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Relationship between central corneal thickness and some ocular and demographic parameters: A cross-sectional study

CCT, ocular and demographic parameters

Olajide OS[1]ID, Ajayi BG[2]ID, Ajibode HA[3]ID, Jagun OO[1]ID, Betiku AO[1]ID, Fingesi UI[1], Godwin MO[1]ID, Olajide LO[4]ID

[1]Ophthalmology Unit, Surgery Department, Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, Nigeria
[2]Eleta Eye Institute, Ibadan, Oyo State, Nigeria
[3]Ophthalmology Department, Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State, Nigeria
[4]Biochemistry Department, Benjamin Carson Senior College of Health Sciences, Babcock University, Ilishan-Remo, Ogun State

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Abstract
Objective: To determine the relationship between central corneal thickness (CCT) and corneal curvature, intraocular pressure, axial length, use of topical glaucoma medications, refractive status, age, race, and gender.
Method: This descriptive cross-sectional study involved 270 new and follow-up patients who were at least 18 years old and had no corneal pathology on slit lamp ocular examination. Non-probability convenient sampling technique was used. Biodata of participants were taken after which visual acuity, slit-lamp examination, auto-refraction, keratometry, subjective refraction, pachymetry (OCT and ultrasound), axial length, tonometry, and dilated fundoscopy were done. Data was analysed using the Statistical Package for the Social Sciences 26.0. Pearson's correlation was used to determine the association between pachymetry and the parameters. Analyses were considered statistically significant when the p-value was less than 0.05.
Results: The mean age of participants was 37.35 ± 17.28 years, the male-to-female ratio was 1:2.1. The mean ultrasound CCT was 524.51 ± 37.65 µm, while the mean OCT CCT was 508.97 ± 35.09 µm. CCT showed a negative correlation with age ($p<0.05$), and a positive correlation with corneal curvature ($p<0.05$) and axial length ($p<0.05$). Participants on topical prostaglandin analogues and combination therapy had lower CCT compared to those on alpha-2 agonists, beta-blockers, and those who were not on any glaucoma medication. No correlation was found between gender, IOP, refractive status, and CCT.
Conclusion: Age, axial length, corneal curvature, use of topical prostaglandin analogues, and combination therapy all affect CCT.

Keywords: Central corneal thickness, Age, Axial length, Corneal curvature, Topical glaucoma medications

Plain English summary

Correspondence:
Olajide Olushola S
Ophthalmology Unit, Surgery Department
Babcock University Teaching Hospital
Ilishan-Remo, Ogun State.
08094676034, olajidesho@gmail.com

The objective was to determine the relationship between central corneal thickness and corneal curvature, eye pressure, eye length, use of glaucoma eye drops, refractive status, age, race, and gender. 270 participants who were at least 18 years old and had no eye disease on examination participated in the study. Their biodata was taken, after which vision, eye examination, corneal curvature, glasses test, corneal thickness measurement (OCT and ultrasound), length and pressure of their eyes were done. Data was analysed using the Statistical Package for the Social Sciences 26.0. Results were considered significant when the p-value was less than 0.05.
The average age of participants was 37.35 ± 17.28 years. The average ultrasound CCT was 524.51 ± 37.65 µm, and the average OCT CCT was 508.97 ± 35.09 µm. CCT showed a negative correlation with age and a positive correlation with corneal curvature and globe length. Participants on prostaglandin analogue eye drops and combination therapy had lower CCT compared to those on alpha-2 agonists, beta-blockers, and those who were not on any glaucoma eye drops. No correlation was found between gender, eye pressure, refractive status, and CCT.

