

Research Article

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Corneal Thickness of Glaucoma Patients in Onitsha, Southeast Nigeria

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ABSTRACT

Background: The assessment of the Central Cornea Thickness (CCT) is crucial in the decision-making process in the management of glaucoma.

Objectives: The objectives of this study were to determine the mean CCT of glaucoma patients of Igbo descent, and to evaluate any relationship of CCT and the patients' demographics.

Materials and Method: This was a cross-sectional study done at a private eye specialist clinic in Onitsha, southeastern Nigeria. Participants were eligible glaucoma patients of Igbo ethnicity. The corneal thickness of each eye was measured using ultrasound pachymeter. The mean CCT was calculated and its relationship with gender and age was studied.

Results: A total of 155 eyes of 79 participants were studied; males constituted 57%. The mean age of the participants was 53.69 ± 16.29 years. The mean CCT for all eyes studied was $529.51 \pm 35.77 \mu\text{m}$ (95% confidence interval (CI): 523.83 – 535.19 μm), while the right and left eyes had mean CCT of $528.99 \pm 36.16 \mu\text{m}$ (95% CI: 520.84 – 537.14 μm) and $530.04 \pm 35.61 \mu\text{m}$ (95% CI: 521.96 – 538.12 μm) respectively. There was no significant difference in mean CCT with increasing age ($P = 0.38$). The mean CCT were thicker in males for both the right and left eyes, however, these differences were not statistically significant ($P = 0.74$, $P = 0.86$ respectively).

Conclusion: CCT values of glaucoma patients of Igbo ethnicity is similar to that of the non-glaucoma individuals. There is no significant relationship between age and CCT in both gender.

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Introduction

The cornea, which is the transparent anterior part of the eye is important in the protection and overall health of the eye. The force necessary to flatten the cornea during tonometry can be influenced not only by the intraocular pressure (IOP) but also by corneal characteristics such as central corneal thickness (CCT), corneal shape and hydration, and rigidity of the sclera and globe [1]. The central region (4 mm from the optic area) is usually thinner than the middle of the corneal periphery (4–9 mm from the optic area), which is in turn thinner than the corneal periphery (9 mm from the optic area). The average thickness is $515 \mu\text{m}$ in the center of the cornea. In the paracentral region, the thickness varies from $522 \mu\text{m}$ to $574 \mu\text{m}$ while the peripheral area thickness ranges from $633 \mu\text{m}$ to $673 \mu\text{m}$ [2–4].

There is a positive correlation between IOP readings and corneal thickness in the general population [5]. This fact stems from the

principle upon which the Goldmann applanation tonometer (GAT), the most widely used and international gold standard of measuring IOP, is based. Hans Goldmann applied the Imbert–Fick principle which states: ‘the existing pressure in a sphere containing a liquid, whose wall is constituted by a very thin and perfectly elastic membrane, can be measured by an external compression sufficient to transform a portion of spheric surface in a plain surface’. This theoretical sphere is dry, thin-walled, and readily flexible, all features not applicable to the cornea [1]. However, in describing some of the possible sources of measurement error Goldmann specifically outlined that the theoretical basis for his instrument was calculated for a mean CCT of $50 \mu\text{m}$ and that the accuracy could vary if CCT was significantly different from this value [1].

A corneal pachymeter measures corneal thickness, a sensitive indicator of endothelial physiology that correlates well with functional measurements. Techniques for measuring central corneal thickness (CCT) include optical pachymetry, ultrasound pachymetry, confocal microscopy, optical light ray passage

