Features of the intraocular pressure and axial length in eyes of infant with different stages of retinopathy of prematurity

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Особливості внутрішньоочного тиску та аксіальної довжини ока дитини при різних стадіях ретинопатії недоношених

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Abstract

Purpose. *To determine the features of intraocular pressure (IOP) and axial length (AL) in eyes with different stages of retinopathy of prematurity (ROP) and their relationships with the course of the disease.*

Material and Methods. *The study consisted of two unrelated parts. Part 1 aimed to determine the relationship between the IOP and the course of ROP and included 61 preterm children (41, 14 and 6 children with no ROP, spontaneous ROP regression, and ROP requiring treatment (e.g., aggressive ROP (AROP)), respectively). The iCare tonometer was used to measure IOP. Part 2 aimed to determine the relationship between the AL and the course of ROP and included an independent sample of 25 preterm children (11, 7 and 7 children with no ROP, spontaneous ROP regression, and ROP requiring treatment (e.g., AROP), respectively). AL was measured by ultrasonography (Accutome). Data were tested for normal distribution and homogeneity of variance using the Kolmogorov-Smirnov-Test and Leven's test, respectively. A one-way analysis of variance with post-hoc Tukey honestly significant difference was used to identify any significant between-group differences. Cohen's d was used to determine effect size. Spearman rank correlation was used to assess correlations between variables. Statistical significance was set at $p < 0.05$ for all analyses.*

Results. *The IOP did not significantly depend on the presence or severity of ROP, gestational age or birth weight ($p > 0.05$). AL was statistically smaller in children with ROP requiring treatment than in those without ROP ($p = 0.007$).*

Conclusion. *The IOP did not significantly depend on the course of ROP, while shorter AL was associated with more severe ROP ($p = 0.007$).*

Keywords: *retinopathy, preterm children, intraocular pressure, axial length, risk factors, laser photocoagulation, screening, retina, tonometry.*

Резюме

Мета. *Вивчити особливості внутрішньоочного тиску та аксіальної довжини ока при різних стадіях ретинопатії недоношених і визначити їхній зв'язок із перебігом захворювання у дітей.*

Матеріал та методи. *Дослідження було розділене на два блоки не пов'язані меж собою. Перший блок дослідження був присвячений оцінці взаємозв'язку внутрішньоочного тиску (ВОТ) та перебігу РН і включав 61 передчасно народжену дитину: 41 – без РН, 14 – із саморегресуючими стадіями РН, 6 – із РН, що потребувала лікування, включаючи АРН. ВОТ вимірювали тонометром iCare. Другий блок включав незалежну вибірку з 25 передчасно народжених дітей і був спрямований на оцінку взаємозв'язку аксіальної довжини (АД) ока з перебігом РН: 11 дітей – без РН, 7 – із саморегресуючими стадіями РН, 7 – із РН, що потребувала лікування, включаючи АРН. АК визначали за допомогою ультразвукового сканера Accutome. Нормальність роз-*

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поділу оцінювали критерієм Колмогорова – Смірнова, однорідність дисперсій – тестом Левена. Для міжгрупових порівнянь застосовували ANOVA з post-hoc тестом Tukey HSD, величину ефекту оцінювали за Cohen's d, кореляції – за коефіцієнтом Спірмена. Статистично значущими вважали результати при p<0,05.

***Результати**. ВОТ статистично значуще не залежав від наявності чи тяжкості РН, гестаційного віку та маси тіла при народженні (p>0,05). Аксіальна довжина була статистично меншою при РН, що потребувала лікування, порівняно з дітьми без РН (p=0,007).*

***Висновки.** Ми встановили, що внутрішньоочний тиск не мав статистично значущого зв'язку з перебігом РН, тоді як менша аксіальна довжина ока асоціювалася з тяжчими формами захворювання (p=0,007).*

***Ключові слова:** ретинопатія, недоношені діти, внутрішньоочний тиск, аксіальна довжина ока, фактори ризику, лазерна коагуляція, скринінг, сітківка, тонометрія.*

Introduction

A severe retinal disorder, retinopathy of prematurity (RoP), has recently become a major eye disease in premature infants. It is a severe retinal vasoproliferative disease that affects premature infants and is associated with the risk of severe RoP that may result in blindness [1, 2].