Background

Corneal thickness is not uniform- the central part is thinner than the periphery (1). Central corneal thickness (CCT) varies based on ocular and demographic factors such as corneal curvature, axial length, use of topical glaucoma medications, refractive status, age, race, and gender (2, 3, 4, 5, 6, 7, 8). The conclusions from studies that have been carried out on the relationship between CCT and these factors are sometimes conflicting. The average CCT for Nigerians, according to studies done by Adegbehingbe et al (3) and Oladigbolu et al (4), is 530 ± 0.032µm and 531.18 ± 38.33 µm, respectively. Average CCT values in the Caucasian population range between 537.8–551.9µm (8, 9). Some studies report that age (7), gender (2, 4, 7, 10), corneal curvature (10), axial length (2), IOP (4, 10), refractive status (2, 4, 7), and topical glaucoma medications (5, 11) have no significant association with CCT. Other studies found an association between age (2, 10), gender (5), corneal curvature (2, 6), axial length (6), IOP (2), refractive status (7), and topical glaucoma medications (12). Hence, there is a need to further evaluate the association between CCT and these ocular and demographic factors. CCT is of great clinical importance when interpreting IOP measurements in glaucoma diagnosis and management (3, 4). It is also important in the assessment of patients for refractive corneal surgery, contact lens wear, corneal diseases, corneal endothelial function, and corneal oedema (1, 13). Instruments that measure CCT use either ultrasound or optical principles (1, 9). The objectives of this study were to determine the CCT of participants using ultrasound pachymetry and optical coherence tomography, determine if an association exists between the mean CCT and corneal curvature, intraocular pressure, axial length, use of anti-glaucoma eye drops, refractive status, age, and gender.

Materials and Methods

This descriptive cross-sectional study was carried out at the Ophthalmology clinic, Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, South-West Nigeria, between March 2022 and July 2022. New and follow-up patients attending the Ophthalmology clinic were recruited for this study. A non-probability convenient sampling technique was used, and every consecutive consenting patient who met the inclusion criteria was recruited into the study. Inclusion criteria included the absence of corneal pathology and participants who are 18 years and above. Exclusion criteria were history of ocular surgery or anterior segment pathology, corneal pathology / ocular infection, contact lens wear within the past 4 weeks of the recruitment date, lack of verbal and written consent, and participants less than 18 years of age. A total of 540 eyes (270 participants) were recruited.
Materials used include Optovue ivue 80 OCT, Suoer SW-1000AP ultrasound pachymeter, SLM-3ER digital Slit lamp, Snellen's chart (alphabet optotype and the E chart), Trial frame, PRK-6000 Potec Autorefractor, Sonomed PacScan 300 A-scan, 0.5% Amethocaine Hydrochloride, Goldmann applanation tonometer.
With the aid of a questionnaire, a detailed history was taken from each participant. History included basic demographic data, past medical history (diabetes mellitus, hypertension), glaucoma diagnosis, year of diagnosis of glaucoma, and use of glaucoma medications. The ophthalmic assessment included visual acuity, slit-lamp examination, IOP measurement, refraction, keratometry, axial length, and pachymetry. The refractive error was calculated in Dioptres as spherical equivalent (spherical refractive error + 0.5 × cylindrical refractive error). An average of 3 readings was obtained to get the mean keratometry value, while the average of 5 readings was taken as the axial length. The non-contact OCT

pachymetry was done first, followed immediately by ultrasonic pachymetry. All the measurements were performed between 9 am and 2 pm. One researcher was involved in the recruitment of willing participants, consent and history taking, and data capturing. Another researcher performed visual acuity test, auto-refraction, axial length and keratometry measurement, while two other researchers were designated to perform subjective refraction. Slit lamp examination, IOP and CCT measurement (OCT & ultrasound) were carried out by a separate researcher.

Data obtained were analysed using SPSS (Statistical Package for Social Sciences) 26.0. Results were presented using frequency tables and percentages as appropriate. The bivariate analysis was done with a t-test. To determine the association between corneal curvature, intraocular pressure, axial length, refractive error, and CCT, Pearson's correlation was used. The analyses were considered statistically significant when the p-value was less than 0.05.

Results

A total of 270 participants (540 eyes) were enrolled in this study. Their mean age was 37.35 ± 17.28 years, and their age range was between 18-81 years (Table 1).

