

# Intraocular pressure and central corneal thickness in full-term newborns

## Medida da pressão intraocular e espessura corneana central em recém-nascidos a termo

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### ABSTRACT

**Objective:** The aim of this study was to determine the central corneal thickness (CCT) and intraocular pressure (IOP) in full-term newborns and to correlate these values with the following variables: weight, sex, and post-conception age (PCA).

**Methods:** IOP and CCT were determined in 52 full-term newborns with a mean gestational age of  $39.43 \pm 1.03$  weeks and a mean birth weight of  $3,273 \pm 558$  g. The mean age of the neonates at the time of taking the measurements was  $1.15 \pm 1.38$  days after birth. IOP was determined with a Tono-Pen, and CCT was determined using a handheld ultrasound pachymeter.

**Results:** The mean overall IOP was  $14.0 \pm 2.91$  mmHg, and the mean IOP in male and female newborns was  $13.77 \pm 2.88$  mmHg and  $14.32 \pm 3.05$  mmHg, respectively. The mean overall CCT was  $605.87 \pm 62.98$   $\mu$ m, and the mean CCT in male and female newborns was  $626.70 \pm 67.46$   $\mu$ m and  $577.45 \pm 45.50$   $\mu$ m, respectively; the mean CCT was higher in male newborns than in female newborns. PCA was negatively associated with CCT, IOP, and weight; however, only the correlation with CCT was statistically significant. Comparisons between the sexes showed significant differences for two variables: weight and CCT.

**Conclusions:** No relationship was found between CCT and IOP; however, we found a positive association between weight and CCT.

**Keywords:** Glaucoma/genetics; Cornea topography; Intraocular pressure; Tonometry, ocular; Humans; Infant, newborn

### RESUMO

**Objetivo:** O objetivo deste estudo foi avaliar a espessura central da córnea (ECC) e a pressão intraocular (PIO) em recém-nascidos (RN) a termo, correlacionando seus valores entre as variáveis peso, sexo e idade pós-concepção (PCA).

**Métodos:** A pressão intraocular e a espessura central da córnea foram determinadas em 52 recém-nascidos a termo com idade gestacional média de  $39,43 \pm 1,03$  semanas, peso médio de nascimento de  $3.273 \pm 558$  g. A média de idade durante as medições após o nascimento foi  $1,15 \pm 1,38$  dias. A pressão intraocular foi determinada com Tono-pen. A espessura central da córnea foi determinada com paquímetro ultrassônico portátil.

**Resultados:** A pressão intraocular média foi de  $14,0 \pm 2,91$  mmHg em ambos os sexos, de  $13,77 \pm 2,88$  mmHg nos recém-nascidos do sexo masculino e  $14,32 \pm 3,05$  mmHg nos recém-nascidos do sexo feminino. A espessura central da córnea média foi de  $605,87 \pm 62,98$   $\mu$ m em ambos os sexos; de  $626,70 \pm 67,46$   $\mu$ m recém-nascidos do sexo masculino e de  $577,45 \pm 45,50$   $\mu$ m nos recém-nascidos do sexo feminino. A maior média da espessura da córnea foi no sexo masculino. A variável idade pós-concepção teve uma relação decrescente com espessura central da córnea, pressão intraocular e peso, porém, a correlação só foi significativa com a espessura central da córnea. Na comparação entre os sexos houve diferenças significativas para duas variáveis: peso e espessura central da córnea.

**Conclusões:** Não houve relação entre a espessura central da córnea e a pressão intraocular neste estudo, entretanto verificou-se que existe uma relação de aumento de peso com a espessura central da córnea.

**Descritores:** Glaucoma/genético; Topografia da córnea; Pressão intraocular; Tonometria ocular; Humanos; Recém-nascido

### INTRODUCTION

Until the 20th century, little was known about ocular pressure in newborns, mainly because of the lack of suitable equipment for measuring ocular pressure. The physical properties of the neonatal cornea appear to be the main factors associated with difficulty in obtaining reliable measurements of intraocular pressure (IOP) using the majority of available tonometers. Corneal thickness is an independent risk factor for glaucoma development in adults with ocular hypertension<sup>(1)</sup>. However, few studies have been conducted in Brazil on IOP values in full-term newborns, and these studies have not reported a correlation between IOP and central corneal thickness (CCT)<sup>(2)</sup>. Glaucoma is an important disease in children, accounting for 2.5%-10% of all cases of childhood blindness<sup>(3)</sup>. Knowledge of the reference values for IOP in newborns, in association with CCT, weight, sex, and post-conception age (PCA), is important for the early diagnosis of glaucoma, especially in children who have not yet developed the

classic signs of primary congenital glaucoma (e.g., cloudy cornea, buphthalmia). The aim of the present study is to fill this knowledge gap.

