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## Central Corneal Thickness in Children With Intellectual Disability: A Controlled Study

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### Abstract

**Purpose**—To evaluate the central corneal thickness (CCT) in children with intellectual disability (ID) and to determine the association between ID-related variables and CCT.

**Methods**—A total of 77 subjects with ID and 38 healthy controls were included in the study. The subjects with ID were subdivided into mild (IQ 50–69; n = 34), moderate (IQ 35–49; n = 30), and severe (IQ <34; n = 13) groups and syndromic (n = 40) versus nonsyndromic (n = 37) distinctions. All children underwent CCT assessment by ultrasound pachymetry, in addition to complete ophthalmologic examination. Analysis of variance,  $\chi^2$  test, and linear regression analysis were used for statistical analysis.

**Results**—CCT was significantly higher in the ID group ( $549.7 \pm 21.4 \mu\text{m}$ ) than that the control group ( $521.6 \pm 16.9 \mu\text{m}$ ;  $P < 0.0001$ ). Linear regression analysis revealed that presence of syndromic etiology significantly predicted higher CCT among the individuals with ID ( $P < 0.0001$ ).

**Conclusions**—Children with ID have an increased CCT compared with healthy controls. Syndromic etiology is the only variable that predicts higher CCT among the individuals with ID. Although the finding of an increased CCT in children with ID is statistically significant, it is not clinically significant.

### Keywords

intellectual disability; central corneal thickness

Ophthalmologic examination of children with intellectual disability (ID) is a serious problem. There have been several studies evaluating the ocular findings in individuals with ID. The most frequently reported ocular findings in these studies included optic atrophy, cataract, keratoconus, strabismus and refractive errors, and hypermetropia.<sup>1–4</sup> Because most of these ocular findings were amblyogenic, ophthalmologic screening of children with ID is advised.

It has been the clinical impression of one of the authors (A.A.) that an increased intraocular pressure (IOP) value was more prevalent among the children with ID. Therefore, central corneal thickness (CCT) measurements were taken. The purpose of this study was to

evaluate the CCT in children with ID and to determine the association between ID-related variables and CCT.

## MATERIALS AND METHODS

The study sample included consecutive children with ID applying to a child psychiatry clinic of a children's hospital. The ID group included 77 subjects (40 males and 37 females; mean  $\pm$  SD  $9.1 \pm 2.9$  years; age range 7–15 years). The control subjects consisted of 38 children (20 males and 18 females;  $10.3 \pm 3.1$  years; age range 7–16 years) of average intelligence recruited from the same child psychiatry out-patient clinic. The controls had IQ scores higher than 80 and without any known neurological or medical disorders. Informed written consent was obtained from the parents of all participants.

The subjects with ID were further divided into 3 groups according to the IQ levels obtained by age-appropriate intelligence tests: (1) mild (IQ of 50–69;  $n = 34$ ), (2) moderate (IQ of 35–49;  $n = 30$ ), and (3) severe (IQ  $< 34$ ;  $n = 13$ ). Full neurological examination was conducted for all subjects with ID and controls. Further investigation was required to determine the possible cause of ID; cranial magnetic resonance imaging, electroencephalography, blood and urea amino acid levels, and chromosomal analysis were carried out whenever clinically necessary.

Based on these results, the subjects with ID were further categorized under syndromic and nonsyndromic groups. The definition of syndromic ID included those children with a defined predisposing cause of ID, such as chromosomal disorders, known exposure to toxins or infections during pregnancy, prematurity complications, lead poisoning or other postnatal exposure to toxins, or evidence of metabolic disorders and head trauma. The nonsyndromic group included children with no defined predisposing cause of ID.

All children underwent CCT assessment (3 times) by ultrasound pachymetry, in addition to complete ophthalmologic examination. The IOP was measured by a portable pneumotonometer. The children were allowed to blink between measurements. The values obtained from the right eyes of each patient were evaluated.

We used analysis of variance (and post hoc Tukey test) and  $\chi^2$  tests to compare the continuous and categorical variables, respectively. In the ID group, we used linear regression analysis to evaluate the relative significance of age, sex, presence of syndromic ID etiology, and severity of ID on the central cornea thickness.  $P$  values  $< 0.05$  were regarded as statistically significant. The SPSS 13.0 statistical program was used for all analysis (SPSS, Inc). All values are stated as means  $\pm$  SD unless noted.

## RESULTS

### Demographic Variables

The sex distribution of the ID and the control groups was not significantly different ( $\chi^2 = 0.86$ ;  $P = 1.0$ ). The control subjects ( $10.3 \pm 3.1$  years) were older than the subjects with ID [ $9.1 \pm 2.9$  years;  $F(1,108) = 4.1$ ;  $P = 0.047$ ]. However, age was not found to be significantly correlated with CCT in the regression analysis ( $r = -0.89$ ;  $P = 0.35$ ). The rate of severe ID was significantly more common in syndromic ID subjects than idiopathic ID cases ( $\chi^2 = 13.9$ ;  $P = 0.001$ ; Table 1). The etiology of ID is summarized in Table 2. The additional ocular findings observed in the children in the ID group are summarized in Table 3.