analysis, topography, and optical coherence tomography. Optical method for determining CCT consider the image projected onto the tear film or anterior corneal surface [2]. It is imprecise and rarely used today. Ultrasonic pachymetry, which is based on the speed of sound in the normal cornea (1640 m/sec), is both easier to perform and more accurate [6]. Values from the optical and ultrasound pachymetries are not interchangeable [7-9]. Corneal thickness affects the measurement of intraocular pressure (IOP), with thicker corneas producing falsely higher IOP readings and thinner corneas producing falsely lower readings. However, Liu and Roberts demonstrated that the biomechanical properties of the cornea, particularly stiffness, may have a greater impact on IOP measurement errors than does corneal thickness or corneal curvature. Adjustment for corneal biomechanical properties may lead to a more accurate measurement of the IOP. Despite these adjustments, low pachymetry measurements have been shown to be an independent risk factor for glaucoma even when the artificial lowering of IOP is accounted for [10,11]. CCT is considered as a possible explanation for glaucoma cases where clinical findings do not match [11]. Pachymetry is an important tool in the assessment of corneal hydration and the function of the corneal endothelium in its dual role as a barrier to aqueous humor and as a metabolic pump. Pachymetry measurements are important in the selection of patients for refractive surgery, contact lens wearing, keratoplasty, and detection of pathologies such as Keratoconus, Pellucid Marginal Corneal Degeneration, Fuchs Dystrophy [12].

The many devices available for measuring IOP can be influenced by variations in CCT. Although GAT was developed based on a 500- μm -thick cornea, however, with cannulation studies a CCT of 520 μm was found to be the most accurate with GAT [1,13]. There is a positive correlation between CCT and IOP in GAT [14, 15]. A deviation of 100 μm from the “ideal” CCT of 520 μm introduces an error of 7 mmHg [13]. To account for this deviation, several correction methods have been devised which unfortunately introduce other errors into the interpretation of the IOP results [16,17]. A thinner CCT was identified as an important independent predictive factor for development of primary open angle glaucoma (POAG) from ocular hypertension (OHTN) [18]. A patient with a CCT of 555 μm or less had a threefold increased risk of developing glaucoma within 5 years compared with someone with a CCT greater than 588 μm [18]. Likewise, with every 40 μm decrease in CCT associated with a twofold increased risk of developing glaucoma over 5 years [19].

Some factors are known to affect CCT. Twin studies have shown that the CCT phenotype is highly heritable with the genes also involved in collagen and extracellular matrix metabolism, collagen fibril organization, and myosin binding [20, 21]. Ethnicity should be considered when interpreting CCT, given the variations in the measured average CCT of different ethnic groups. Africans, African Americans and Japanese have thinner CCT consistently compared with Caucasian, Hispanic, Latino, Chinese, Filipino, Korean, Malay, and Iranian populations who have thicker CCT [22-31]. Age has a significant inverse correlation with CCT, decreasing ~2–10 μm per decade [14, 29, 32, 33]. There are variable correlations of sex and CCT wherein there is no difference between the sexes; males having thicker CCT than females and females having thicker CCT than males [14,22,24,29,34]. Certain systemic disorders are correlated with thicker CCT: diabetes mellitus, metabolic syndrome, an increased body mass index and chronic kidney disease [35, 36]. Topical anti-glaucoma medications can cause thinning, thickening, or no change to the CCT; the effects are mostly reversible [37-40]. In addition, glaucoma and OHTN

patients with thicker CCT show significantly less decrease in IOP than those with thinner CCT following the use of anti-glaucoma medications or selective laser trabeculoplasty over time [41-44].

The southeast zone in Nigeria, populated by predominantly the Igbo ethnic group, was reported to have the highest prevalence of glaucoma (6.1%) according to a nationwide survey done more than 15 years ago [45, 46] without any data on CCT. Subsequently, several community and hospital based studies on CCT of Nigerians were on mixed ethnicities [23, 47, 48]. However, there was a recent study on CCT among the Igbo people but was focused only on the non-glaucomatous adults [22]. To the best of the authors’ knowledge no research has been carried out in the southeastern Nigeria to determine the mean CCT of glaucoma patients.