Table 1: Age distribution of participants

Age	Number of participants	Percentage (%)
< 30	113	41.9
30 – 39	26	9.6
40 – 49	62	23.0
50 – 59	38	14.1
60 and above	31	11.4
Total	270	100
Mean age	37.35 ± 17.28 years	

Eighty-six participants (31.9%) were males while 184 (68.1%) participants were females, giving a male to female ratio of 1:2.1. Five participants (1.9%) had no formal education, thirty-two (11.9%) had only Primary / Secondary education, two hundred and eighteen participants (80.7%) had a 1st degree or were in a higher institution at the time of participating in the study while fifteen (5.5%) possessed a Masters / Ph.D. degree. Most of the participants, 177 (65.6%) were Yorubas, 55 (20.3%), and 3 (1.1%) of them were Igbos and Hausas, respectively, and 35 (13%) belonged to other Nigerian tribes that are not among the 3 major tribes. Most of the participants had normal IOP (10 – 21 mmHg), 246 for the right eye (91.1%) and 251 (93%) for the left eye. Ten participants (3.7%) had elevated IOP (> 21mmHg) in the right eye, nine of them (3.3%) had elevated IOP in the left eye, while fourteen participants (5.2%) considering the right eye and ten participants (3.7%) considering the left eye had IOP less than 10mmHg. Most of the participants had myopia, one hundred and thirty-four (49.6%) in the right eye and one hundred and thirty (48.2%) in the left eye. Seventy-eight (28.9%) and seventy-nine (29.3%) participants had hypermetropia in the right and left eyes, respectively, while fifty-eight (21.5%) and sixty-one (22.5%) participants had no refractive error, considering the right and left eyes, respectively. Refractive error of -0.25 and above was considered as myopia, while +0.25 and above was considered as hypermetropia.

A clear correlation was found between CCT in the right and left eyes. For OCT ($r = 0.955$, $p < 0.05$) and USS ($r = 0.969$, $p < 0.05$) (Table 2). Hence, for further analysis, the CCT of the right eye will be used.

Table 2: Mean values of ocular parameters of participants

	Right Eye		Left Eye	
Variable	Mean ± SD	Range	Mean ± SD	Range
Corneal curvature(mm)	7.92 ± 0.29	7.20-9.90	7.90 ± 0.26	7.18-8.66
Axial length (mm)	23.65 ± 1.09	20.80-30.06	23.58 ± 1.02	20.81-30.23
USS CCT (µm)	523.88 ± 38.16	414.00-635.00	525.14 ± 37.14	439.00-629.00
OCT CCT (µm)	509.91 ± 36.08	430.00-656.00	508.03 ± 34.10	429.00-611.00

Data presented as mean ± standard deviation; USS CCT = Ultrasonic central corneal thickness; OCT CCT = Optical coherence tomography central corneal thickness

A statistically significant increase in CCT (OCT and USS) was noticed with an increase in corneal curvature (F = 2.971, p = 0.036) for OCT CCT and (F = 2.984, p = 0.033) for USS CCT. As the axial length increases, so does the CCT (USS and OCT). The increment is statistically significant for OCT CCT (F = 1.044, p = 0.042) and for USS CCT (F = 1.246, p = 0.034). Participants who had myopia had a higher CCT (OCT and USS) than those who had hypermetropia. The difference, however, was not statistically significant, for OCT CCT (F = 2.312, p = 0.130), while for USS CCT (F = 3.581, p = 0.060) (Table 3).

Table 3: CCT stratified based on ocular/demographic factors

Age	n=270	OCT CCT Mean(µm) ±SD	USS CCT Mean(µm) ±SD
< 30	113	518.14 ± 35.44	533.97 ± 39.83
30 – 39	26	515.08 ± 34.19	531.87 ± 41.38
40 – 49	62	514.80 ± 33.40	526.03 ± 35.38
50 – 59	38	501.21 ± 31.41	516.03 ± 31.08
60 & above	31	500.32 ± 45.09	515.87 ± 32.97
Gender			
Male	86	508.65 ± 35.04	510.51± 36.63
Female	184	523.86 ± 38.37	523.89 ± 38.17
Corneal	Curvature		
< 7.70	54	502.19 ± 32.93	515.20 ± 37.84
7.70 - 7.90	75	504.45 ± 32.51	517.67 ± 35.45
> 7.90	141	519.50 ± 36.51	533.70 ± 37.23
Axial	Length		
< 22	10	491.80 ± 30.60	507.00 ± 8.39
22-24	181	508.72 ± 34.75	522.45 ± 8.09
> 24	79	514.95 ± 39.02	529.28 ± 38.86
Refractive	Error		
Hypermetropia	78	504.15 ± 32.99	516.24 ± 33.19
Myopia	134	511.84 ± 36.88	526.63 ± 41.30