IOP as measured by a portable pneumotonometry was similar in the ID ( $19.8 \pm 4.3$  mm Hg) and the control groups ( $17.3 \pm 2.4$  mm Hg;  $t = 1.92$ ;  $P = 0.76$ ). Seven patients in the study

group had IOP greater than 21 mm Hg and were referred to the glaucoma section for further investigation. However, none of them were diagnosed with glaucoma. None of the patients in the study group already had the diagnosis of glaucoma.

### Comparison of CCT

CCT was significantly higher in the ID group ( $549.7 \pm 21.4 \mu\text{m}$ ) than in the control group [ $521.6 \pm 16.9 \mu\text{m}$ ;  $F(1,108) = 45.1$ ;  $P < 0.0001$ ]. CCT was significantly higher in subjects with syndromic ID ( $n = 40$ ;  $559.6 \pm 23.3 \mu\text{m}$ ) than in the subjects with idiopathic ID [ $n = 37$ ;  $539.0 \pm 12.1 \mu\text{m}$ ;  $F(1,75) = 23.1$ ;  $P < 0.0001$ ].

CCT was significantly different among the ID severity subgroups [ $F(2,74) = 5.0$ ;  $P = 0.009$ ]. Post hoc Tukey test revealed that the CCT of subjects with severe ID ( $n = 13$ ;  $565.5 \pm 22.5 \mu\text{m}$ ) was significantly higher than that of the subjects with mild ( $n = 34$ ;  $544.7 \pm 21.3 \mu\text{m}$ ;  $P = 0.007$ ) and moderate ID ( $n = 30$ ;  $548.5 \pm 18.0 \mu\text{m}$ ;  $P = 0.036$ ), whereas there was no significant difference between the latter 2 groups ( $P = 0.74$ ).

### Multivariate Regression Analysis

To evaluate the effects of age, sex, presence of syndromic ID, and the severity of ID on CCT in the ID group, we conducted linear regression analysis. The model was statistically significant [ $F(5,71) = 5.2$ ;  $P < 0.0001$ ]. Results showed that in the ID group, presence of syndromic etiology significantly predicted higher CCT ( $\beta = 0.42$ ;  $t = 3.7$ ;  $P < 0.0001$ ). The effects of other variables, including age ( $\beta = -0.01$ ;  $t = -0.10$ ;  $P = 0.92$ ), sex ( $\beta = 0.04$ ;  $t = 0.38$ ;  $P = 0.70$ ), and the severity of ID (moderate ID:  $\beta = -0.02$ ;  $t = -0.13$ ;  $P = 0.89$  and severe ID:  $\beta = 0.18$ ;  $t = 1.47$ ;  $P < 0.15$ ) were not significant when the presence of syndromic etiology was controlled (Table 4).

The corneal thickness variable was not skewed and normally distributed indicated by skewness (0.22) and kurtosis (0.50) values. Corneal thickness was different among patients with syndromic or idiopathic ID [ $F(2,74) = 13.5$ ;  $P = 0.001$ ; Table 5]. The corneal thickness of patients with Down syndrome and patients with syndromic ID other than Down syndrome was significantly higher when compared with the idiopathic group ( $P = 0.008$  and  $P = 0.001$ , respectively), but there was no significant difference between patients with Down syndrome and other syndromic ID etiology ( $P = 0.18$ ; Table 5).

## DISCUSSION

Children with ID, particularly those with syndromic etiology, may have a predisposition for glaucoma and other ocular findings as a component of the syndrome.<sup>5</sup> The reliability of IOP measurements is low in these children because of the lack of cooperation. In addition, an increased CCT may cause an overestimation of IOP. This study showed that the children with ID had an increased CCT compared with healthy controls. Among the children with ID, the subjects with syndromic ID had significantly higher CCT. Regression analysis clearly showed that the presence of syndromic etiology was the only ID-related variable that significantly predicted higher CCT. The children in the syndromic ID group had not been diagnosed with syndromes such as mucopolysaccharidosis or other disorders that are known to cause increased CCT.

The overall difference in CCT between groups was about  $30 \mu\text{m}$ , with the ID group having a mean CCT of  $549.7 \mu\text{m}$  and the control group having a CCT of  $521.6 \mu\text{m}$ . Although this difference may be highly statistically significant, it is not clinically significant. One study suggests that there should be a 0.4 mm Hg adjustment for every  $10 \mu\text{m}$  of deviation in thickness from a CCT of  $550 \mu\text{m}$  as measured by ultrasound pachymetry.<sup>6</sup> This means that in the current study, the IOP does not have to be adjusted at all for the children with ID, who

really fall within the normal range of CCTs. If one were, however, to make an adjustment, the adjustment would only be about 1.2 mm Hg. Therefore, this data would not make much difference in patient management. If pachymetry matters in these patients, it should be measured along with the IOP and clinical decisions should be made on the data collected from the individual patient.