Although numerous studies on the disease have been published, data is limited on early changes in biometric parameters of the eye and intraocular pressure (IOP) in this category of children. Of special interest is the assessment of axial length (AL) and IOP, because these characteristics may demonstrate the features of postnatal development of the eye and be associated with the course of RoP. Therefore, studies on these parameters are important for better understanding of the anatomic and functional changes in the eye in premature infants [3, 4].

Congenital glaucoma is a complication of prematurity which may result from embryological developmental abnormalities and trabecular immaturity at birth. Elevated IOP in preterm children may be found as early as at birth, and develop in the first weeks or months of life or even a few years after birth. In preterm children, glaucoma was observed in 0.11% (3/2660) of the infants with very low birth weight (BW < 1500 g) [3].

Glaucoma in RoP is an important clinical concern. Most commonly, it is secondary to RoP, but may be associated with primary congenital glaucoma. The causes of ROP-induced glaucoma are multifactorial, and its mechanisms and severity are likely to depend on the stage of RoP, time of its manifestations and treatment interventions performed [5].

Important etiopathogenetic factors of RoP include maternal rubella, measles, influenza, other acute viral infections, toxoplasmosis, and exposure to ionizing radiation, heavy metal poisoning and other adverse factors. Glaucoma in premature infants is a problem of increasing clinical significance. Congenital glaucoma is associated with elevated IOP due to impaired aqueous humor outflow from the anterior chamber to Schlemm's canal secondary to a developmental abnormality of the anterior chamber angle. These abnormalities include the persistence of embryonic mesodermal tissue that covers the trabecular meshwork; anomalous cleavage or differentiation of the angle structures, or a combination of these developmental abnormalities. Primary congenital glaucoma originates from incomplete or abnormal development of the drainage system of the eye leading to elevated IOP. The most common causes of the obstruction of the trabecular meshwork and Schlemm's canal are the persistence of embryonic mesodermal tissue, poor differentiation of the angle structures, an anteriorly inserted iris root, and their combination [6-9].

RoP has been reported to be associated with changes in ocular biometric parameters including the AL and posterior segment length. Higher stages of acute ROP were associated with shorter AL ($p < 0.05$ for all stages of both eyes) but the rate of growth during the study period did not demonstrate significant differences between stages. Stage 3 infants reaching the threshold for cryotherapy had shorter AL than stage 3 infants not receiving treatment [4].

AL measurements in neonates and early infants are still methodically challenging, because non-contact measurements are often unavailable in children younger than 3 years, and clinicians have to use ultrasound or other imaging techniques. In a meta-analysis by Groot and colleagues [10], the authors obtained AL measurements for a total number of 6575 eyes in 27 papers. They demonstrated that average AL increases from 5.1 mm to 16.2 mm from week 12 to week 38 gestational age (GA) and the growth rate decreases thereafter. AL measurements in preterm infants have several limitations including a small size of the eye, unstable condition of the infant at the neonatal intensive care unit (NICU), eye movements, the need for transpalpebral or contact ultrasound measurements, and the dependence of measurement results on the position of the sensor and operator's experience. Due to these limitations, different studies used different AL measurement methods including A-scan ultrasound, B-scan biometry, transpalpebral AL measurements, and serial measurements, which partially explains the heterogeneity of results reported [10].

A prospective study was conducted within the framework of the national ROP screening program [11]. It was concluded that ROP is associated with delayed ocular development, as eyes of premature infants with ROP have shorter AL and thicker corneas than eyes of premature infants without ROP. Weekly increase of AL < 0.095 mm, weekly reduction of central corneal thickness (CCT) < 0.5

μm, or weekly weight gain < 7% was associated with ROP development. The association of AL, CCT, and weight gain with ROP could be of value for future development of predictive models for ROP [11].

Cauduro and colleagues [12] conducted an observational prospective study on preterm infants in the NICU to document ocular growth using ultrasound biometry measurements in conditions of prematurity with or without retinopathy. The biometric parameter showed a positive correlation relationship with GA. None of the variables evaluated (anterior chamber depth, anterior-posterior lens diameter (lens thickness), vitreous chamber depth, and AL) showed a significant difference between newborns with ROP and those without ROP ($P > 0.05$). This indicates that, in early postnatal development, ocular growth in preterm infants may be determined more by gestational maturity than the presence of RoP per se [12].

