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Original research

Distribution of corneal thickness and its determinants in 6−12-year-old children in an Iranian general population

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Abstract

Purpose: To determine the central corneal thickness (CCT), apex, and paracentral thicknesses and their determinants in children aged 6−12 years.
Methods: The present study was part of the phase 1 of Shahroud School Children Eye Cohort Study in 2015. Cluster sampling was done in urban areas while all children were invited to participate in the study in rural areas. The Pentacam HR was used for measurements. CCT was measured within the central 3 mm zone of the cornea, and corneal thickness 3 mm further from the center was considered paracentral thickness.
Results: Of 6624 students who were selected, 5620 (84.8%) participated in the study. Among 4956 students, studied in this report, 52.2% were boys, and the mean age of the study participants was 9.75 ± 1.71 years (6−12). The mean CCT and apical thickness was 556.29 ± 34.04 and 557.43 ± 34.03 μm, respectively. The mean paracentral thickness was 657.62 ± 39.11 μm in the superior, 632.65 ± 37.63 μm in the inferior, 648.64 ± 38.75 μm in the nasal, and 617.36 ± 37.19 μm in the temporal region. A multiple regression model showed that CCT decreased by 4.70 μm with every 1 diopter increase in the mean keratometry and increased by 20.06 μm with every 1 mm increase in the anterior chamber depth (ACD) (Both *P*-Value < 0.001). Age, sex, ethnicity and residence place were also found to be associated with CCT.
Conclusions: This study is the first to describe the distribution of corneal thickness in Iranian children with a large sample size. This study showed that corneal thickness was significantly correlated with younger age, female gender, urban residence, and a number of biometric variables.

Keywords: Central corneal thickness; Children; Cornea; General population; Iran

Introduction

Corneal thickness is an important index in corneal evaluation and a well-known factor in the assessment and determination of the prognosis of diseases like glaucoma, keratoconus, and degenerative diseases of the eye.[1−3] On the other hand, knowledge of the normal values of central and paracentral corneal thickness and the corneal thinnest point is of clinical significance, for example in refraction surgery. Few studies have addressed corneal thickness and its determinants in children in recent years.[4−7] These studies have shown that congenital diseases, race and ethnicity, body mass index, nutritional status, gestational age at birth, refractive errors, and

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corneal curvature radius are the most important determinants of central and paracentral corneal thicknesses.[4,8−10]

Among all corneal thickness measurement methods, ultrasound has been accepted as a standard method[11,12]; however, due to some limitations, non-contact methods like the Pentacam are more commonly used. The most important limitations of ultrasound include a feeling of discomfort in the eye due to the need for contact with the eye, applying pressure on the cornea as a result of moving the probe and the probability of corneal thickness underestimation, lack of pachymetry and thinnest corneal point information, and probability of corneal thickness overestimation due to different measurements of the central cornea.[13] The most important characteristic of the Pentacam is that it uses a rotating Scheimpflug camera to provide valid and reliable biometric data of the cornea and anterior segment.[11] Corneal thickness has been mostly studied in young adults and adults in Iran,[14−16] and few studies have evaluated corneal thickness and its determinants in children. For this reason, we performed a cross-sectional study to investigate the distribution of corneal thickness in schoolchildren aged 6−12 years.

Methods

The present study was part of the phase 1 of Shahroud School Children Eye Cohort Study conducted in Shahroud in 2015.[17] The target population of this cross-sectional study was the primary school students of the urban and rural areas of Shahroud. Considering the low number of children in rural areas and in order for them to benefit from eye examinations, all rural primary school students (n = 1214) were invited to take part in the study. Cluster sampling with unequal cluster was applied for random selection of about 5300 out of 12800 primary school children in urban areas of Shahroud. There were 473 classes with an average of 27 students in each class in urban areas of Shahroud, of which 200 classes were selected randomly. The students were transported to the clinic to receive optometric and ophthalmic examinations as well as imaging studies after obtaining their parents' written informed consent.

First, all students underwent the measurement of distance uncorrected visual acuity using the Nidek CP-770 chart projector at 3 m. Then non-cycloplegic refraction was measured with an auto refractometer (ARK-510A, Nidek, Japan). To refine the results of refraction, manifest refraction was measured using the Heine Beta 200 retinoscope (HEINE Optotechnik, Herrsching, Germany). Finally, all students underwent subjective refraction.