### METHODS

The study protocol was approved by the Ethics Committee of the Federal University of São Paulo. The parents/guardians of the newborns were informed about the tests, and provided their written consent.

IOP and CCT were measured in 52 full-term newborns with a mean gestational age (GA) of  $39.43 \pm 1.03$  weeks and a mean birth weight of  $3,273 \pm 558$  g. The mean age of the neonates at the time of taking the measurements was  $1.15 \pm 1.38$  days after birth (Table 1). Newborns with abnormalities in biomicroscopy (deformities and abnormalities in the transparency of the cornea and defects of the iris, such as aniridia or coloboma), red reflex changes, or systemic syndromes were excluded.

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**Table 1. Description of the variables under analysis in newborns**

	Interval		Mean ± SD
	Minimum	Maximum	
Age (days)	0	7	1.15 ± 1.38
CCT (µm)	483	794	605.87 ± 62.98
IOP (mmHg)	8	20.0	14.00 ± 2.91
GA (weeks)	37	41.6	39.46 ± 1.03
Weight (g)	1960	4435	3273.56 ± 558.20

PCA= post-conception age; CCT= central corneal thickness; IOP= intraocular pressure; GA= gestational age; SD= standard deviation.

The newborns were placed on a wheeled stretcher in the supine position. After the administration of topical anesthesia (one drop of 0.5% proparacaine), their eyelids were carefully parted by the operator's fingers while avoiding placing the weight of the hand on the ocular globe, which can influence the accuracy of optical measurements. The measurement was only performed when the newborn was quiet and still. The mean IOP was calculated after three measurements with a Tono-Pen AVIA (Reichert, Depew, NY, USA). If the IOP results from the three measurements differed by >3 mmHg, the measurement was repeated. The mean CCT was calculated after eight measurements in each eye with an SP-100 portable pachymeter (Tomey, Nagoya, Japan). All measurements were centrally performed, and all tests were performed by the same operator during the same period of the day (between 13 h and 16 h).

Statistical analyses were initiated by the characterization of variables through measures of central tendency and variability. The Kolmogorov-Smirnov test was used to verify the normality of the data. Multiple linear regression was used to evaluate the relationship between variables. The premises of normality of the residuals (Kolmogorov-Smirnov), absence of serial autocorrelation (Durbin-Watson), absence of heteroscedasticity [(variance inflation factor (VIF)], and the absence of multicollinearity (robust standard error) were verified. The differences between the sexes of the tested variable. were determined by the Mann-Whitney test. The level of significance adopted was 5%, with a confidence interval of 95.0%. SPSS Statistics software (version 21; IBM Corp., Armonk, NY, USA) was used to perform all statistical analyses.

**RESULTS**

The overall mean IOP was 14 ± 2.91 mmHg (range 8-20 mmHg) (Table 1), and the mean IOP in male and female newborns was 13.77 ± 2.88 mmHg (range 8-19 mmHg) and 14.32 ± 3.05 mmHg (range 8-20 mmHg), respectively. The overall mean CCT was 605.87 ± 62.98 µm (range 483-794 µm), and the mean CCT in male and female newborns was 626.70 ± 67.46 µm (range 483-794 µm) and 577.45 ± 45.50 µm (range 521-686 µm), respectively. The mean CCT was significantly higher in male newborns (Tables 2 and 3).

Multiple linear regression analysis showed statistical significance for weight, female sex, and PCA. There was a positive relationship between weight and CCT. Female neonates had significantly lower CCT than male neonates. Further, CCT decreased as the PCA increased (Table 4). Male weight was significantly associated with CCT; as the mean weight increased, the CCT also increased (Table 5). Conversely, no significance was found for any of the variables in the female neonates; that is, weight, IOP, and PCA were independent of CCT (Table 6).

The Mann-Whitney test showed significant differences between the sexes for two variables only, namely weight and CCT, and male sex obtained significantly higher means and median for both variables (Table 7).

