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Conclusion: The study confirms there was no significant relationship between central cornea thickness

and specific open angle glaucoma.

Key words: Central cornea thickness, glaucoma, open angle glaucoma, non glaucoma

1. INTRODUCTION

Central cornea thickness (CCT) is the measurement of the thickness of the central part of the cornea. It has an influence on cornea rigidity and consequently could affect the accuracy of intraocular pressure (IOP) measurement by Goldmann applanation tonometry (GAT).[1] The influence of CCT on the accuracy of IOP measurements was acknowledged in the first description of the Goldman tonometer by Goldman and Schmidt in 1957 and has become a topic of much interest. [2]IOP is one of the most important parameters in the detection and monitoring of response to treatment of glaucoma in routine clinical practice.[3,4] Studies have shown that open angle glaucoma (OAG) is an important cause of blindness worldwide and glaucoma is the second leading cause of blindness globally.[5,6] Over 8.4 million people globally were bilaterally blind from primary glaucoma in 2010. This number may rise to 11.1 million by 2020.[5] OAG has been said to disproportionately affect those of African derivation. [5]The prevalence rate of OAG is higher in Africans, it seems to begin in the younger age group and is more aggressive than in Caucasians.[7] Reports from Africa also indicate that most people with glaucoma are not aware of having the disease and at least half of eyes are already blind at presentation.[8,9] The Nigeria national blindness and visual impairment survey revealed that glaucoma was the second commonest cause of blindness in Nigeria.[10]And as the proportion of those over age 40 years increases, the proportional increase in glaucoma will challenge our resources and ingenuity. Therefore information on the pattern of CCT in our indigenous African population is pertinent so as to aid our diagnosis and management of glaucoma patients. The knowledge of CCT will be important in managing our patients either suspected of having OAG, normal tension glaucoma (NTG) or diagnosed with it because IOP is arguably the most important and only modifiable risk factor for glaucoma progression and it is known to be influenced by CCT.

2. MATERIAL AND METHODS

This is a hospital based case control study was conducted in the Eye clinic and General Outpatient Department (GOPD) of the UCH, Ibadan, Oyo State, Nigeria. The hospital offers quality patient care in all specialties of Medicine and Surgery and serves as a major referral centre for other hospitals in south-western Nigeria and other parts of the country.

All consecutive new and follow up patients that met the inclusion criteria below and who were seen at the eye clinic and GOPD of the hospital from August 2009 to June 2010 and from whom written consent were obtained, formed the study population.

45 INCLUSION CRITERIA FOR GLAUCOMA SUBJECTS

46 Patients were recruited from the glaucoma clinic of the eye clinic

- 47 i) Adults 40 years and above, both newly diagnosed cases of OAG and those already on treatment for glaucoma.
- 48 ii) Diagnosis of primary glaucoma in these patients was based on optic disc changes (assessment of the thickness,
49 symmetry, colour of neuroretinal rim, notching and retina nerve fibre loss) associated with glaucoma typically
50 examined with non contact examination lens (+78D).
- 51 iii) Visual field defects on automated perimetry typical of glaucoma that cannot be explained by other pathology
52 (minimal change of paracentral, small, relatively steep depressions, most commonly superonasally)
- 53 iv) Gonioscopically open angles in at least 270°.
- 54 v) No evidence of corneal pathology.

55 NTG patients had IOP $\leq$ 21mmHg after diurnal phasing with visual field and disc changes of glaucoma.

56 INCLUSION CRITERIA FOR NON-GLAUCOMA SUBJECTS

- 57 i) Healthy adults, 40 years and above with no suspicion of any form of glaucomatous optic nerve damage and visual
58 field changes attributable to glaucoma or eye disease.
- 59 ii) Subjects not on any treatment for glaucoma and did not have elevated IOP, (IOP $\leq$ 21mmHg in both eyes) or
60 family history of glaucoma.
- 61 iii) Subjects with no evidence of cornea or anterior segment disease, contact lens wear or previous eye surgery.

62 EXCLUSION CRITERIA FOR GLAUCOMA SUBJECTS

- 63 i) Adults younger than 40 years of age, and
- 64 ii) Those who had concomitant ocular disease, previously used contact lens or steroids.
- 65 iii) Patients with systemic disease or on medications known to affect visual field or associated with corneal pathology.
- 66 iv) All angle closure, pseudoexfoliation, pigmentary glaucoma and ocular hypertension patients.
- 67 v) Patients who declined recruitment into the study.