Therefore, the relevance of the present study stems from the fact that the anatomical and functional features of the eye in preterm infants remain insufficiently understood. The data available on changes in IOP and AL in different courses of RoP are limited and at times contradictory. This highlights the need for further research on these characteristics and an assessment of their potential association with RoP severity.

The purpose of this study was to determine the features of IOP and AL in eyes with different stages of RoP and their relationships with the course of the disease.

Material and Methods

This retrospective study consisted of two unrelated parts that were designed taking into account the availability of relevant diagnostic modalities. The first was a two-center unit, and the second was a one-center unit. In both parts of the study, GA and BW were used as major perinatal characteristics, which enabled assessing their relationships with the course of RoP and relevant ocular characteristics.

Part 1 aimed to determine the relationship between the IOP and the development of different stages of ROP and included 61 preterm children that were followed up in the Odesa Regional Clinical Pediatric Hospital and Municipal Clinical Pediatric Hospital No. 2, Odesa, in 2021. The preterm infants were divided into three groups: group 1 of 41 infants with avascular retinal areas (without ROP); group 2 of 14 infants with autoregressive ROP (stage 1 ROP, stage 2 ROP or type 2 pre-threshold ROP); and group 3 of 6 infants that required treatment for ROP (type 1 pre-threshold ROP, AROP). All these infants underwent ROP screening in accordance with international standards in due time [13]. Infants with stage 4 ROP or stage 5 ROP were excluded from the study. Tonometry was performed at rest using the Icare HOME (Icare Oy, Vanda, Finland) tonometer.

Part 2 aimed to determine the relationship between the AL and different stages of ROP and included an independent sample of 25 preterm children who were followed up in SI “The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine”, Odesa, Ukraine in 2020. These preterm infants were divided into three groups: group 1 of 11 infants with avascular retinal areas (without ROP); group 2 of 7 infants with autoregressive ROP (stage 1 ROP, stage 2 ROP or type 2 pre-threshold ROP); and group 3 of 7 infants that required treatment for ROP (type 1 pre-threshold ROP, AROP). Infants with stage 4 ROP or stage 5 ROP were excluded from the study. Transpalpebral AL measurements were performed using the Accutome (A-Scan Plus Connect; Accutome, Malvern, PA) A scan ultrasonography.

In both units of the study, indirect ophthalmoscopy was conducted using a binocular ophthalmoscope, 30 D-lens, eyelid speculum and scleral depressor after topical anesthetic (oxybuprocaine hydrochloride 0.4%) was instilled. A combination of eye drops, 0.5% tropicamidum and 0.2% phenylephrine, was used to achieve mydriasis.

Samples of patients across the two parts of the study were not overlapping and the results of these parts were analyzed independently for each part. For each part, appropriate descriptive and comparative statistical methods were used depending on the type of variables and data distribution. Kolmogorov-Smirnov test showed no statistically significant deviation from a normal distribution for the IOP and AL. The Leven’s test was used to determine homogeneity of variance before parametric tests were performed. A one-way analysis of variance (ANOVA) was used to compare the independent groups for mean values, with the Tukey HSD test for post-hoc pairwise comparisons. Cohen’s d was used to assess the effect size, and the Spearman rank correlation coefficient (r) was used to assess correlations between variables. Statistical significance was set at $P < 0.05$ for all analyses.

Results

In part 1 of the study, IOP values were analyzed in 61 preterm infants divided into groups differing in the course of RoP. In this cohort, mean GA and mean BW were 31.95 ± 2.89 weeks and 1641.48 ± 534.55 g, respectively.

The average IOP for the right and left eyes was used. Mean IOP was 14.8 ± 4.8 mmHg for infants with RoP and 14.9 ± 5.9 mg for those without RoP, but the difference was not significant ($p = 0.8$). Additionally, mean IOP was 14.97 ± 4.67 mmHg for infants not requiring treatment for RoP and 13.53 ± 6.51 mg for those requiring treatment for RoP (Table 1).

Because results from Levene’s test indicated that the assumption of homogeneity across groups was not violated ($p = 0.07$), ANOVA was used to compare means across groups. The Tukey HSD test was used for post-hoc pairwise comparisons. There was no significant between-group difference in IOP (Table 1), i.e., no tendency to a change of IOP with increasing severity of RoP was found.

