Special Focus, Cornea, Original Article

A cross-sectional study to compare the normal corneal epithelial thickness in various age groups of Indian population using 9 mm wide optical coherence tomography scans

Abhishek Hoshing[1,5], Seema Bhosale[2], Monica Samant[3], Aditya Bamne[4], Huma Kalyankar[4]

Purpose: To compare the corneal epithelial thickness among various age groups of normal Indians with 9-mm-wide optical coherence tomography scans. **Methods:** This cross sectional, observational study recruited patients in the age groups of 5–20 years (group 1), 21–35 years (group 2), 36–50 years (group 3), and more than 51 years (group 4). They underwent a detailed ophthalmic examination and were excluded if found to have any ocular surface or intraocular disease (except cataract and refractive error), undergone any ophthalmic surgery, corneal topography changes suggestive of corneal ectasias, or been continuously using any topical medication in either eye for a period of 3 months or more with the last instillation being within 1 month of inclusion in the study. Corneal epithelial thickness (CET) was measured using anterior segment optical coherence tomography (AS-OCT). The CET data from 25 sectors in each eye were analyzed for each age group. **Results:** There were 71 subjects in group 1, 76 subjects in group 2, 59 subjects in group 3, and 57 subjects in group 4. The mean (± standard deviation) ages in the groups 1, 2, 3, and 4 were 14.04 ± 5.10, 26.63 ± 4.71, 42.66 ± 3.92, and 61.65 ± 7.47 years, respectively. The central corneal thickness in all age groups was comparable. Maximum variance in CET parameters was seen in superior cornea. **Conclusion:** Central corneal thickness remains fairly stable over various age groups. The maximum variance in CET over age is seen in superior cornea. The findings from the Indian population correlate well with racially and geographically distinct subjects.

Access this article online

Website:
www.ijo.in

DOI:
10.4103/ijo.IJO_1621_21

Quick Response Code:

Key words: ASOCT, corneal epithelial thickness, corneal epithelium, normative data

Corneal epithelial thickness (CET) parameters and their changes are a subject of interest vis-à-vis ectasia diagnosis and treatment, orthokeratology lenses, and advanced surface ablations for correction of refractive errors.[1,2] However, having a normative database is essential prior to understanding and analyzing effects secondary to disease entity or treatment modalities.

Most studies that aimed to assess the CET in normal individuals using optical coherence tomography (OCT) have been limited by having a scan diameter of only 6 mm.[3-6] This leads to poor assessment of extreme peripheral CET and can have a bearing on the assessment of CET changes in peripheral ectasias, wider ablation zones in kerato-refractive surgery, and orthokeratology lenses. Furthermore, the studies that aimed to compare the CET in various age groups did not include pediatric subjects.[7,8]

In this study, we aim to compare the CET parameters in various age groups, measured using a 9-mm-wide OCT scan, including a comparable representation of the pediatric population.

[1]Department of Cornea and Refractive Surgery, [2]Cataract Services, [3]Pediatric Ophthalmology, Strabismus and Neuro-Ophthalmology, [4]Clinical Optometry, Laxmi Eye Institute, Panvel, Maharashtra, [5]Department of Ophthalmology, Apollo Hospitals, Navi Mumbai, Maharashtra, India

Correspondence to: Dr. Abhishek Hoshing, Laxmi Eye Institute, Uran Road, Panvel - 410 206, Maharashtra, India. E-mail: abhishekhoshing@gmail.com

Received: 11-Jun-2021 Revision: 22-Aug-2021
Accepted: 01-Sep-2021 Published: 27-Jan-2022

Methods

This was a prospective, cross-sectional observational study carried out in a tertiary care eye hospital in western India over an 18-month period from August 2017 to February 2019. Clearance from the institutional review board and ethics committee was obtained prior to the commencement of the study. The adult subjects provided written informed consent to participate in the study. Informed consent was obtained from the parents/guardians of the children and minor subjects.

