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Original Article

Intraocular Pressure of Premature Newborns – A 2 Year Follow up

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ABSTRACT

Background: The intraocular pressure (IOP) ranges of premature newborns are not the same as those in full-term newborns and adult population. There are no unified standards for IOP in infants, much less premature newborn. Research on the topic is very conflicting and needs to be expanded upon. To assess IOP in premature and full-term newborns and factors influencing it.

Methods: Using a hand-held rebound tonometer, IOP was measured in 548 eyes of 274 preterm infants (gestational age ranging from 26 to 32 weeks) shortly after birth and at weekly intervals for one month.

Results: The mean gestational age for premature newborns was 30.23±2.34 weeks (25-35 weeks), for full-term newborn it was 39.19±0.91 weeks (37-41 weeks). Mean IOP values in preterm infants were 21.95±4.36 mmHg (ranging from 11.1 to 32 mmHg), while for full-term were 13.5±2.9 (from 10.5 to 25.1 mmHg). At the end of the first month the mean IOP decreased to 17.66 ± 2.21 mm Hg ($P < .001$) for preterm newborns, while not changing in a statistically significant way for the full-term ones ($P>0.5$). Central corneal thickness was found to be among the major factors associated with increased IOP ($P<.001$).

Conclusion: Measured values of IOP are well outside the normal range for newborns. There is a tendency for decreasing IOP observed during the first month screening which decreases the value of the initial findings. The exact causes of the decrease of IOP are not completely clear up to this point. Use of eyelid speculum needs to be avoided to prevent artificial increase of IOP.

Keywords: Central corneal thickness, Infants, Intraocular pressure, Preterm

Introduction

Premature birth poses significant health risks across various organs and systems. Understanding the anatomical and physiological variances from full-term newborns is crucial for physicians to ensure accurate diagnosis and appropriate treatment. Among these systems, the visual system is particularly vulnerable to serious consequences associated with prematurity. While retinopathy of prematurity stands out as the most severe and prevalent issue, other conditions such as strabismus (1), myopia (2), and cerebral vision impairment (3) can also manifest.

In a retrospective study conducted by Thiagarajah et al. involving 247 premature patients, a 2% occurrence of congenital glaucoma was observed. This finding indicates a significantly higher prevalence compared to the general population (4), suggesting potential disruption in the development of the trabecular meshwork or angle. However, it's worth noting that other studies (5, 6) did not establish a clear link between primary congenital glaucoma and prematurity.

Both conditions may coexist (5) and, given

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their severity and potential to cause blindness, necessitate thorough screening, diagnosis, and treatment. Differentiating between primary congenital glaucoma and large disc cupping, which can be common in premature infants (7), presents an additional challenge. Some authors speculate that elevated intraocular pressure (IOP) is not only associated with a higher risk of glaucoma but could also lead to a significant reduction in ocular perfusion pressure, potentially exacerbating the development of retinopathy of prematurity (8).

Screening for glaucoma involves measuring IOP, yet there are currently no standardized protocols for IOP measurement in infants, particularly premature newborns. Studies conducted over the years have yielded varying results, contributing to conflicting findings in research on this topic. Therefore, there is an urgent need for further investigation and expansion of research in this area. Our objective is to evaluate IOP in both premature and full-term newborns, as well as identify factors influencing it.

Methods

Study Design

The study adopts a longitudinal case-controlled analytic approach.

Study Population

Our study encompassed a cohort of 274 preterm infants (548 eyes) and 292 (584) full-term infants who were treated at the neonatology clinic between March 2020 and April 2022.

Inclusion/Exclusion criteria

Infants born at less than 32 weeks' gestational age were categorized into the pre-term group, whereas those born at 36 weeks' gestation or later were classified into the full-term group.

Individuals presenting with ocular abnormalities such as corneal, iris, lens, and retinal pathologies, as well as glaucomatous optic nerve head changes, or systemic abnormalities including chromosomal disorders, visceral anomalies were excluded from the study.

Examination

Using a handheld rebound tonometer, intraocular pressure (IOP) was assessed immediately after birth and subsequently at weekly intervals for one month with a SW-500 portable tonometer. These evaluations were conducted, with the infants in a supine position following the administration of local anesthesia and placement of a lid retractor. Additionally, corneal diameter measurements were obtained using corneal templates, while central corneal thickness (CCT) was gauged using a portable pachymeter (Pachpen Accutome Pachymeter).