IOP was found to have no significant correlation with GA ($\rho = –0.019$; $p = 0.887$), BW ($\rho = 0.021$; $p = 0.870$) or the severity of RoP ($\rho = –0.041$; $p = 0.753$). Therefore

Table 1. Intraocular pressure (IOP) measured in mm Hg in preterm infants with no retinopathy of prematurity (ROP), spontaneous ROP regression, and ROP requiring treatment (M ± SD)

Group	n	IOP (M ± SD)	p
Group 1 (infants with no ROP)	82	14.8 ± 4.8	p_{1-2} = 0.8 p_{1-3} = 0.7 p_{2-3} = 0.5
Group 2 (infants with spontaneous ROP regression)	28	15.5 ± 5.8	
Group 3 (infants with ROP requiring treatment)	12	13.5 ± 6.3	

Notes: n, number of eyes; M, mean value; ROP, retinopathy of prematurity; SD, standard deviation; p, significance of between-group difference

Table 2. Correlation of intraocular pressure with gestation age, birth weight and severity of RoP

Characteristic	Spearman rank correlation coefficient (r)	p
Gestation age	–0.01	0.9
Birth weight	0.027	0.9
Severity of RoP	0.03	0.6

Notes: ROP, retinopathy of prematurity. Statistical significance was set at $p < 0.05$ for all analyses.

in the examined sample of infants, IOP demonstrated no dependence on the degree of prematurity, the presence of RoP or the severity of RoP (Table 2).

There was a strong positive correlation between right and left eye IOP ($\rho = 0.738$; $p < 0.0001$), with no significant difference between the eyes ($p = 0.301$), which is consistent with the similar ophthalmoscopic appearance of the fundus between the eyes. This justifies the use of the average IOP of both eyes for analysis. However, IOP was not statistically significantly correlated with GA, BW, the presence of RoP or the need for RoP treatment. Therefore, within this cohort, IOP did not show independent informativeness with regard to RoP severity, i.e., within this cohort, the pathological changes in RoP were not accompanied by impairment in mechanisms of IOP regulation.

In part 2 of the study, axial lengths in 25 preterm infants were analyzed depending on the presence and severity of RoP. In this cohort, mean GA and mean BW values were 30.64 ± 3.11 weeks and 1433.60 ± 467.14 g, respectively. Group 1 included 11 infants with avascular retinal areas, whereas group 2 included seven infants with autoregressive ROP, and group 3, seven infants that required treatment for ROP.

AL was measured separately for the right and left eyes, and the average value for both eyes was used for the between-group analysis. The AL tended to decrease with an increase in the severity of RoP. Mean AL was 17.25 ± 0.43 mm for infants without RoP, 17.05 ± 0.55 mm for infants with autoregressive ROP, and 16.81 ± 0.22 mm for infants that required treatment for ROP.

An ANOVA found a significant difference in AL between the three examined groups ($F(2;47) = 4.86$; $p = 0.012$). Levene's test confirmed homogeneity of variance ($p > 0.05$), allowing for post hoc pairwise comparisons among the group means using Tukey's HSD test.

The mean AL was 0.45 mm shorter in group 3 than in group 1, and the difference was significant (2.6%, p1-2 = 0.008). The difference in mean AL between groups 1 and 3 was large (Cohen's d = 1.22) enough to be not only statistically significant, but potentially clinically significant as well.

The differences between groups 1 and 2 (17.25 ± 0.42 mm versus 17.05 ± 0.53 mm; $p_{1-2} = 0.33$), and between groups 2 and 3 (17.05 ± 0.53 mm versus 16.80 ± 0.24 mm; $p_{2-3} = 0.30$), however, were not significant. The mean AL for infants of groups 2 and 3 was 16.92 ± 0.42 mm, which was 0.33 mm shorter than for infants in group 1 (1.9%, p = 0.008) (Table 3).

More advanced GA and larger BW at delivery were associated with longer AL (i.e., longer AL was associated with greater maturity of the infant), whereas an unfavorable course of RoP was associated with shorter AL. This may indicate slower AL growth in premature infants and be considered a morphometric manifestation of incomplete or RoP-associated retarded growth of the eye globe (Table 4).