Data presented as mean ± standard deviation; OCT CCT = Optical coherence tomography central corneal thickness; CCT USS = Ultrasonic central corneal thickness

As seen in Table 4 below, a positive correlation exists between CCT (measured through OCT and USS), corneal curvature, and axial length. Age of the participants had a negative correlation with CCT measured through the 2 methods. No correlation was found between gender, intraocular pressure, refractive status, and the CCT measured through the two methods.

Table 4: Pearson's correlation coefficient for CCT and ocular and demographic parameters of participants

Parameter	OCT		USS	
	R	P	r	P
Age	-0.176	0.004	-0.217	-0.000
Gender	0.024	0.695	0.000	0.996
Intraocular pressure	0.015	0.814	-0.017	0.783
Corneal curvature	0.176	0.004	0.166	0.006
Refractive status	0.032	0.603	0.017	0.783
Axial length	0.100	0.046	0.104	0.044

r = Pearson's correlation coefficient; USS = Ultrasonic central corneal thickness; OCT = Optical coherence tomography central corneal thickness

Only forty (14.9%) of the participants had been diagnosed with glaucoma. Participants on prostaglandin analogues and combination therapy had reduced CCT compared to those on alpha-2 agonist, beta blocker and those who were not on any glaucoma medication. In Table 5, the ANOVA test shows this reduction to be statistically significant (F = 2.434, p = 0.048) for OCT CCT and

(F = 3.906, p = 0.004) for USS CCT. Even though participants who have used topical glaucoma medications for more than 5 years had higher CCT (measured using both OCT and USS) when compared to those who have used topical glaucoma medications for only 5 years or less, the difference was not statistically significant. (F = 2.339, p = 0.111) for OCT CCT and (F = 1.335, p = 0.276) for USS CCT.

Table 5: ANOVA of CCT of participants on topical glaucoma medications/ number of years of use

	N	OCTCCT(μm) Mean ± SD	F	P	USSCCT(μm) Mean ± SD	F	P
Topical		Medications					
Prostaglandin analogue	14	491.57 ± 28.44	2.434	0.048	499.79 ± 29.88	3.906	0.004
Beta-blocker	4	510.50 ± 14.84			530.25 ± 10.05		
Alpha-2 agonist	5	499.65 ± 38.04			509.60 ± 48.29		
Combination therapy	17	493.65 ± 38.04			504.29 ± 35.04		
No glaucoma medication	230	512.60 ± 36.10			527.32 ± 37.91		
Number of		years of use					
< 1	9	488.00 ± 35.43	2.339	0.111	504.33±40.84	1.335	0.276
1-5	26	491.30±26.50			499.73±29.45		
>5	5	506.40±45.53			516.40±39.73		

N = number of participants; USS CCT = Ultrasonic central corneal thickness; OCT CCT = Optical coherence tomography central corneal thickness; Data presented as mean ± standard deviation

Discussion

The mean age of participants in this study was 37.35 ± 17.28 years, it is similar to 40.01 ± 13.86 years and 40.34 ± 14.47 years reported in studies done in Nigeria by Oladigbolu et al (4) and Mbatuegwu et al (14), and to 34.75 ± 14.55 years reported by Toptan et al in a Caucasian study (15). All these studies used 18 years as the minimum age limit of participants included in their studies, just like this study. The minimum age limit of participants in the study by Adegbehingbe et al (3) and Tsikripis et al (16) is 40 and 50 years respectively, it is therefore not surprising that the mean age of participants reported by Adegbehingbe et al (3) (54.5 ± 9.15 years) and Tsikripis et al (16) (51 ± 9 years) is higher when compared to the mean age of participants in this study.