Stratified sampling technique was used by dividing the subjects into four age groups, *viz.* 5–20 years (group 1), 21–35 years (group 2), 36–50 years (group 3), and more than 51 years (group 4), to have comparable representation. We aimed to recruit at least 50 subjects in each group to have a predetermined convenient sample of 200 subjects (400 eyes). The age completed at last birthday was considered while including the subject in the study.

Patients presenting to the hospital for correction of refractive errors and cataract surgery were included in the study. Detailed

Cite this article as: Hoshing A, Bhosale S, Samant M, Bamne A, Kalyankar H. A cross-sectional study to compare the normal corneal epithelial thickness in various age groups of Indian population using 9 mm wide optical coherence tomography scans. Indian J Ophthalmol 2022;70:505-10.

refraction, slit-lamp, and biomicroscopic examinations were done for all patients prior to inclusion in the study. Presence of ocular surface or intraocular disease conditions (except cataract and refractive error), history of undergoing any ophthalmic surgery in the past, corneal topography changes suggestive of ectasias (screened in patients with astigmatism more than 3 D), or history of continuous use of any topical medication in either eye for a period of 3 months or more with the last instillation being within 1 month of inclusion in the study were criteria for exclusion.

The subjects who fulfilled all the criteria underwent corneal epithelial thickness measurement with anterior segment optical coherence tomography (AS-OCT) on the Avanti OCT (Model RTVueXR1002, Optovue, USA) using the Cam-L (low-magnification corneal lens adapter). The scans were performed by the same person. A 735-nm infrared LED on gooseneck cable was used to externally illuminate the cornea and pupil, and the subjects were asked to look at the internal fixation target. The best of three consecutive scans with good demarcation of corneal boundaries and good measurement reliability rating with signal strength index (SSI) >60 was included in the study for analysis.

The OCT corneal epithelial thickness (CET) output map generates automatic thickness data and comprises four concentric zones. The innermost or the central zone is a circle of 2-mm diameter. The paracentral, midperipheral, and peripheral zones are concentric rings created by circles of the diameters 5, 7, and 9 mm, respectively. The outer three zones are further divided into eight pie segments (PS) by eight radiating lines. Thus, each PS, *viz.* superior, superotemporal, temporal, inferotemporal, inferior, inferonasal, nasal, and superonasal, has a paracentral, midperipheral, and peripheral zone. We chose to call each of these areas a sector. Thus, the machine presents the CET (in microns) for a total of 25 sectors including the central circle.

The CET data from each of these sectors were analyzed separately for each age group by using IBM SPSS Statistical Software version 23. The demographic data and refraction data were also captured and analyzed. The paired *t*-test was performed for intereye comparison of the mean CET of each sector within an age group. The one-way ANOVA test was done to assess the variance of the mean CET of each sector across the various age groups.

All data are presented in tables and figures.

Results

In total, 263 right and left eyes of 263 patients were analyzed as a part of the study.

There were 71 subjects in group 1, 76 subjects in group 2, 59 subjects in group 3, and 57 subjects in group 4. The mean (± standard deviation) ages in groups 1, 2, 3, and 4 were 14.04 ± 5.10, 26.63 ± 4.71, 42.66 ± 3.92, and 61.65 ± 7.47 years, respectively.

The male:female ratio of subjects was 35:36 in group 1, 27:49 in group 2, 27:32 in group 3, and 34:23 in group 4.

Table 1 presents the median (with minimum and maximum) spherical and cylindrical errors refractive errors in the various age groups.