Table 3. Axial length of the eye (mm) in preterm infants with no retinopathy of prematurity (ROP), spontaneous ROP regression, and ROP requiring treatment (M ± SD)

Group	n	AL	AL	p
		M ± SD	95% CI	
Group 1 (infants with no ROP)	22	17.25±0.42	17.06-17.44	p_{1-2} = 0.33 p_{1-3} = 0.008 p_{2-3} = 0.3
Group 2 (infants with spontaneous ROP regression)	14	17.05±0.53	16.7-17.35	
Group 3 (infants with ROP requiring treatment)	12	16.8±0.24	16.6-16.9	

Notes: AL, axial length; n, number of eyes; M, mean value; ROP, retinopathy of prematurity; SD, standard deviation; p, significance of between-group difference

Table 3. Axial length of the eye (mm) in preterm infants with no retinopathy of prematurity (ROP), spontaneous ROP regression, and ROP requiring treatment (M ± SD)

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Group 2 (infants with spontaneous ROP regression)	14	17.05±0.53	16.7-17.35	
Group 3 (infants with ROP requiring treatment)	12	16.8±0.24	16.6-16.9	

Notes: AL, axial length; n, number of eyes; M, mean value; ROP, retinopathy of prematurity; SD, standard deviation; p, significance of between-group difference

Table 4. Correlation of the axial length of the eye with gestation age and birth weight in preterm infants

Characteristic	r		
	ROP	Gestation age	Birth weight
Axial length	–0.39	0.28	0.32

Notes: r, Spearman rank correlation coefficient; ROP, retinopathy of prematurity. Plus ("+") and minus ("–") indicate positive and negative correlation, respectively.

Discussion

The issue of early changes in the biometric parameters of the eye and IOP in patients with RoP has been insufficiently studied although the disease is of particular interest to ophthalmologists. Of the available studies, most have a relatively small sample size and some have been conducted before recent advancements in the field and do not take into account modern approaches to the care and management of preterm infants, which limits the ability to extrapolate their findings to current clinical practice. Additionally, their findings (especially those with regard to the relationship of RoP with AL and IOP) are inconsistent and at times contradictory. Consequently, further research on early postnatal changes in these parameters is essential for clarifying the mechanisms of RoP and enhancing methods for predicting the disease [3, 4].

Because preterm infants must undergo eye examination on a regular basis, the IOP can be measured with a portable tonometer at recommended screening time points. Understanding the patterns of natural maturation of the visual system, establishing normative ranges for IOP in preterm infants, and identifying internal and external determinants of IOP are essential for early assessment of development disorders and diagnosing an eye disease [14].

Current practice shows that the issue related to IOP measurements in children involves not only difficulty and even impossibility of performing instrumental measurement of IOP due to the infant's restless behavior. It is of not less importance to interpret digital tonometry readings correctly. Biomechanical properties of the fibrous capsule of the eye, especially in patients with congenital glaucoma, should be taken in account while interpreting the readings. For this reason, the selection of the tonometry technique and the selection of the tonometer are of fundamental importance. Goldmann applanation tonometry (the Perkins applanation tonometry in infants), non-contact pneumotonometry, Tonopen tonometry and Icare tonometry are most commonly used in foreign clinical practice. Icare rebound tonometry is an advanced IOP measurement technique that is commonly reported to be well tolerated by infants [15].

In the current study, we selected Icare rebound tonometry for IOP measurements in preterm infants. This choice allowed IOP measurements to be performed in infants at rest and obtaining quantitative IOP readings suitable for the comparative analysis of groups that differed in the course of RoP.

In a study by Turkish researchers [16], the mean IOP was 16.2 ± 2.7 mmHg in premature and 16.6 ± 2.3 mmHg in full-term newborns ($p = 0.27$), and there was no correlation between IOP and GA, BW or age at measurement. Ng and colleagues [17] demonstrated a gradual decrease in IOP with an increase in postconceptual age, from 16.9 mm Hg at 26.1 weeks to 14.6 mm Hg at 46.4 weeks. This is in line with a report by Ricci [18] on a decrease in IOP over the first month of life in premature infants. A prospective study [19] found that baseline IOP was significantly lower in preterm infants that required laser treatment compared to those with no RoP or those that had untreated RoP, with a transient increase postlaser treatment that typically normalized without needing IOP treatment. This justifies the rationale for monitoring IOP in preterm infants.