Statistical analyses

Results from the two groups were compared using the two-tailed t-test. The Chi-square test was employed for assessing qualitative data such as gender distribution. Descriptive statistical techniques, including mean and standard deviation calculations, were utilized, along with multiple regression analysis and Pearson correlation analysis. A significance level of $P < 0.05$ was deemed statistically meaningful.

Ethical approval

The Study was approved by the Ethics Committee of Trakia University Hospital (Ethical Commettee Aproval N19/03.2020). Written informed consent was obtained from every parent/ guardian following a comprehensive explanation regarding the purpose and scope of the study.

Results

Out of the 566 patients examined, 274 (48.40%) were born prematurely, while 292 (51.60%) were born at term. The male gender was slightly more represented, accounting for 288 (50.88%) of the total sample. In the premature group, the mean gestational age was 30.23±2.34 weeks (ranging from 25 to 35 weeks), with a mean birth weight of 1231.3±497.8 grams (ranging from 680 to 2500 grams). In contrast, the full-term group had a mean gestational age of 39.19±0.91 weeks (ranging from 37 to 41 weeks) and a mean birth weight of 2565±826.5 grams (ranging from 1350 to 4200 grams). Both groups exhibited a weight gain of over 600 grams within the first month.

Significant differences were observed between the two groups in terms of gestational age, birth weight, age, and weight at the time of measurement ($P < 0.05$), while no significant difference was found in gender distribution ($P>0.05$) (Table 1).

Due to a high correlation of central corneal thickness (CCT) and intraocular pressure (IOP) between the right and left eyes, only data from the right eye were utilized for further analysis (Table 2, Table 3).

A statistically significant high correlation was noted between IOP and CCT in both preterm ($p < 0.001$, Pearson correlation = 0.637) and full-term newborns ($P < 0.001$, Pearson correlation = 0.733)

Table 1. Characteristics of the screened population

	Premature newborn	Full-term newborn	P value
Eyes (n) - OD	274	292	
Sex			0.79
Male	140 (51.1%)	148 (50.7%)	
Female	134 (48.9%)	144 (49.3%)	
Gestational age (weeks)			<0.01
Mean±SD	30.23±2.34	39.19±0.91	
Range	25-35	37-41	
Gestational weight at birth (grams)			<0.01
Mean±SD	1231.3±497.8	2565±826.5	
Range	680-2500	1350-4200	
Weight at one month measurement (grams)			<0.01
Mean±SD	1891.4±698.3	3015±906.2	
Range	1450-3000	2050-4670	
IOP (mmHG) initial			<0.01
Mean±SD	21.95±4.36	13.5±2.9	
Range	11.1-32	10.5-25.1	
IOP at one month measurement			<0.01
Mean±SD	17.66±2.21	12.9±2.35	
Range	10.7-23	10.5-21.2	
CCT (μm)			<0.01
Mean±SD	616.66±74.95	506.34±36.60	
Range	470-800	430-620	

Table 2. Correlation between the IOP in right/ left eye in preterm newborn

Correlation preterm	IOP OD	IOP OS
IOP OD		
Pearson correlation	1	0.880
Sig. (two-tailed)		<0.001
N	274	274
IOP OS		
Pearson correlation	0.880	1
Sig. (two-tailed)	<0.001	
N	274	274

Table 4. Correlation between the IOP and CCT in preterm newborn

Correlation preterm	IOP	CCT
IOP		
Pearson correlation	1	0.637
Sig. (two-tailed)		<0.001
N	274	274
CCT		
Pearson correlation	0.637	1
Sig. (two-tailed)	<0.001	
N	274	274

(Tables 3-5). Additionally, a reverse correlation was observed with gestational age (Pearson correlation = -0.703, Pearson correlation = -0.653) and weight (Pearson correlation = -0.676, Pearson correlation = -0.653) for preterm and full-term infants, respectively.