The Pentacam HR (Oculus Inc., Lynnwood, WA) with the Oculus software 6.03r19/1.18r08 was used to measure corneal thickness. The examinations (both eyes) were performed between 8:00 a.m. and 4:00 p.m., at least 2 h after waking up to avoid diurnal variations.

The corneal thickness at the pupil center, as generated by the device, was recorded as the central corneal thickness (CCT), and the average corneal thickness at 4 points within 3 mm from the center (superior, temporal, inferior, and nasal) was considered (apical thickness and the paracentral thickness were considered 3 mm further than CCT). The corneal apex was defined as the point of maximum elevation.

In this study, a spherical equivalent ≤ -0.5 Diopter (D) was considered myopia, and a spherical equivalent ≥ 2 D was considered hyperopia based on the cycloplegic refraction results.[18]

Exclusion criteria

A positive history of ocular surgery, tropia, Pentacam measurement errors, trauma, and lack of Pentacam data were the exclusion criteria.

Statistical analysis

Corneal thickness is reported as mean ± standard deviation (SD) and 95% confidence intervals (CI) in different parts of the eye. Considering the correlation of the left and right eye ($r = 0.83$ $P < 0.001$), the results of the right eye were used for analysis.

The design effect was considered for calculation of the standard error, and the sampling weight was considered when calculating mean values and other analyses.

T-test and one-way analysis of variance were used to investigate the difference between mean CCT and apical thickness according to the study variables. Then the post-hoc Scheffe test was applied to determine the means differences. Moreover, univariate linear regression was done to evaluate the relationship between variables. A backward stepwise linear regression model was employed to determine the final model of the variables affecting CCT. All analyses were performed at a significance level of 0.05 using the Stata 11 (Stata Corp, College Station, TX, USA) statistical software.

Ethical issues

The Ethics Committee of Shahroud University of Medical Sciences approved the study protocol, which was conducted in accordance with the tenets of the Declaration of Helsinki. Written informed consent was obtained from all parents.

Results

Of 6624 students who were selected, 5620 participated in the study (response rate: 84.8%). After applying the exclusion criteria, the final analysis was performed on the data of 4956 students. Boys comprised 52.2% of the subjects of this study, and the mean age of study participants was 9.75 ± 1.71 years (6−12).

Table 1 shows the distribution of the study variables in children. The distribution of CCT is presented through a histogram in Fig. 1. The mean CCT and apical thickness was 556.29 ± 34.0 and 557.43 ± 34.0 μm, respectively. Table 1 shows the mean CCT and apical thickness according to sex, age, refractive error status, residence place, and race. The results showed that the mean CCT and apical thickness had a significant difference between boys (558.5 ± 33.8 μm) and

Table 1
Distribution of central corneal and apex thickness in 6−12 year-old children of Sharoud, 2015.

Independent Variables		N	Central Thickness			Corneal Thickness in Apex		*P*-value
			Mean ± SD	95% CI	*P*-value	Mean ± SD	95% CI	
Gender	Boy	2688	558.53 ± 33.76	556.64−560.42	<0.001*	559.74 ± 33.73	557.86−561.63	<0.001*
	Girl	2420	553.82 ± 34.19	552.14−555.49		554.89 ± 34.18	553.21−556.56	
Age (Year)	6	203	559.91 ± 36.90	555.21−564.61	<0.001**	561.05 ± 37.04	556.33−565.77	<0.001**
	7	761	559.59 ± 33.99	556.47−562.72		560.81 ± 33.89	557.67−563.95	
	8	928	556.81 ± 34.35	554.14−559.49		557.90 ± 34.37	555.18−560.62	
	9	975	560.01 ± 34.59	557.08−562.94		561.17 ± 34.58	558.23−564.11	
	10	818	554.24 ± 33.11	551.36−557.13		555.39 ± 33.14	552.52−558.27	
	11	850	553.56 ± 32.31	551.03−556.09		554.74 ± 32.35	552.25−557.23	
	12	573	550.94 ± 34.47	547.51−554.36		551.99 ± 34.32	548.60−555.38	
Refractive Errors	Emmetopia	4560	556.49 ± 33.82	555.11−557.86	0.004**	557.64 ± 33.79	556.26−559.01	0.002**
	Myopia	216	550.08 ± 35.06	544.68−555.49		550.82 ± 35.26	545.36−556.28	
	Hyperopia	182	562.71 ± 34.42	557.40−568.03		564.36 ± 34.32	559.05−569.67	
Residence Place	Urban	4076	557.36 ± 31.88	555.99−558.74	<0.001*	558.50 ± 31.88	557.12−559.88	<0.001*
	Rural	1032	546.27 ± 48.44	543.34−549.20		547.50 ± 48.38	544.58−550.41	
Ethnicity	Fars	4968	556.47 ± 34.04	555.15−557.78	0.012**	557.60 ± 34.03	556.28−558.92	0.016**
	Turk	54	544.58 ± 32.58	535.92−553.24		546.19 ± 32.42	537.58−554.80	
	Other	84	551.09 ± 32.91	544.22−557.96		552.55 ± 33.00	545.65−559.46	