More females participated in this study. Studies done in Nigeria by Adegbehingbe et al (3), Oladigbolu et al (4), Mbatuegwu et al (14), and that done among Caucasians by Tsikripis et al (16) all reported that more females participated in their studies. This implies that more women tend to access health care compared to men (17).

CCT is known to be lower in Blacks as compared to Caucasians, and this study affirms this as the mean CCT obtained using the ultrasound pachymeter (USS CCT) in this study (524.51 ± 37.65 μm) is lower than what was reported in available Caucasian studies. For example, Pateras and Kouroupaki (9) reported a mean USS CCT of 547.26 ± 44.24 μm, Ayala and Strandas (18) reported a mean USS CCT of 532 ± 30 μm, while Toptan and Simsek (15), Tsikripis et al (16) and Bechmann et al (19) reported mean USS CCTS of 541.21 ± 29.24 μm, 532.5 ± 36 μm, and 581 ± 34 μm, respectively.

The mean CCT obtained using optical coherence tomography (OCT CCT) in this study was 508.97 ± 35.09 μm, which is similar to 505.86 ± 39.27 μm reported by T van der lecq (20) in a South African study but as noticed with the USS values, it is lower than mean OCT CCT values from Caucasian studies by Pateras and Kouroupaki (9) (536.42 ± 40.35 μm), Ayala and Strandas (18) (536 ± 29 μm), Toptan and Simsek (15) (532.21 ± 29.53 μm), Tsikripis et al (16) (523 ± 31.7 μm) and Bechmann et al (19) (530 ± 32 μm).

In this study, the mean corneal curvature of participants was 7.91 ± 0.28 mm, which is similar to 7.85 mm obtained by Hashemi et al (21) but higher than 7.69 mm obtained by AlMahmoud et al (22). A positive correlation between corneal curvature and CCT was seen. While some studies (2, 6) also found the same correlation between CCT and corneal curvature, others found no correlation (10). The relationship between corneal curvature and CCT can be ambiguous, as other factors like axial length, corneal diameter, and refractive error also influence the corneal curvature value. AlMahmoud et al (22), for instance, reported a positive correlation between corneal curvature and CCT in myopes, but no such correlation was found in hyperopes.

Another parameter that showed a positive correlation with CCT in this study was the axial length. This implies that as axial length increases, CCT tends to increase as well. However, the relationship between axial length and CCT can vary and may be influenced by factors such as age and refractive error (6). Axial length increases with increasing myopic refractive error (6) and decreases with increasing age (23). The mean value of axial length in this study was 23.62 ± 1.6 mm. Muthu-Krishnan et al (6) obtained a similar value of 23.52 mm and, just like this study, also reported a positive correlation between CCT and axial length, but this was not the case in the Varghese et al (2) study, as they did not find any association between axial length and CCT. The age range of participants in this study was 18 to 81 years (average age of 37.35 ± 17.28 years). for the Varghese et al (2) study, the age range was between 30 to 70 years (average age of 47.8 ± 10.1 years). This disparity in the mean average age may contribute to the difference in findings, as both axial length and CCT have been shown to decrease with age (2, 3, 4, 23).

CCT showed a negative correlation with age in this study, indicating that as the age of participants increased, CCT measured through both USS and OCT decreased. Previous studies have also reported a negative correlation between age and CCT (2, 3, 4). Keratocytes, the major cellular component of the cornea stroma, decrease in density with increasing age (24). Breakdown of collagen fibres that help to maintain the shape and transparency of the cornea also occurs, leading to loss of corneal integrity (24). A decrease in keratocyte density and breakdown of collagen fibres are considered the most likely reasons for the observed reduction in CCT with age (24).