There have been few reports about the CCT in individuals with ID.<sup>7,8</sup> Evereklioglu et al<sup>7</sup> investigated the CCT in children with Down syndrome. A total of 28 children with Down syndrome and 20 age- and sex-matched healthy control subjects were evaluated. CCT values were below 500  $\mu\text{m}$  in 19 (67.8%) of the 28 children with Down syndrome, 4 of which were less than 450  $\mu\text{m}$ . However, all CCT measurements in the control eyes were more than 500  $\mu\text{m}$ . The mean CCT in the children with Down syndrome was significantly less than that in the healthy control subjects ( $488.39 \pm 39.87$  vs.  $536.25 \pm 20.70$   $\mu\text{m}$ ;  $P < 0.001$ ). Mean keratometric values were significantly higher in the eyes of the children with Down syndrome than in the eyes of the control subjects ( $46.35 \pm 1.28$  vs.  $43.32 \pm 1.15$  diopters;  $P < .001$ ). They concluded that children with Down syndrome had a decreased CCT compared with healthy control subjects, which should be kept in mind for IOP measurements and when developing approaches for keratorefractive treatment of patients with Down syndrome.<sup>7</sup>

Karadag et al<sup>8</sup> evaluated the CCT in individuals with ID. A total of 25 individuals with ID and 25 controls were enrolled. In the ID group, mean CCT value was  $554.0 \pm 39.7$   $\mu\text{m}$  in the right eye and  $556.8 \pm 38.7$   $\mu\text{m}$  in the left eye. In the control group, mean CCT value was  $535.7 \pm 24.2$   $\mu\text{m}$  in the right eye and  $536.5 \pm 24.8$   $\mu\text{m}$  in the left eye. CCT value in the ID group was significantly greater than that in the control group for both right ( $P < 0.05$ ) and left eyes ( $P < 0.02$ ). They concluded that CCT should be kept in mind during measurements of IOP in individuals with ID because their CCTs may be greater than those in the general population.

In conclusion, children with ID, particularly those with syndromic ID, have an increased CCT compared with healthy control subjects. Because the difference in the IOP is not clinically significant, elevated IOPs in children with ID still need further investigation.

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**TABLE 1**

Severity of ID in Idiopathic and Syndromic Subjects

ID Etiology	ID Severity, n (%)		
	Mild	Moderate	Severe
Idiopathic	23 (62.2)	13 (35.1)	1 (2.7)
Syndromic	11 (27.5)	17 (42.5)	12 (30.0)

**TABLE 2**

## Etiologies of ID Among Subjects

<b>Etiology of ID</b>	<b>Frequency, n (%)</b>
Nonsyndromic	37 (48)
Down syndrome	23 (29.9)
Tuberous sclerosis	5 (6.5)
Laurence Moon Biedl syndrome	4 (5)
Prader-Willi syndrome	1 (1.3)
Ehler Danlos syndrome	1 (1.3)
Goldenhar syndrome	1 (1.3)
Congenital hypothyroidism	3 (3.9)
Septo-optic dysplasia	1 (1.3)
Mythochondrial cytopathia	1 (1.3)
Total	77 (100.0)

**TABLE 3**

## Additional Ocular Findings in Children With ID

Variables	ID Group (n = 77)	
	Idiopathic (n = 37)	Syndromic (n = 40)
Astigmatism	7	10
Hypermetropia	6	11
Myopia	3	2
Anisometropia	2	4
Nystagmus	1	5
Horizontal	—	4
Rotatory	1	1
Strabismus		
Exotropia	—	2
Esotropia	1	3
Optic disc coloboma	—	1
Optic disc hypoplasia	—	1
Microcornea	—	1
Retinitis pigmentosa	—	1
Congenital cataract	—	1
Ectopic pupilla	—	1

**TABLE 4**

## Regression Analysis Results

	$\beta$ Value	<i>t</i> Value	<i>P</i>
Constant		56.494	0.000
Age	−0.011	−0.105	0.917
Sex	0.039	0.383	0.703
Syndromic etiology	0.420	3.725	0.000
Moderate ID	−0.015	−0.129	0.898
Severe ID	0.178	1.469	0.146



**TABLE 5**

CCT in Patients With Syndromic or Idiopathic ID

	<b>N</b>	<b>Mean CCT (μm)</b>	<b>SD</b>
Idiopathic	37	539.0000	12.14953
Syndromic other than Down syndrome	18	565.4444	30.32417
Down syndrome	22	554.8182	14.53284