Fig. 1a presents the mean and standard deviation of the CET values in each sector for the right and left eye in group 1. Fig. 1b presents the same data for group 2. In group 1

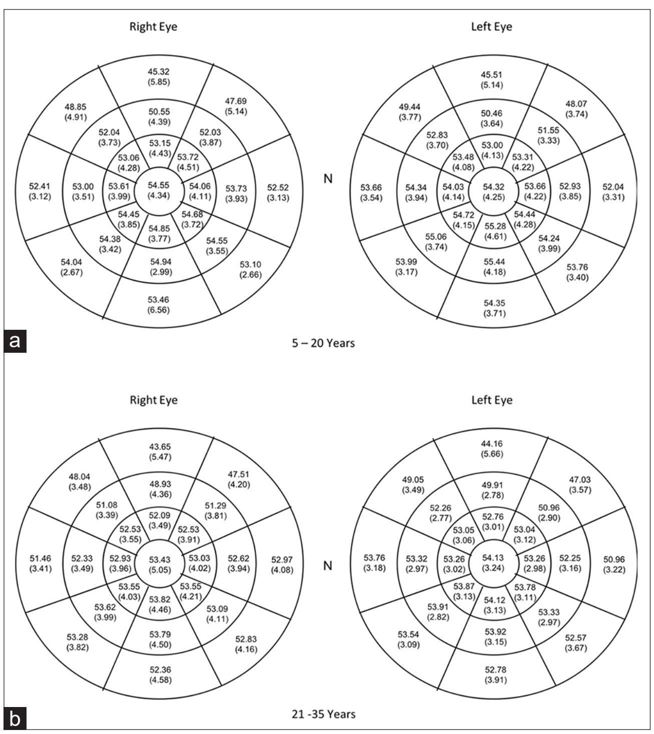

Figure 1: Mean CET of the 25 sectors in the right and left eye of the subjects in group 1 (5–20 years) in (a) and in group 2 (21–35 years) in (b) *(values in parenthesis depict the standard deviation)*

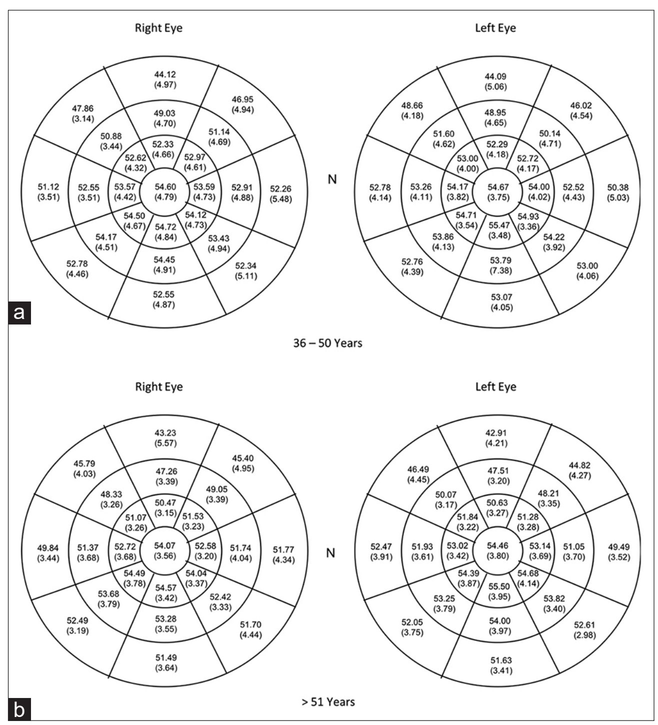

Figure 2: Mean CET of the 25 sectors in the right and left eye of the subjects in group 3 (36–50 years) in (a) and in group 4 (>51 years) in (b) *(values in parenthesis depict the standard deviation)*