In the current study, IOP in preterm infants did not statistically significantly depend on the presence or severity of ROP, GA or BW. Additionally, IOP was found to have no significant correlation with GA ($\rho = –0.019$; $p = 0.887$), BW ($\rho = 0.021$; $p = 0.870$) or the severity of RoP ($\rho = –0.041$; $p = 0.753$). This indicates that, within the cohort examined, IOP cannot be considered an independent

index reflecting the degree of prematurity of the severity of RoP. There was a strong positive correlation between right and left eye IOP ($\rho = 0.738$; $p < 0.0001$), with no significant difference between the eyes ($p = 0.301$), which is consistent with the similar ophthalmoscopic appearance of the fundus between the eyes. This symmetry of findigs is consistent with a similar ophthalmoscopic appearance in both eyes and justifies the use of the average IOP of both eyes for analysis. Therefore, within the cohort examined, the pathological changes in RoP were not accompanied by statistically significant changes in IOP, and IOP did not show independent informativeness with regard to RoP severity.

Because AL seemed to be a more promising factor of RoP severity, we gave attention to the analysis of its potential association the course of RoP. Literature data suggests that, in preterm infants, the AL changes rapidly in the early postnatal period and may be associated with the severity of RoP. Some studies found advanced RoP to be associated with smaller AL and delayed ocular growth, whereas others did not find significant difference between infants with and without RoP. This controversy of results could stem from varying evaluation time points, ultrasound biometry techniques, infants age and clinical severity of RoP [20].

A meta-analysis by Groot and colleagues [10] showed that eyes of newborns and early infants increase their AL rapidly during prenatal and early postnatal development periods, but the AL measurements in preterm infants are still methodically challenging due to a a small size of the eye, unstable condition of the infant, eye movements, the need for transpalpebral or contact ultrasound measurements, and the dependence of measurement results on the position of the sensor and operator's experience. A prospective study conducted within the framework of the national ROP screening program [11] concluded that ROP is associated with delayed ocular development, as eyes of premature infants with ROP have shorter AL. Specifically for AL, weekly increase <0.095 mm was correlated with ROP development [11].

In a prospective study by Caduro and colleagues [12], however, none of the variables evaluated (anterior chamber depth, anterior-posterior lens diameter, vitreous chamber depth, and AL) showed a significant difference between newborns with ROP and those without ROP ($P > 0.05$). This indicates that, in early postnatal development, ocular growth in preterm infants may be determined more by gestational maturity than the presence of RoP per se [12].

Our findings generally support the view that the AL of the premature eye reflects the degree of morphological maturation of the globe and may be associated with the severity of RoP. In the sample examined, older GA and larger BW were associated with a longer AL, whereas a shorter AL was seen in infants with advanced RoP. The greatest magnitude of difference in AL was seen between infants without RoP and those requiring treatment for RoP, with the mean AL being 0.45 mm shorter for the former than for the latter infants, and the size of the effect was large. The absence of significant difference in AL between individual groups, however, indicates that the relationship between the AL and the progression of RoP is non-linear across the full spectrum of disease severity. Therefore, these findings allow us to consider a shorter AL as a morphometric manifestation of RoP-associated incomplete or retarded growth of the eye.

Limitations of the study

Major limitations of the study include a relatively small sample size and uneven distribution of participants across groups. An additional limitation is that the study consisted of two independent parts, which was due to the availability of different diagnostic techniques.

Conclusion

The presence and stage of RoP were not associated with statistically significant changes in IOP. IOP was not statistically significantly associated with GA or BW. The mean AL was 0.45 mm shorter in infants requiring treatment for RoP than in infants without RoP ($p = 0.008$). The AL ranged from 16.6 mm to 16.9 mm in the former infants and from 17.06 mm to 17.44 mm in the latter infants. Older GA and larger BW were found to be associated with longer AL, which reflects the relationship between the size of the eye and the degree of maturation of the preterm infant.

Conflict of interest

The author declares no conflict of interest that could influence her views on the subject matter or materials described and discussed in this manuscript.

Ethical Declaration

This study involved human subjects, was approved by the Bioethics Committee of SI "The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine" (Meeting Minutes No.4 dated April16, 2019), and followed ethical standards as outlined in the Declaration of Helsinki. Informed consent was not obtained due to the retrospective nature of the study. This study did not include animal experiments.

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Abbreviations

AL, axial length; AROP, aggressive retinopathy of prematurity; BW, body weight; GA, gestational age; IOP, intraocular pressure; ROP, retinopathy of prematurity

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