The mean IOP for preterm newborns was 21.95±4.36 mmHg (ranging from 11.1 to 32 mmHg), whereas for full-term newborns, it was 13.5±2.9 mmHg (ranging from 10.5 to 25.1 mmHg). A consistent decrease in IOP was observed during the interim measurements, with an average of 0.89±0.25 mmHg per week for the per-term. The end result was a reduction of approximately 4 mmHg for preterm infants and 1 mmHg for full-term infants at the one-month follow-up. The mean CCT was 616.66±74.95 micrometers (ranging from 470

Table 3. Correlation between the IOP in right/ left eye in full-term newborn

Correlation full-term	IOP OD	IOP OS
IOP OD		
Pearson correlation	1	0.810
Sig. (two-tailed)		<0.001
N	292	292
IOP OS		
Pearson correlation	0.810	1
Sig. (two-tailed)	<0.001	
N	292	292

Table 5. Correlation between the IOP and CCT in full-term newborn

Correlation full-term	IOP	CCT
IOP		
Pearson correlation	1	0.733
Sig. (two-tailed)		<0.001
N	292	292
CCT		
Pearson correlation	0.733	1
Sig. (two-tailed)	<0.001	
N	292	292

to 800 micrometers) and 506.34±36.60 micrometers (ranging from 430 to 620 micrometers) for preterm and full-term infants, respectively.

While the inclination toward decreasing intraocular pressure (IOP) is more pronounced among pre-term infants, our analysis observes a statistically significant difference in IOP values between both groups across all measurement points (P < 0.005). Notably, the gap in IOP is progressively narrowing, diminishing from 8.4 mmHg initially to 4.7 mmHg at one month.

A multiple regression analysis was conducted with IOP as the dependent variable and gestational age, birth weight, age, and weight at the time of measurement as predictors for both right and left eyes in both groups (Table 6). The analysis confirmed a significant correlation between these parameters (P < 0.05) (Table 7, Figure 1).

Table 6. Variable's coefficients

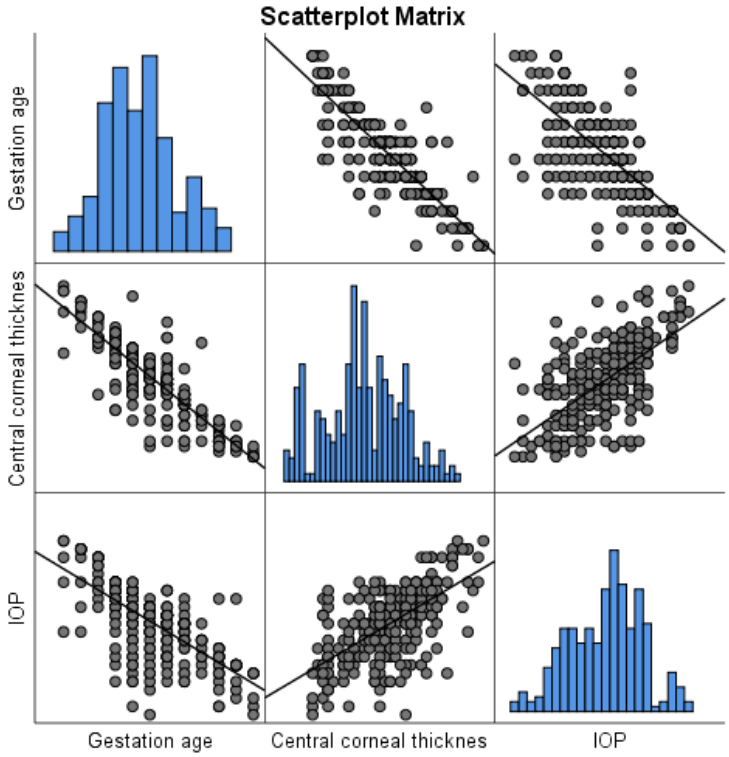
	Coefficients Std. error	Standardized Coefficients Beta	Sig.
Constant	3.271		<0.001
Birth weight	.393	.268	<0.001
Gestation age	.135	-.925	<0.001
Measurement weight	.324	.301	<0.001
Measurement age	.167	-.798	<0.001

Furthermore, ANOVA analysis affirmed that the data fit well with the regression model and demonstrated that the independent variables significantly predict the dependent variable (p < 0.005) (Table 8).