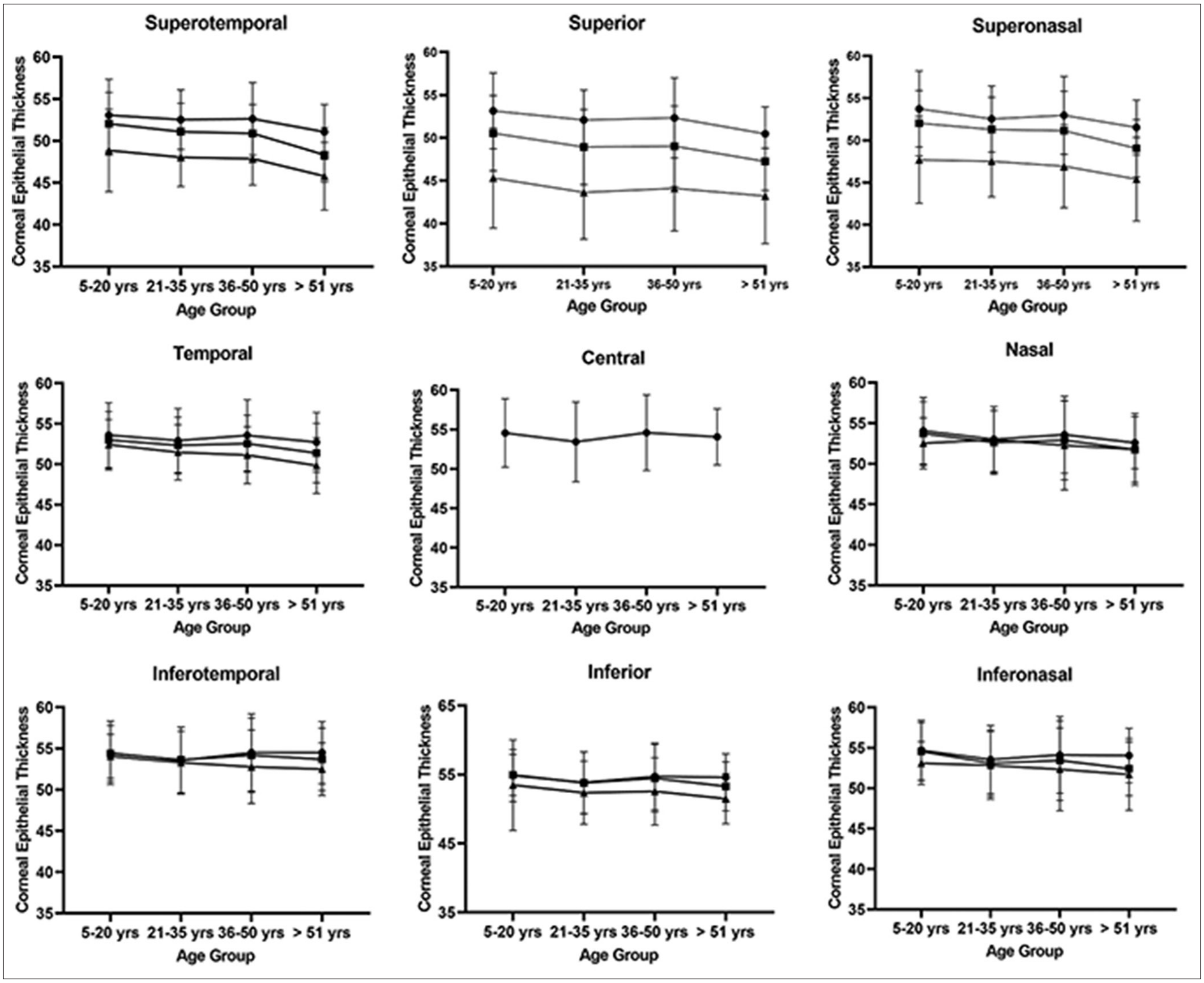

Figure 3: Dot-and-whisker plot depicting the age-group-wise trends in the mean CET values of each sector plotted for individual pie segments of the right eyes of the subjects *(whisker depicts the standard deviation; ● represent the paracentral sectors; ■ represents the midperipheral sectors; and ▲ represents the peripheral sectors)*

(5–20 years), a significant difference in the mean CET value was found between the superonasal peripheral ($P = 0.002$), nasal peripheral ($P = 0.001$), and inferonasal peripheral ($P < 0.001$) sectors of the right and left eye. In group 1, no other sector in the right eye had a significantly different CET value when compared to the left eye.