*P-value was calculated by independent sample t-test; **P-value was calculated by ANOVA.
SD: Standard Deviation; CI: Confidence Interval; N: Number.

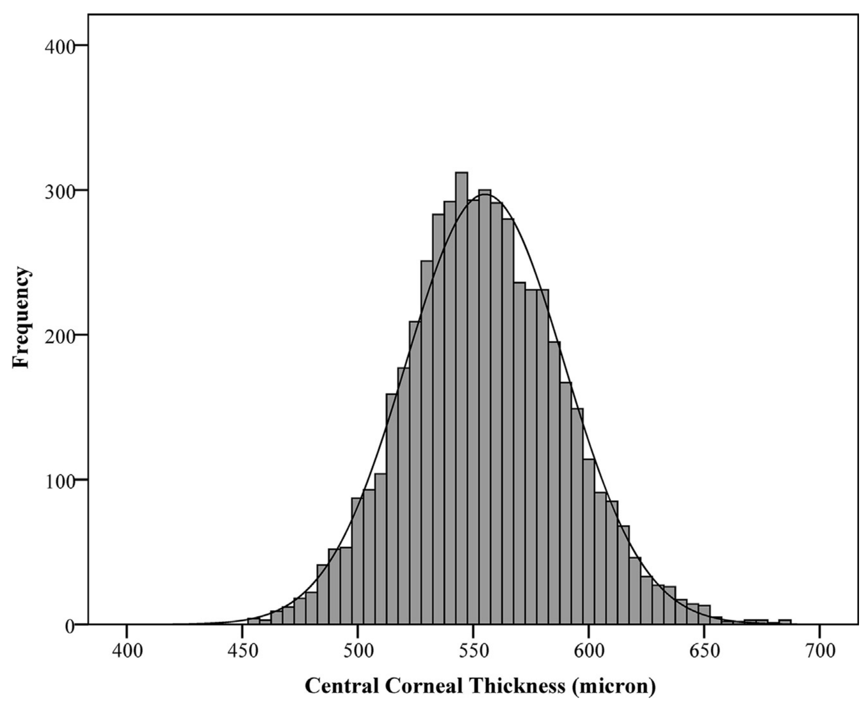

Fig. 1. Distribution of central corneal thickness (CCT) in children aged 6-12 years in Shahroud, Iran, 2015.

girls (553.8 ± 34.2 μm) ($P < 0.001$). The highest and lowest CCT and apical thickness was seen in children aged 6 and 12 years, respectively. The mean CCT and apical thickness had a significant correlation with the refractive error status ($P < 0.001$) as children with hyperopia had the highest and children with myopia had the lowest CCT and apical thickness.

CCT and apical thickness were significantly higher in urban children in comparison with rural children ($P < 0.001$). The mean CCT and apical thickness was significantly higher in Fars children as compared to other ethnicities ($P = 0.012$ and $P = 0.016$).

The mean paracentral corneal thickness was 657.6 ± 39.1, 632.7 ± 37.6, 648.6 ± 38.8, and 617.4 ± 37.2 μm in the superior, inferior, nasal, and temporal region, respectively. These values are presented according to the study variables in Table 2. Univariate linear regression analysis showed that sex, age above 10 years, ethnicity, anterior chamber depth (ACD), and mean keratometry were associated with CCT (Table 3). It was also found that for each diopter increase in refraction, corneal

Table 2
Distribution of peripheral corneal thickness in 6–12 year-old children of Shahroud, Iran, 2015.