**Table 2. Mean CCT and sex**

Variable	n	Mean CCT ± SD
Newborns	52	605.87 ± 63.69
Sex		
F	22	577.45 ± 45.50
M	30	626.70 ± 67.46

n= number of newborns; CCT= central corneal thickness; SD= standard deviation; F= female; M= male.

**Table 3. Relationship between PCA and CCT**

PCA days	n	CCT		IOP	
		Mean ± SD µm	Interval µm	Mean ± SD mmHg	Interval mmHg
0	17	632.35 ± 66.69	530-794	14.41 ± 2.67	8-18
1	22	607.36 ± 60.29	521-749	13.64 ± 3.26	8-19
2	9	569.44 ± 48.27	524-661	14.44 ± 2.70	12-20
3	1	603.00	-	18	-
4	1	483.00	-	13	-
6	1	573.00	-	10	-
7	1	609.00	-	12	-
Total	52	605.86	483-794	14 ± 2.94	8-20

PCA= post-conception age; CCT= central corneal thickness; IOP= intraocular pressure; SD= standard deviation; n= number of newborns.

**Table 4. Association between CCT and the variables under analysis (overall)**

Independent variable	Model (with robust standard error)	R <sup>2</sup>	p	95.0% confidence interval for B		VIF
				Lower limit	Upper limit	
Weight (g)	y= 655.83 + 0.05x	0.356	<b>0.005</b>	0.02	0.090	1.031
Sex (female)	y= 655.83 - 43.40x		<b>0.006</b>	-73.78	-13.013	1.025
IOP (mmHg)	y= 655.83 - 1.51x		0.560	-6.69	3.670	1.032
PCA (days)	y= 655.83 - 11.89x		<b>0.034</b>	-22.83	-0.950	1.034

Durbin-Watson= 2.128; Kolmogorov-Smirnov (p) = 0.200.

R<sup>2</sup>= Adjusting the model; IOP= intraocular pressure; PCA= post-conception age; VIF= variance inflation factor. Dependent variable: CCT= central corneal thickness.

**Table 5. Association between CCT and the variables under analysis (male newborns)**

Independent variable	Model (with robust standard error)	R <sup>2</sup>	p	95.0% confidence interval for B		VIF
				Lower limit	Upper limit	
Weight (g)	y= 654.58 + 0.55x	0.303	<b>0.014</b>	0.12	0.10	1.019
IOP (mmHg)	y= 654.58 - 1.42x		0.726	-9.69	6.85	1.104
PCA (days)	y= 654.58 - 11.86x		0.092	-25.77	2.06	1.115

Durbin-Watson = 1.932; Kolmogorov-Smirnov (p) = 0.200.

R<sup>2</sup>= Adjusting the model; IOP= intraocular pressure; PCA= post-conception age; VIF= variance inflation factor; Dependent variable: CCT= central corneal thickness.

**Table 6. Association between CCT and the variables under analysis (female newborns)**

Independent variable	Model (with robust standard error)	R <sup>2</sup>	p	95.0% confidence interval for B		VIF
				Lower limit	Upper limit	
Weight (g)	y= 599.93 + 4.25x	0.167	0.814	-33.26	41.77	1.086
IOP (mmHg)	y= 599.93 - 1.63x		0.652	-9.08	5.82	1.087
PCA (days)	y= 599.93 - 10.78x		0.467	-41.24	19.69	1.175

Durbin-Watson = 2.214; Kolmogorov-Smirnov (p) = 0.200.

R<sup>2</sup>= Adjusting the model; IOP= intraocular pressure; PCA= post-conception age; VIF= variance inflation factor; Dependent variable: CCT= central corneal thickness.

**Table 7. Comparison of the variables between the sexes**

	Sex				p*
	Female		Male		
	Median	Mean	Median	Mean	
IOP (mmHg)	14.00	14.32	14.00	13.77	0.570
PCA (days)	1.00	1.14	1.00	1.17	0.208
Weight (g)	2985.00	3079.50	3520.00	3415.80	<b>0.026</b>
CCT (µm)	571.50	577.45	619.50	626.70	<b>0.005</b>

\* Mann-Whitney test; IOP= intraocular pressure; PCA= post-conception age; CCT= central corneal thickness; F= female; M= male; p= significance.

## DISCUSSION

In the present study, we assessed the effect of CCT on IOP, weight, sex, and PCA in full-term newborns. The mean IOP was 14.42 ± 2.91 mmHg, which is lower than that observed in previous similar studies<sup>(4-6)</sup>.