Table 7. Multiple regression analysis

Model	R	R square	Adj. R square	Std. error of the estimate
1	0.758	0.574	0.556	4.691

Constant: central corneal thickness, gestational age, birth weight, age and weight at measurement Dependent: IOP



*At baseline IOP

Figure 1. Central corneal thickness, gestational age, birth weight, age and weight at measurement Dependent: IOP

Table 8. ANOVA Analysis

Model	Sum of squares	Df	Mean square	F	Sig.
Regression	904.514	21	43.072	15,123	<0.001
Residual	717.709	252	2.848		
Total	1622.223	273			

Discussion

Screening and diagnosing glaucoma primarily involves measuring intraocular pressure (IOP), a practice also applicable to pediatric patients. However, the gold standard, Goldman tonometry, is unsuitable for newborns. Alternatives, such as Tono-Pen and ICare, have proven to be adequate replacements for measuring IOP in newborns. Studies comparing these methods vary, with Gandhi et al. (9) reporting slightly higher IOP measurements with Tono-Pen, Iester et al. (10) finding no significant difference, and McKee (11) and Haus (12) teams showing lower Tono-Pen results. Due to the edematous corneas in premature newborns, ICare and Tono-Pen may be considered superior in measuring IOP (13, 14).

Several studies have investigated IOP in premature newborns. Our study found a mean IOP of 21.95±4.36 mmHg. In comparison, Uva et al. (15) reported 18.9 mmHg, Murasella et al. (16) reported 18.04 mmHg, Muslubas et al. (17) reported 16.2±2.7 mmHg, and Acar et al. (18) reported 18.28 ± 2.78 mmHg. Although our IOP results were slightly higher, mean central corneal thickness (CCT) remained relatively consistent across all studies.

Ricci et al. (8) reported a decrease in mean IOP during the first month of life from 13.25 mmHg to 10.96 mmHg in premature newborns. Ng et al. (19) further supported this finding, suggesting a two-fold decrease from 16.9 mmHg to 14.6 mmHg at 26.1 weeks and 46.4 weeks of postconceptional age, respectively. Our study also supports this hypothesis, with an average decrease of 4 mmHg for premature newborns and 1 mmHg for full-term infants.

Similarly, CCT decreases in the first month of life. The findings of our study are further supported by Kirwan et al. (20) and Autzen et al (21).

One limitation of our study is the exclusion of other factors that may influence IOP (e.g., oxygen levels, other diseases, artificial reproductive technology, pregnancy complications, and the effects of the eye speculum). We must also consider the possible artificial increase in IOP due to increased venous pressure caused by the Valsalva maneuver produced by resisting examination, forced closure of the eyelids, or the use of an eyelid speculum. The effects of the eyelid speculum were studied by several teams, showing an increase in IOP between 2.6 to 4 mmHg (22, 23).

Intubation is also a concern. According to Mikhail et al. (24), at least 3-5 minutes need to pass before measuring intraocular pressure for a proper assessment.

Conclusion

The precise reference ranges for intraocular pressure (IOP) in premature newborns have yet to be definitively established. Our findings demonstrate a statistically significant elevation of IOP in premature infants compared to their full-term counterparts. While our results are corroborated to some extent by existing literature, they do not offer conclusive agreement.

Most authors prefer employing Tono-Pen or iCare as the primary modalities for measuring IOP. However, it is imperative to refrain from using an eyelid speculum during measurements to prevent artificially inflated readings.

The underlying mechanisms driving the observed decrease in IOP remain incompletely understood. It is plausible that this phenomenon is associated with the gradual reduction in central corneal thickness during neonatal maturation. Additionally, factors such as mode of delivery, Apgar score, blood pressure, and medication regimen merit consideration in further analyses to comprehensively elucidate the intricacies of IOP dynamics in newborns.

Limitations

The utilization of topical anesthetics has the potential to introduce variability in central corneal thickness (CCT) measurements. Furthermore, the employment of a lid speculum during intraocular pressure (IOP) assessment can significantly impact the recorded values. The relationship between postconceptual age, CCT, and IOP are not thoroughly explored..

Acknowledgments

None.

Conflicts of interest

The authors declare that there is no conflict of interest.

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