Independent Variable		Superior		Inferior		Nasal		Temporal	
		Mean ± SD	95% CI	Mean ± SD	95% CI	Mean ± SD	95% CI	Mean ± SD	95% CI
Gender	Boy	660.34 ± 39.09	658.42–662.27	635.56 ± 37.57	633.54–637.58	649.93 ± 38.96	647.75–652.12	619.41 ± 36.94	617.37–621.44
	Girl	654.61 ± 38.91	652.70–656.52	629.44 ± 37.43	627.60–631.28	647.21 ± 38.47	645.22–649.21	615.11 ± 37.34	613.25–616.97
Age Group (year)	6	655.57 ± 42.35	650.19–660.96	634.09 ± 40.78	628.75–639.43	651.14 ± 42.93	645.52–656.75	620.63 ± 40.24	615.27–626.00
	7	656.52 ± 40.04	653.02–660.02	635.31 ± 37.62	631.94–638.68	652.07 ± 38.85	648.87–655.27	620.52 ± 37.73	617.11–623.93
	8	656.24 ± 39.05	653.26–659.23	633.30 ± 38.86	630.36–636.24	649.66 ± 38.75	646.79–652.54	617.41 ± 37.35	614.42–620.39
	9	660.99 ± 40.65	657.69–664.30	636.24 ± 38.00	632.81–639.66	652.72 ± 40.09	649.12–656.33	621.27 ± 37.69	618.12–624.42
	10	656.13 ± 38.34	652.80–659.46	631.16 ± 36.60	627.98–634.34	646.13 ± 37.73	642.79–649.48	615.09 ± 36.59	611.89–618.29
	11	657.61 ± 36.04	654.97–660.25	630.14 ± 35.60	627.46–632.81	645.01 ± 36.37	642.02–648.00	614.97 ± 35.22	612.14–617.80
	12	658.34 ± 39.67	654.34–662.35	627.70 ± 37.65	624.02–631.38	644.09 ± 38.82	640.07–648.10	612.58 ± 37.22	608.86–616.29
Refractive Errors	Emmetopia	657.74 ± 39.04	656.25–659.24	632.71 ± 37.30	631.20–634.21	648.86 ± 38.57	647.29–650.43	617.53 ± 36.86	616.05–619.02
	Myopia	651.63 ± 37.68	646.02–657.23	626.56 ± 38.21	620.86–632.26	641.28 ± 37.54	635.65–646.91	610.60 ± 39.54	604.50–616.71
	Hyperopia	663.30 ± 39.39	657.40–669.20	640.36 ± 40.33	634.37–646.35	656.04 ± 40.62	650.10–661.97	624.41 ± 37.48	618.64–630.18
Residence Place	Urban	658.44 ± 36.70	656.94–659.93	633.79 ± 35.25	632.28–635.30	650.01 ± 36.30	648.44–651.58	618.41 ± 34.90	616.92–619.91
	Rural	649.97 ± 56.07	646.82–653.11	621.99 ± 53.55	618.75–625.24	635.83 ± 54.28	632.48–639.18	607.59 ± 52.43	604.53–610.65
Ethnicity	Fars	657.84 ± 39.10	656.43–659.25	632.86 ± 37.63	631.43–634.30	648.90 ± 38.75	647.40–650.40	617.56 ± 37.22	616.14–618.98
	Turk	642.82 ± 39.94	631.48–654.16	618.20 ± 36.22	608.50–627.90	631.60 ± 36.54	621.87–641.32	604.13 ± 34.93	594.71–613.56
	Other	651.49 ± 36.12	644.07–658.91	626.76 ± 35.57	619.30–634.23	641.16 ± 35.78	633.36–648.95	611.96 ± 33.82	604.73–619.19

thickness increased by 1.86 μm ($P = 0.002$) in simple linear regression model.

Multiple linear regression after adjustment of the results for confounders revealed that age, sex, and residence place were associated with CCT. Linear regression model also showed that with every 1 mm increase in the ACD, CCT increased by 20.06 μm, and with every 1 mm increase in mean keratometry, CCT decreased by 4.70 μm.