This research aims to explore the central corneal thickness profiles of glaucoma patients in this region. The objectives include:

- To determine the mean CCT of glaucoma patients of Igbo descent,
- To evaluate any relationship of CCT and the patients’ demographics.

Data generated from this study will contribute to a better understanding of the characteristics of glaucoma in the southeast, ultimately leading to improved diagnosis and treatment strategies for the local population.

Materials and Method

Study design: A cross-sectional prospective study

Study Population: The study was conducted among glaucoma patients of Igbo origin.

Study site: The study was carried out at a well-equipped private eye clinic in Onitsha which runs comprehensive outpatient and surgical services. Onitsha is the most populous city in the southeastern Nigeria.

Sample size: A sample size of participants was determined using the formula

$$N = z^2pq/d^2$$

Where,

N = Minimum sample size.

Z = The standard normal deviate, usually set at 1.96 corresponding to 95% confidence interval

p = Assumed prevalence of glaucoma among the southeastern Igbo people taken from a study done in Nigeria which was 6.1% [45].

$$q = 1.0 - p \quad (1.0 - 0.061) = 0.939$$

d = Precision level acceptable = 5% (0.05).

This gives a minimum sample size of approximately 88 participants.

Inclusion Criteria: Consenting glaucoma patients of Igbo ethnicity.

Exclusion Criteria: Patients less than 5 years, those with penetrative /perforative ocular injuries and those who did not give their consent.

Sample Technique: Simple random sampling technique was used. Consenting glaucoma patients were selected alternately from the list of patients present on each day. For any patient who declined consent the next alternate patient was recruited. For patients less than 18years consent was sought from a legitimate adult parent/guardian.

Procedures Involved: Each selected patient underwent full clinical assessment including: biodata, clinical history and ocular examination. The average of three CCT readings were recorded for each patient into a pro forma (appendix 1). All CCT measurements were taken by the same qualified person.

Consent: The participants were duly informed of the aim and nature of the study, and the details of the various procedures that were involved. Patient information was obtained with no identifier, and confidentiality was maintained. All consenting patients were required to sign a consent form. A patient was free to withdraw his/her consent at any point.

Data Processing and analysis: All collected data were analyzed using Microsoft Excel spreadsheet (2013).

Result

There were more male participants 45 (57%) than females 34 (43%) out of a total of 79 participants in a ratio of 1.3:1 respectively. A total of 155 eyes were studied. An only eye was studied in a male while two female participants had each an only eye. The mean age of all participants was 53.69 years (SD ±16.29). The age range was from 9 to 82years. Table 1 shows that the mean CCT for all eyes studied was 529.51±35.77µm.

Table 1: Statistics of CCT Measured in all Participants			
Variable	Count	Mean ± SD (µm)	95% CI (µm)
CCTRE	78	528.99 ±36.16	520.84 – 537.14
CCTLE	77	530.04 ±35.61	521.96 – 538.12
CCTCombined	155	529.51 ±35.77	523.83 – 535.19

CCTRE = central corneal thickness right eye; CCTLE = central corneal thickness left eye; CCTcombined = central corneal thickness of all eyes; SD = standard deviation; CI = confidence interval; µm = micron meter.

The CCT values for all eyes studied were not normally distributed as shown in figure 1.

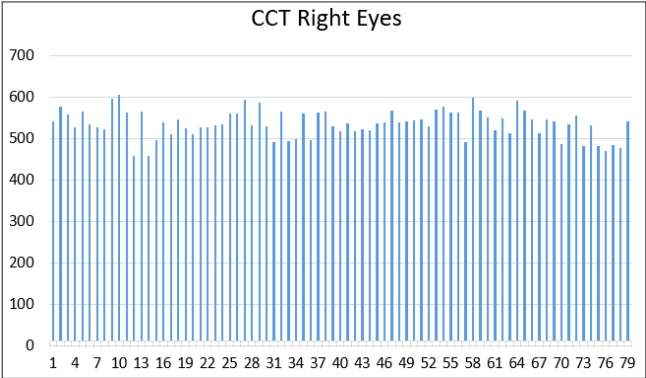


Figure 1: Distribution of CCT of Right Eyes

A summary of the descriptive statistics of the CCT of all eyes is shown in Table 2.