Forty glaucoma patients participated in this study, and they were on the following medications: alpha-2 agonists, beta-blockers, prostaglandin analogues, and combination therapy (those using more than one class of glaucoma drugs). Participants on topical prostaglandin analogues, and combination therapy had lower CCT compared to those on topical alpha-2 agonists, beta blockers and those not on any topical medication. The finding in this study corroborates the findings of studies that have reported a decrease in CCT with the use of prostaglandin analogues and combination therapy (25, 26). Prostaglandin analogues, when used in the treatment of glaucoma, have been found to stimulate the release of matrix metalloproteinases in the cornea (25). The metalloproteinases lead to the breakdown and remodelling of collagen fibres in the cornea, which will result in a reduction in CCT over time (25). It is a well-known fact that decreased CCT results in underestimation of IOP (4). Therefore, serial CCT measurement is recommended in patients on prostaglandin analogues and combination therapy to avoid underestimation of IOP.

Participants who had used topical glaucoma medications for more than 5 years had a higher CCT (OCT and USS) than those who had used topical glaucoma medications for 5 years or less, but the difference was not statistically significant. No association was found between CCT and gender in this study, just like the findings of some other studies (2, 4, 7, 10). This study and some other studies (4, 10) found no correlation between CCT and IOP. However, some studies (2, 27) have reported a positive correlation between CCT and IOP. One reason given by both Mbatuegwu et al (28) and Yasukawa et al (29) for this inconsistency in the finding is that other factors affect IOP, such as blood pressure, which has been reported to be high in patients with raised IOP. There was no correlation between CCT and refractive status as corroborated by Varghese et al (2) and Divya et al (7). In contrast, AlMahmoud et al (22) reported that CCT correlated directly with refractive status when the analysis was done for all the participants in their study, but no correlation was seen when a separate analysis was done for those who had myopia or hypermetropia. The fact that in the study by AlMahmoud et al (22), cycloplegic refraction and not manifest refraction was used as the spherical refractive error, while in this study, manifest refraction (subjective refraction) without cycloplegia was used as the refractive error, creates a bias that may account for the different findings.

Study Limitation

The number of participants on topical glaucoma medications was small. Moreover, their baseline CCT were not measured before they commenced topical medications, nor were follow-up CCT measurements done, as participants' CCT was only measured once

Conclusion

This study has been able to demonstrate that age, axial length, corneal curvature, use of topical prostaglandin analogues and combination therapy all affect CCT, hence, these factors should be considered in interpreting CCT measurements.

Intraocular pressure, refractive status, and gender have no correlation with CCT.

List of abbreviations

CCT: Central corneal thickness
IOP: Intraocular pressure
OCT: Optical coherence tomography
OCT CCT: Optical coherence tomography central corneal thickness
USS CCT: Ultrasonic central corneal thickness

Declaration

Ethics approval and consent to participate

This study was approved by the Babcock University Health Research and Ethics Committee (BUHREC) with reference number 657/21. All tests/procedures were done at no cost to the patients. Participants were adequately informed about the study, and written informed consent was obtained from each participant before being recruited. The Tenet of the Helsinki declaration was strictly adhered to. All data were protected to maintain patient confidentiality by ensuring that participants wrote only their initials on the datasheet and only the researchers had access to the datasheet.

Consent for publication

Availability of data and materials

The data and materials associated with this research will be made available by the corresponding author upon reasonable request.

Competing interests

Nil.

Funding

Nil.

Authors' contributions

OSO: Conceptualisation, methodology, data acquisition, data curation, formal analysis, writing, review and editing, project administration
ABG: Conceptualisation, methodology, data curation, formal analysis, writing, review and editing.
AHA: Conceptualisation, methodology, data curation, formal analysis, writing, review and editing.
JOO: Conceptualisation, methodology, data acquisition, data curation, formal analysis, writing, review and editing.
BAO: Conceptualisation, methodology, data acquisition, data curation, formal analysis, writing, review and editing
FUI: Conceptualisation, methodology, data acquisition, data curation, formal analysis, writing, review and editing
GMO: Conceptualisation, methodology, data acquisition, data curation, formal analysis, writing, review and editing
OLO: Conceptualisation, methodology, data curation, formal analysis, writing, review and editing.

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