Discussion

In this cross-sectional study, we used the Pentacam to evaluate the distribution of corneal thickness and its determinants in the age group 6–12 years for the first time in Iran. For this reason, we had some limitations in comparing our results with the findings of other domestic studies. Our results showed that the mean CCT was 556.29 μm in the study population. The values obtained in other studies (Table 4) indicate a controversy in the results of CCT measurement in children. Ma et al.[5] reported a CCT of 532.96 μm in Chinese children aged 7–15 years while these values were 550.70 and 553.00 μm in other studies in China, which are closer to our results.[6,29] Tong et al.[30] reported a CCT of 543.6 μm in Singaporean children aged 9–11 years, which is lower than our result. Age is one of the most important reasons for differences in corneal indices. Findings indicate that age is a determinant of CCT. A study conducted by Pediatric Eye Disease Investigator Group on children aged 0–17 years showed that CCT increases with age in 1 to 11-year-old children and then remains unchanged.[7] Moreover, Husain et al.[31] found that CCT increased with age in children while Ma et al.[5] found no increase in CCT in the age group 7–15 years. Our finding is in contrast to the above results. We noted a decrease in CCT with age. For example, CCT showed a mean decrease of 8.97 μm when comparing children aged 12 with 6 years. Some researchers believe that the increase or decrease in the corneal thickness with age is not a steady trend and may be unpredictable considering the lifestyle and environmental exposures.[32]

According to Table 4, different studies have used different devices like the Pentacam, ultrasound, BioGraph, etc., or different versions of the same device. On the other hand, the differences in the expertise of the technicians and their familiarity with each device as well as their ability in interpreting the results may be other reasons for different results.

Finally, it seems that ethnic and racial differences are other factors contributing to different results in different populations. Bradfield et al.[7] reported that the cornea was thicker in white children in comparison with East Asian children whereas East Asian children had thicker corneas than African-American black children and South Asian children. A study in Singapore showed that despite living in a common environment, Chinese children had thicker central corneas than Malaysian or Indian children living in Singapore.[29]The results of current study also indicates that CCT differ in ethnicity groups (Table 3).

The results of different studies on the effect of sex on CCT are contradictory. Some studies with an adequate sample size and strong methodology have shown a thicker cornea in men.[22,29] According to our results, central cornea was 4.71 μm

Table 3
Simple and multiple linear regression analysis of demographic factors and ocular indexes to predict central corneal thickness, Shahroud, Iran, 2015.

Independent Variables		Simple linear regression				Multiple linear regression				Overall *P*-value[a]
		coefficient	95% CI		*P*-value	coefficient	95% CI		*P*-value	
Gender	Boy	Reference				Reference				0.003
	Girl	−4.71	−7.25	−2.18	<0.001	−3.62	−6.01	−1.22	0.003	
Age group (year)	6	Reference				Reference				<0.001
	7	−0.32	−6.04	5.41	0.913	−0.71	−6.36	4.93	0.804	
	8.	−3.09	−8.46	2.27	0.257	−3.23	−8.31	1.84	0.210	
	9	0.10	−5.47	5.67	0.972	−0.24	−5.50	5.02	0.928	
	10	−5.66	−11.17	−0.15	0.044	−6.35	−11.63	−1.08	0.018	
	11	−6.35	−11.69	−1.01	0.020	−6.21	−11.59	−0.83	0.024	
	12	−8.97	−14.79	−3.14	0.003	−8.04	−13.80	−2.29	0.006	
Residence Place	Urban	Reference				Reference				<0.001
	Rural	−11.09	−14.34	−7.85	<0.001	−9.56	−12.82	−6.29	<0.001	
Biometric Components	Corneal Volume (microL)	−0.17	−0.21	−0.14	<0.001	0.94	−2.45	4.33	0.585	
	Mean keratometry (diopter)	−3.16	−3.86	−2.45	<0.001	−4.70	−5.47	−3.93	<0.001	
	Anterior Chamber Depth (mm)	−14.44	−18.03	−10.84	<0.001	20.06	13.98	26.14	<0.001	
	Anterior Chamber Volume (microL)	−0.17	−0.21	−0.14	<0.001	−1.30	−4.69	2.10	0.452	
Refractive Errors	Emmetropia	Reference								0.581
	Myopia	−6.40	−11.91	−0.90	0.023	−0.78	−6.22	4.67	0.779	
	Hyperopia	6.23	0.74	11.71	0.026	2.72	−2.66	8.09	0.321	
Ethnicity	Fars	Reference								0.027
	Turk	−11.89	−20.61	−3.17	0.008	−10.21	−19.12	−1.31	0.025	
	Other	−5.38	−12.29	1.54	0.127	−5.44	−11.87	0.98	0.096	

[a] Adjusted Wald test.

Table 4
Comparison of mean central corneal thickness (CCT) values in different studies.