Table 2: Descriptive Statistics of CCT Combined	
Mean	529.5084
Standard Error	2.873429
Median	532.3
Mode	564
Standard Deviation	35.7739
Sample Variance	1279.772
Kurtosis	-0.44673
Skewness	-0.04114

Range	173.3
Minimum	448.7
Maximum	622
Sum	82073.8
Count	155

The mean central corneal thickness (CCT) for RE was 528.99 ± 36.16µm (95% CI: 520.84 –537.14µm) and 530.04 ± 35.61µm for LE (95% CI: 521.96 – 538.12µm). Table 3 shows the mean CCT for the right and left eyes when discriminated into male and female groups.

Although, the mean CCT were higher in males for both the right and left eyes, however, these differences were not statistically significant (p=0.74, p=0.86 respectively).

Table 3: Gender Distribution of Mean CCT for Right and Left Eyes

	CCTRE (µm) ± SD (95% CI)	CCTLE (µm) ± SD (95% CI)
Males	530.22 ± 30.70 (520.89 – 539.55)	530.64 ± 29.73 (521.71 – 539.57)
Females	527.38 ± 42.63 (512.52 – 542.26)	529.19 ± 43.05 (513.67 – 544.71)
Combined	528.99 ± 36.16 (520.84 – 537.14)	530.04 ± 35.61 (521.96 – 538.12)
p value	0.74	0.86

Level of significance set at p< 0.05.

Figure 2 shows that the ages of the patients were not normally distributed. There was a consistent decrease in CCT with increasing age up to the fourth decade (Figure 3, Table 4). A one-way analysis of variance (ANOVA) test showed no statistically significant correlation (p=0.38) between the age categories and mean CCT (Table 5). Further analysis of the ranked ages and CCT using the Spearman’s rank correlation test also showed no significant correlation (rs = -0.13, p= 0.11).

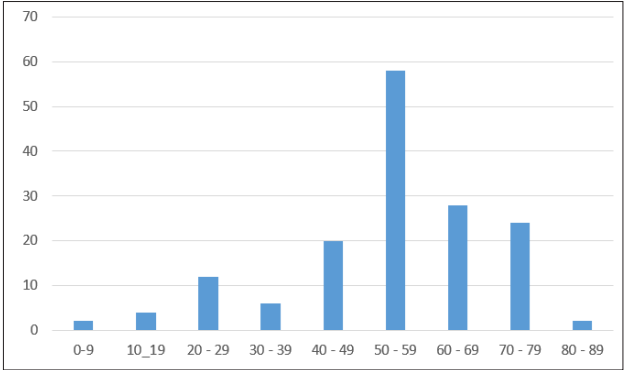


Figure 2: Age Frequency Distribution of the Patients (156 eyes)

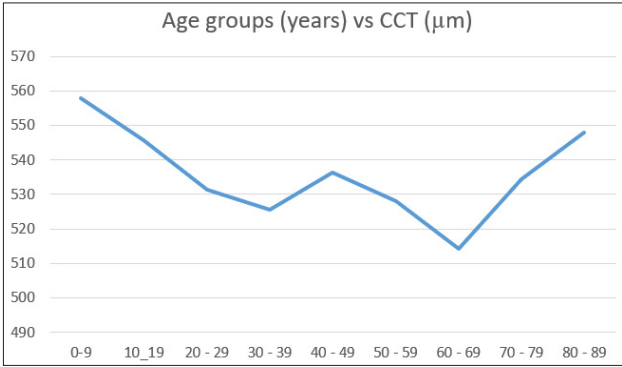


Figure 3: Age Groups vs CCT

Table 4: Age Frequency and Mean CCT

AGE Groups	Frequency (Eyes)	Mean CCT
0-9	2	557.8
10_19	4	545.75
20 – 29	12	531.4
30 – 39	6	525.6
40 – 49	20	536.23
50 – 59	58	528.18
60 – 69	28	514.36
70 – 79	24	534.51
80 – 89	2	548