In group 2, significant difference in the CET values between right and left eyes was found in superior paracentral ($P = 0.029$), superior midperipheral ($P = 0.020$), superonasal midperipheral ($P = 0.017$), inferonasal midperipheral ($P = 0.042$), superonasal peripheral ($P = 0.002$), and superotemporal peripheral ($P = 0.011$) sectors.

Fig. 2a and b present the mean and standard deviation of CET values for each sector of the right and left eyes of subjects in groups 3 and 4, respectively. In group 3, the mean CET values were significantly different between right and left eyes only in the superonasal peripheral ($P = 0.035$) and superotemporal peripheral ($P = 0.006$) sectors. The inferior paracentral and the superonasal midperipheral sectors of right and left eyes in

Table 1: Table depicting the Median (Minimum, Maximum) Spherical and Cylindrical refractive errors in four age groups

Parameter	Right eye	Left eye
Median (Min, Max) Spherical error (in Diopters)		
5-20 years	0.00 (−7.00, 4.00)	0.00 (−6.00, 6.00)
21-35 years	0.00 (−5.00, 0.25)	0.00 (−5.00, 6.00)
36-50 years	0.00 (−5.75, 2.00)	0.00 (−9.00, 2.50)
>51 years	0.75 (−8.50, 4.75)	0.75 (−7.25, 3.75)
Median (Min, Max) Cylindrical error (in Diopters)		
5-20 years	−0.50 (−5.00, 3.00)	−0.75 (−4.00, 3.00)
21-35 years	−0.50 (−2.25, 0.00)	−0.50 (−4.50, 2.00)
36-50 years	−0.50 (−3.50, 0.00)	−0.625 (−3.00, 0.00)
>51 years	−0.75 (−3.00, 0.00)	−1.00 (−1.75, 1.25)