Study year and country	Age group (year)	Mean ± SD of CCT (μm)	Measurement tools
2014, Turkey[19]	1–12	556.00 (In 1–2 years old) 555.00 (In 11–12 years old)	Ultrasound biometry
2016, Mexico[20]	Under 20	558.82 ± 37.39	Ultrasonic pachymetry
2016, Iran[21]	6–13	513.47 ± 33.88	Specular microscopy
2012, Turkey[22]	5–18	557.91 ± 34.26	Ultrasonic pachymeter
2011, Malaysia[23]	8–16	530.87 ± 30.79	Specular microscopy
2010, Italy[24]	7–17	570.61 ± 37.4 (In patients with growth defect) 546.00 ± 24.9 (In healthy group)	Hand held ultrasound pachymeter
2009, Turkey[25]	mean age: 10.3	576.9 ± 41.8(In diabetes mellitus group) 521.00 ± 16.6 (Control group)	Ultrasound pachymeter
2008, USA[26]	10–18	535.00 ± 35 (In African American) 559.00 ± 38 (In white children)	Contact ultrasound
2002, Iran[27]	14–19	575.10 ± 44.50	Orbscan II
2012, Iran[28]	6–18	549.33 (95% CI: 546.59–552.07)	LENSTAR/BioGraph

CCT: Central corneal thickness.
CI: Confidence intervals.

thicker in boys than girls on average ($P < 0.001$). When adjusted for other variables, we found also that the central cornea was 3.62 μm thicker in boys than girls, too (Table 3). Tong et al.[30] also reported that the central cornea was 6.5 μm thicker in boys than girls. Similarly, some other studies have also shown that boys have thicker corneas than girls.[6,32] Considering the adjustment for age in this study, it seems that anatomical differences in the ocular structure between boys and girls are the reason for the difference in CCT. However, some authors believe that the effect of sex on CCT is not significant.[5,33]

According to our results, the central cornea was 11.09 μm thicker in urban residents versus rural residents ($P < 0.001$). Vijaya et al.[34] showed the central cornea was 17.4 μm thicker in the urban versus the rural population of India. They also reported a greater decrease in CCT per decade of life in the rural population in comparison with city dwellers. It seems that environment, lifestyle, exposure to environmental factors like sunlight, and nutritional status play an important role in CCT. Alsbrik et al.[35] conducted a study on 868 adults and reported that city residents had thicker corneas than their rural counterparts and attributed the difference mainly to environmental exposures. It should be noted that given the large sample size in this study, some differences may be statistical significance while they are not important in current clinical application.

According to our findings, with every 1 mm increase in ACD, CCT decreased by 14.44 μm in simple linear regression, but when adjusted with other variable in multiple model, CCT increased by 20.06 with every 1 mm increase in ACD. This finding is in contrary with the results of Tehran Eye Study, indicating a 12.20 μm decrease in CCT with every 1 mm increase in ACD.[27] Curtin[36] and Suzuki et al.[37] also reported a positive correlation between a deeper anterior chamber and thinner central cornea, while Chen et al.[38] found no significant relationship between ACD and CCT. Few studies have addressed the relationship between ACD and CCT, and no convincing reason has been proposed for the reported associations. However, some authors have attributed lack of relationship between ACD and CCT to lack of relationship between axial length and CCT in their findings.[39] More studies are required to investigate the relationship between ACD and CCT.

There are contradictory reports on the relationship between corneal curvature and CCT in some population-based studies. Shimmyo et al.[39] reported a positive association between CCT and corneal curvature. Moreover, Ma et al.[5] evaluated children aged 7−15 years and found that with every 1 mm increase in corneal curvature, CCT increased by 14.8 μm. Population-based studies in Singapore[9] and India[40] have also shown a positive association between CCT and corneal curvature radius while Suzuki et al.,[37] Cho et al.,[41] and Chen et al.[38] found no relationship between CCT and corneal curvature. Contrary to these studies, we found that with every 1 mm increase in mean keratometry, CCT decreased by 4.70 μm. However, the decrease in CCT was much less in univariate analysis than the final model, indicating the considerable effect of confounders. Attention should also be paid to the role of the measurement device in the relationship between CCT and corneal curvature as studies that used ultrasound found no association.[38,41]

As a limitation, the present results may only be generalized to Shahroud children and cannot be generalized to all Iranian children. Abnormal corneal shapes were not excluded in this study, which may be considered another limitation. However this study, as one of the largest eye studies on children, showed that CCT decreases with age, and boys have thicker corneas than girls. Moreover, the cornea is thicker in city dwellers than rural residents. Among biometric indices, important variables like ACD and corneal curvature have an inverse effect on CCT. In other words, CCT decreases with an increase in ACD and corneal curvature.

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