Table 5: One-Way ANOVA test of Age Groups and Mean CCT

Summary						
Groups	Count	Sum	Average	Variance		
0-9	2	1115.6	557.8	612.5		
10_19	4	2183	545.75	344.8433		
20 - 29	12	6376.8	531.4	2243.078		
30 - 39	6	3153.6	525.6	67.832		
40 - 49	20	10724.5	536.225	935.5851		
50 - 59	54	28521.6	528.1778	1369.309		
60 - 69	27	13887.7	514.3593	1026.655		
70 - 79	24	12828.3	534.5125	1778.992		
80 - 89	2	1096	548	0.18		
ANOVA						
Source of Variation	SS	df	MS	F	P-value	F crit
Source of Variation	11238.48	8	1404.81	1.080509	0.380167	2.004177
Source of Variation	184619.6	142	1300.138			
Total	195858	150				

Diabetes mellitus was found in 12 (15.19%) of the participants. One participant has a history of tobacco smoking, and none had any previous eye surgery.

Discussion

CCT is a dynamic parameter. The ocular and systemic factors known to influence CCT are varied, and include age, gender, ethnicity, diurnal variation, contact lens wear, topical medication, corneal disease, ocular surgery, systemic disease (e.g. DM) as well as the technical factors (instrument, observer or technique related) [49]. In this study the CCT of 79 (155eyes) confirmed POAG patients of Igbo ethnicity were measured. The participants had a mean age of 53.69 ±16.28 years and a male to female ratio of 1.3:1 (57% males, 43% females). The average CCT of 529.51 ± 35.77μm for all the eyes is similar to 527.57 ± 37.42μm recorded in a study

done in Enugu among non-glaucomatous Igbos with similar mean age (50.29 ± 16.58 years) [22], but thicker than that measured ($523.10\mu\text{m} \pm \text{SD } 41.3$) for glaucoma eyes in Zaria, northern Nigeria [48]. This may be due to the greater proportion of females (M/F = 1:3) and mixed ethnicity in their study. In a study done in a larger sample size in southwestern Nigeria there were no significant differences between glaucoma and non-glaucoma in the CCT measurements. The mean for both groups was $530\mu\text{m}$ for both eyes [25]. However, another study in southwestern Nigeria, which compared mean CCT between POAG and normal control for both myopes and hypermetropes showed statistically no significant difference [50]. The mean CCT in the index study is also similar to that documented by La Rosa for African Americans ($531 \pm 37\mu\text{m}$) in a comparative study of Whites and African Americans with glaucoma [28]. In contrast, the mean CCT in this study is higher than the mean CCT ($521\mu\text{m}$) recorded in another African American study by Aghaian et al in a glaucoma clinic [29]. It was suggested that a higher mean age accounted for this. Compared with non-Black racial groups the mean CCT of this study is thinner: in the European Glaucoma Prevention Study the mean CCT was $574.2\mu\text{m} \pm 38.48$ for OHT patients on dorzolamide and $571.0\mu\text{m} \pm 36.21$ for the control. There was no statistically significant difference in the mean CCT of the groups [51].

