikų grupėje trumparegystė pasireiškė labiausiai ( $p < 0,001$ ). Astigmatizmas ( $>2D$ ) labiau dominavo neišnešiotų vaikų grupėje (39 %) nei išnešiotų (0 %) ( $p < 0,05$ ). 65 % reikšminga ir 35 % didelė anizotropija pasireiškė neišnešiotiems vaikams ir 5 % reikšmingos anizotropijos atvejų nustatyta išnešiotiems vaikams ( $p = 0,014$ ). Neišnešiotų ir nuo NNR gydytų vaikų grupėje daugiausia buvo anizotropijos ir žvairumo atvejų ( $p = 0,001$ ). Regėjimo aštrumas buvo geresnis išnešiotų vaikų nei neišnešiotų ( $p < 0,001$ ). Trys (7,7 %) vaikai neišnešiotų ir nuo NNR gydytų vaikų grupėje buvo silpnaregiai.

**Išvados.** Refrakcinės ydos, astigmatizmas, anizotropija ir žvairumas dažniau pasitaikė neišnešiotų vaikų grupėje, ypač tarp nuo NNR gydytų vaikų. Ikimokyklinio amžiaus neišnešiotiems vaikams regėjimo sistemos sutrikimo rizikos veiksniais išlieka NNR ir neišnešiotumas.

**Raktažodžiai:** priešlaikinis gimimas, neišnešiotų naujagimių retinopatija, gydymas, regėjimo sutrikimas