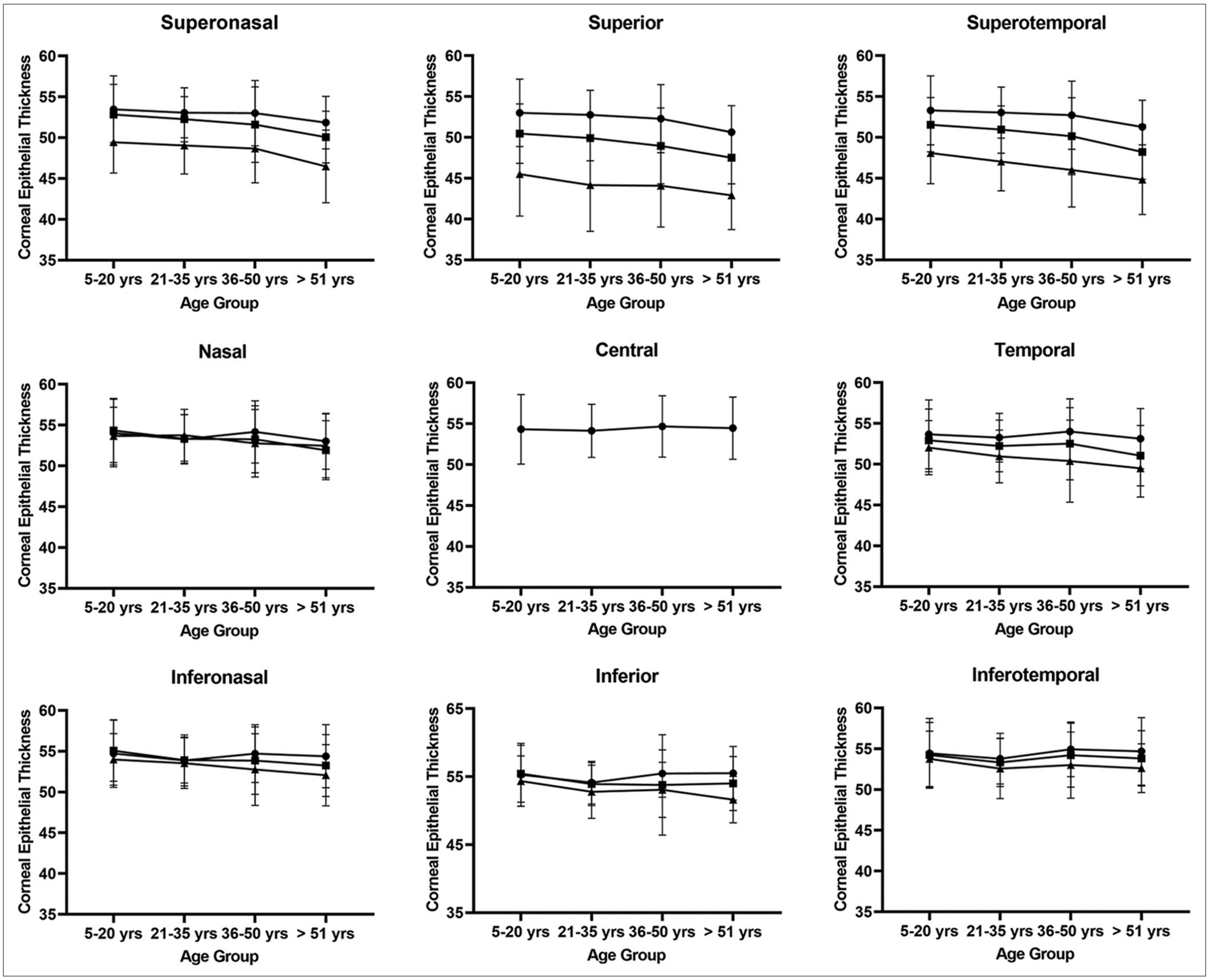

Figure 4: Dot-and-whisker plot depicting the age-group-wise trends in the mean CET values of each sector plotted for individual pie segments of the left eyes of the subjects *(whisker depicts the standard deviation; ● represent the paracentral sectors; ■ represents the midperipheral sectors; and ▲ represents the peripheral sectors*)

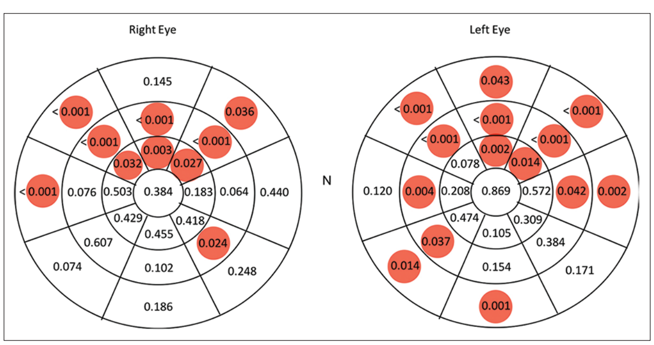

Figure 5: Plot depicting the significance levels (*p*) obtained by testing the variance of mean CET of each sector across the four age groups for right and left eyes. Sectors showing statistically significant variance are highlighted

group 4 had significantly different mean CET values ($P = 0.008$ and 0.005, respectively).

Figs. 3 and 4 depict the trend of mean CET values of each sector across the various age groups. As is evident from both figures, for each age group, the separation in the line graphs depicting each sector was maximum for the superior, superonasal, and superotemporal pie segments. This means that for every age group, the variation of CET from the central to the peripheral cornea is maximum in the three superior pie segments.

One-way ANOVA was done to look for the variance of mean CET values of each sector among various age groups. The significance level of the variance for each sector is plotted in Fig. 5. The sectors that showed statistically significant variance across the age groups are highlighted in the plot. It is evident that the CET values of the superior cornea showed consistently significant variance across the age groups.