As per the existing literature, IOP values obtained in the supine position tend to be higher than those measured in the sitting position as a result of changes in scleral venous pressure<sup>(7)</sup>. Although Goldmann applanation tonometry is the gold standard method for measuring IOP, it only provides estimated values<sup>(8,9)</sup>. Accuracy for this measurement depends on the use of correct technique, and in particular, the use of adequate amounts of fluorescein<sup>(10)</sup>. However, errors resulting from changes in the corneal thickness and rigidity cannot be avoided when using Goldmann applanation tonometry<sup>(8,9)</sup>. The Tono-Pen is the preferred instrument for pediatric patients because it is less affected by corneal thickness, according to a study by Yildirim et al.<sup>(10)</sup>.

In the present study, the mean CCT in full-term newborns was 605.87 ± 62.98 µm. This value is higher than that reported in several previous studies<sup>(4,11-14)</sup> but similar to that reported by Rushood et al.<sup>(15)</sup>. Other studies have shown that CCT is significantly lower in children with congenital glaucoma or childhood glaucoma<sup>(16,17)</sup>.

In a study by Uva et al.<sup>(4)</sup>, premature and full-term newborns were compared; the results showed that IOP increased with an increase in CCT, and that CCT decreased with an increase in birth weight. The authors concluded that the main factor affecting IOP was CCT. In the present study, there was no correlation between CCT and IOP. Although a correlation between CCT and IOP has not been demonstrated in the literature, there is little information about this correlation in full-term newborns. Studies such as that conducted by Karahan et al.<sup>(6)</sup> have similarly not shown an effect of CCT on IOP in premature newborns; however, these previous studies were limited by their small sample sizes.

In the present study, there was a significant negative correlation between PCA and CCT (Table 5). This finding corroborates

the results found by Ehlers et al.<sup>(19)</sup>, who observed that corneal thickness in newborns is highest during the first 24 h and significantly decreases after 48h. Moreover, they reported a decrease in the mean CCT between the day-of-birth group and the 48h group of full-term newborns (from 632 µm to 569 µm, i.e., a 10% reduction after birth), possibly owing to improved regulation of corneal hydration and evaporation and corneal remodeling, with an increase in corneal diameter and a decrease in curvature<sup>(12,14)</sup>. This process of corneal thinning steadily continues until 3 years of age, when the corneal thickness becomes the same as that of an adult. Thereafter, there is a gradual, but non-significant, decrease in the corneal thickness<sup>(18)</sup>. Remon et al.<sup>(14)</sup> also observed significant differences in corneal thickness between 1-day-olds and older children, and Ehlers et al.<sup>(19)</sup> reported that corneal thickness decreases after birth. CCT is a sensitive parameter for early diagnosis of congenital glaucoma, and its measurement is important for monitoring suspected cases; CCT measurement is also important for the interpretation of IOP in acute cases, with or without corneal edema, and chronic cases of childhood glaucoma<sup>(15)</sup>.

In the present study, weight was correlated with CCT. There were significant differences between the sexes for the variables of weight and CCT; however, other authors<sup>(6)</sup> have not reported any correlation between CCT and sex. We found that the mean CCT and mean weight were higher in male newborns than in female newborns. It is not surprising that weight correlates with CCT, since male newborns are typically heavier on average than their female counterparts; however, the difference found between the sexes might be explained by differences in GA between these groups.

The few studies published on this topic confirm that there are several variables and many questions to be explored in order to determine the factors that are associated with a predisposition for glaucomatous disease in newborns.

The present study had several limitations, such as the small sample size as a consequence of excluding newborns with systemic conditions and abnormalities on biomicroscopy, which could have affected the results of the study by introducing selection bias; moreover, the measurements could be performed only when the newborns were quiet or in the absence of any movement that could trigger a Valsalva maneuver. Moreover, the chosen technique of parting the eyelids with the operator's fingers requires great care to avoid placing the weight of the hand on the ocular globe. Therefore, eyes with intense palpebral edema had to be excluded. Finally, the lack of reliable equipment to quickly measure ocular pressure in newborns and obtain reliable mean values led to the need for repeated measurements, which is problematic because it is difficult to keep newborns quiet and still for long periods of time.

In conclusion, we found a relationship between weight and CCT, that is, as the mean weight increases, the CCT also increases. The mean CCT in Brazilian full-term newborns was 605.87 µm and the mean IOP was 14.42 mmHg, and we found no relationship between these variables in the present study.

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