In this study, females had numerically thicker CCT (530.04 ± 35.61 (95% CI: $521.96 - 538.12$)) than males (528.99 ± 36.16 (95% CI: $520.84 - 537.14$)) for both left and right eyes ($p=0.86$, $p=0.74$ respectively) although with no significant difference. The gender difference in CCT is tripodal, with some studies reporting thicker male CCT, or thicker female CCT or no difference at all. The Enugu study reported a significantly thicker CCT among males ($533.59\mu\text{m}$ vs $522.38\mu\text{m}$, $p=0.004$ and $p=0.007$ for right and left eyes respectively) in contrast to the present study [22]. Similarly, marked significantly thicker mean CCT in males was found by Mercieca and co-workers in a hospital-based study in Port Harcourt, South south Nigeria (males $541.0\mu\text{m}$ vs females $522.0\mu\text{m}$) [23]. Consistent with this study several studies also documented thicker mean CCT in females which are not statistically significant [25, 29, 48]. These were attributed to higher proportion of female participants. The relationship of age and CCT is controversial. The present study showed a non-significant negative correlation between age and CCT whereby the CCT decreased with increased age up to the fourth decade in both male and females. This may be a result of the non-normal distribution of the data. However, employing the Spearman rank correlation test also failed to show a significant correlation. This trend was also reported by Prasad and co-workers in New Jersey in their study ($r = 0.00645$) of the relationship of CCT with age and refraction [52]. In addition, The Rotterdam Study similarly reported that CCT did not significantly correlate with age in normal controls, OHT and POAG [53]. Although Siu and Herse in Auckland, New Zealand reported no significant correlation of age and CCT in their 108-sample study, however, power analysis may help explain the conflicting reports available in literature. They posited that diversity in data interpretation may be due to the statistically small sample sizes used in most studies [54]. In their study power analysis shows that at least 80 subjects are needed in each age group (480 subjects in total) before a statistically reliable test of the null hypothesis is possible thus emphasizing the importance of power analysis in calculating an adequate sample size [54]. Some authors have reported definite negative relationship between age and CCT in both gender [22, 23, 25, 51, 54]. According to Hahn et al, the probable cause supported by histologic evidence is the decline in the density of keratocytes and a breakdown in the

collagen fibres in the aging cornea. In addition, there is a probable environmental factor that older individual may have been exposed to longer than younger ones that could have affected the structure or the integrity of the cornea [54].

Conclusion

This study has found that the CCT values in the glaucoma patients of Igbo ethnicity, a group with the reported highest prevalence of glaucoma in Nigeria, are similar to that reported for the non-glaucoma individuals. It also shows that there is no significant relationship between age and CCT as seen in some studies for both gender.

Limitation

The small sample size and non normal distribution of the data set. CONSENT Informed consent was obtained from each patient.

Ethical Approval

Study approval was obtained from the ethics committee of the Chukwuemeka Odumegwu Ojukwu University Teaching Hospital Awka.

Competing Interests

Authors have declared that no competing interests exist.

Funding

No funding was received for conducting this study.

APPENDIX 1

NAME—		
AGE		
SEX		
SMOKING/TOBACCO HABITS		
SYSTEMIC ILLNESS		
DURATION OF SYSTEMIC ILLNESS		
FAMILY HISTORY OF GLAUCOMA		
FAMILY HISTORY OF OTHER OCULAR DISEASES		
HISTORY OF OCULAR TRAUMA	YES	NO
LATERALITY OF OCULAR TRAUMA	(R)	(L);
PROCEDURE/FINDINGS:		
VA AIDED	(R)	(L)
VA UNAIDED	(R)	(L)
PUPILLARY EXAMINATION/REACTION		
IOP	(R)	(L)
SLIT-LAMP FINDINGS		
FUNDUS FINDINGS (UNDILATED)		
CORNEAL THICKNESS	(R)	(L)
USE OF ANAESTHETIC DROPS	YES	NO
ANY ASTIGMATISM	YES	NO
POWER OF ASTIGMATISM & AXIS		
ANY OTHER OCULAR PATHOLOGIES		
HISTORY OF EYE SURGERIES	YES	NO
TYPE OF SURGERY		
USE OF TOPICAL MEDICATIONS	YES	NO
TYPES OF TOPICAL MEDICATIONS		

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