Discussion

The aim of our study was to present a comparison of the CET parameters in various age groups of normal individuals, including the pediatric age group. Few other studies in the past have attempted to compare the CET parameters obtained by OCT among various age groups. In the study by Samy *et al*., 240 eyes of 120 individuals of an Egyptian population were studied.[7] However, they did not include children and the youngest subject included in their study was 18 years old. A similar age grouping was employed by Kim *et al*. in their study involving 210 healthy Korean individuals.[8] The study that most closely mimics our age grouping was the one done by Yang *et al*.[9] They included pediatric subjects too and the lowest age limit was set at 0 years. They compared the CET parameters in the age groups 0–20 years (A), 21–40 years (B), 41–60 years (C), and >60 years (D). However, all these studies differed from our study in the fact that they used a 6-mm-wide scan of the corneal epithelium to measure the thickness.

In the study by Yang *et al*.,[9] the mean CETs in the central 2 mm were 53.4 ± 2.8, 53.4 ± 2.7, 53.2 ± 3.0, and 52.9 ± 3.3 μm in the age groups A, B, C, and D, respectively. These values are fairly comparable to those found in our study for right and left eyes of subjects in all age groups. As evident from Figs. 3 and 4, the central CET values remained fairly constant across all age groups. This echoes the findings of the study by Yang *et al*.

Figs. 3 and 4 show the dot-and-whisker plot depicting the age-group wise trends in the mean CET values of each sector plotted for individual pie segments of the right and left eyes of the subjects, respectively. It is evident from these figures that both for the right and left eye, the maximum change in the mean CET from paracentral to peripheral sectors was seen in the superior, superonasal, and superotemporal pie segments for all age groups. For all other sectors, the mean CET values for each sector in individual pie segments were clustered close to each other.

Fig. 5 plots the significance levels (*P*) obtained by testing the variance (using ANOVA test) of mean CET of each sector across the four age groups for right and left eyes. As evident, the sectors showing significant variance in CET over different age groups were more consistently clustered in the superior halves of both eye corneas. Similar plots were presented in the study by Kim *et al*. and Yang *et al*. based on results obtained from the one-way ANOVA test.[8,9] In the former study, significant variance in the mean CET values was found in all sectors except the central and a single inferotemporal sector in both eyes. In the latter study, the inferior, inferotemporal, and temporal sectors showed no significant variance in addition to the central CET, for both right and left eyes. While our study concurs with the general theme of significant variance in the superior halves of both eyes, it failed to obtain such consistency between the two eyes as reported in the abovementioned studies.

Our study reiterates the fact that the central corneal thickness is not susceptible to age and it stays fairly stable. Similar conclusions have been drawn by other authors using different imaging modalities.[3,10-12] Yang *et al*. attributed this to the purported stem cell-like or progenitor cell-like properties of the central corneal epithelium, which helps to maintain the central corneal thickness and is thus devoid of effects of age.[9]

In our study, the CET parameters of the superior sectors were found to be significantly varying with age with progressive thinning of the superior CET. The thinner CET values in the superior pie segments are attributed to the upper eyelid dynamics. The constant excursion of the upper eyelid during blinking causes friction, leading to desquamation of the epithelium in the superior cornea.[13] We hypothesize that increasing age and the resultant longer period of upper eyelid trauma faced by the superior corneal epithelium causes this significant variance.

Our study has shown that for every age group, the superior corneal CET changes more drastically from the center to the periphery. This needs to be borne in mind while developing CET-based algorithms to detect primarily superior ectasias such as Terrien marginal degeneration or superior pellucid marginal corneal degeneration (PMCD). In contrast, the inferior cornea does not suffer from drastic CET changes from the center to the periphery. Hence, the slightest change in CET may be a useful indicator in algorithms detecting ectasias such as keratoconus, PMCD, or post-refractive surgery ectasia, which primarily affect the inferior halves of the cornea.

Our study is not completely devoid of shortcomings. The study population was selected from the individuals seeking eye care; thus, it is a hospital-based study. Hence, the CET parameters, though extremely unlikely, may not be entirely representative of the entire population.

The age groups in our study include subjects from more than one decade of life and therefore are not representative of a particular age-group decade. This distribution of the age groups was selected to be able to include the youngest possible children while maintaining a regular class interval. We believe that regrouping the study subjects according to chronological age group decades did not affect or change the outcome of the study.

Conclusion

To conclude, our study accomplishes its objective of comparing the CET values among various age groups in normal Indian subjects. The values correlate well with data published by other researchers from other parts of the world. Therefore, any future guidelines pertaining to diagnostic algorithms and treatment protocols based on CET parameters can be extrapolated to Indian subjects too.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Salomão MQ, Hofling-Lima AL, Lopes BT, Canedo ALC, Dawson DG, Carneiro-Freitas R, *et al*. Role of the corneal epithelium measurements in keratorefractive surgery. Curr Opin Ophthalmol 2017;28:326-36.
2. Kim WK, Kim BJ, Ryu I-H, Kim JK, Kim SW. Corneal epithelial and stromal thickness changes in myopic orthokeratology and their relationship with refractive change. PLoS ONE 2018;13:e0203652.
3. Kanellopoulos AJ, Asimellis G. *In vivo* three-dimensional corneal epithelium imaging in normal eyes by anterior-segment optical coherence tomography: A clinical reference study. Cornea 2013;32:1493-8.
4. Wu Y, Wang Y. Detailed distribution of corneal epithelial thickness and correlated characteristics measured with SD-OCT in myopic eyes. J Ophthalmol 2017;1018321. doi: 10.1155/2017/1018321.

5. Li Y, Tan O, Brass R, Weiss JL, Huang D. Corneal epithelial thickness mapping by Fourier-domain optical coherence tomography in normal and keratoconic eyes. Ophthalmology 2012;119:2425-33.
6. Ma Y, He X, Zhu X, Lu L, Zhu J, Zou H. Corneal epithelium thickness profile in 614 normal Chinese children aged 7-15 years old. Sci Rep 2016;6:23482. doi: 10.1038/srep23482.
7. Samy MM, Shaaban YM, Badran TAF. Age- and sex-related differences in corneal epithelial thickness measured with spectral domain anterior segment optical coherence tomography among Egyptians. Medicine (Baltimore) 2017;96:e8314.
8. Kim BJ, Ryu IH, Kim SW. Age-related differences in corneal epithelial thickness measurements with anterior segment optical coherence tomography. Jpn J Ophthalmol 2016;60:357-64.
9. Yang Y, Hong J, Deng SX, Xu J. Age-related changes in human corneal epithelial thickness measured with anterior segment optical coherence tomography. Invest Ophthalmol Vis Sci 2014;55:5032-8.
10. Reinstein DZ, Archer TJ, Gobbe M, Silverman RH, Coleman DJ. Epithelial thickness in the normal cornea: Three-dimensional display with Artemis very high-frequency digital ultrasound. J Refract Surg 2008;24:571-81.
11. Patel S, McLaren J, Hodge D, Bourne W. Normal human keratocyte density and corneal thickness measurement by using confocal microscopy *in vivo*. Invest Ophthalmol Vis Sci 2001;42:333-9.
12. Haque S, Simpson T, Jones L. Corneal and epithelial thickness in keratoconus: A comparison of ultrasonic pachymetry, Orbscan II, and optical coherence tomography. J Refract Surg 2006;22:486-93.
13. Hashmani N, Hashmani S, Saad CM. Wide corneal epithelial mapping using an optical coherence tomography. Invest Ophthalmol Vis Sci 2018;59:1652-8.