68 EXCLUSION CRITERIA FOR NON- GLAUCOMA SUBJECTS

- 69 i) Subjects who are younger than 40 years
- 70 ii) Those with evidence of glaucomatous optic nerve damage and visual field changes attributable to glaucoma or
71 eye disease
- 72 iii) Subjects with any evidence of recent or previous treatment for glaucoma or elevated IOP $\geq$ 21mmHg, contact lens
73 wear, previous eye surgery, glaucoma suspects or family history of glaucoma.
- 74 iv) Subjects with any systemic diseases associated with corneal pathology
- 75 v) Subjects who refused to participate in the study.

SAMPLE SIZE

Using an anticipated minimum difference of 10 (μ) in CCT and a standard deviation of CCT in non glaucoma subjects of 30.3 (μ), a sample size of 160 subjects was arrived at assuming an alpha (α) error of 0.05 and a power of 80%. 170 subjects in each group completed the study and were included in further analysis.

STUDY PROCEDURE AND DATA COLLECTION

Information with the aid of the structured questionnaire included basic demographic data, past medical history (diabetes mellitus, hypertension), family history of glaucoma, history of ocular surgery, number of glaucoma medications and year of diagnosis of glaucoma.

Detailed ocular examinations of the anterior and posterior segments were performed Visual acuity was tested using a Snellen chart or an illiterate E chart.

Slit lamp examination of the anterior segment was performed using Haag Streit Slit Lamp BM 900 and a Goldman applanation tonometer was used to measure the IOP. CCT was measured using ultrasonic pachymeter (Sonomed PACSCAN 300AP) after instillation of amethocaine 0.4% eyedrop.

The CCT measurement was recorded from a seated patient by using the hand held ultrasonic pachymeter probe gently placed in the mid-pupillary axis of the cornea with the pupil undilated. Three measurements expressed in micrometers were taken and the mean was recorded.

IOP was measured twice in each eye, in the morning and afternoon (a minimum four hours difference) because of the diurnal variation in IOP. An average of the two measurements was taken. It was measured three times in patients suspected to have NTG with a minimum of two hours difference. The average of the measurements were taken..

On gonioscopy, the angle of the anterior chamber was considered open when at least the sclera spur could be identified.

Dilated funduscopy was performed using +78D non contact lens on all the participants. Pupillary dilation was achieved with a drop of 1% tropicamide eye drop and 2.5% phenylephrine eye drop in eyes whose anterior chamber was not shallow and gonioscopy showed open angles.

Central Visual Field (CVF) was performed on all glaucoma patients who could fixate and on non glaucoma patients using the Humphrey Field Analyzer perimeter (Carl Zeiss Meditec HFA Model 740 U) and standard 24-2 SITA strategy. The median deviation (MD) and pattern standard deviation (PSD) values were recorded. As a preliminary requirement, the perimetry had to fulfill the reliability criteria defined by fixation losses $\leq$ 20%, false positive $\leq$ 33% and false negative $\leq$ 33%. All patients had auto refraction done using the Acuitus 5015 autorefractor.

For ease of classification of glaucoma, the following criteria were used based on cup disc ratio and mean deviation:

- i) Mild glaucoma: Cup Disc Ratio 0.5 – 0.6 and or Mean Deviation $\leq$ - 6dB
- ii) Moderate glaucoma: Cup Disc Ratio 0.7 – 0.8 and or Mean Deviation $>$ -6 to -12dB

iii) Severe glaucoma: Cup Disc Ratio 0.9 – 1.0 and or Mean Deviation > -12dB

3. RESULTS AND DISCUSSION

A total of 340 eyes of 170 glaucoma patients in the eye clinic and 340 eyes of 170 non-glaucoma patients from the GOPD were studied between August 2009 and June 2010.

The gender distribution by age group for the glaucoma and non-glaucoma patients is shown in table 1. There were more females in both study groups (52.9% in the glaucoma group, 56.5% in the non glaucoma group) than the males (47.1% in the glaucoma group, 43.5% in the non glaucoma group) as shown in table 1. This difference was not statistically significant. ($p=0.513$). The male to female ratio was 1:1.2.

A higher proportion of males with glaucoma were aged 40 - 49 years (40.0%) compared to 21.1% of females while a similar proportion of males and females among non glaucoma were aged 40-49 years.

There was a higher proportion of glaucoma cases with hypertension (25.9% compared to 22.9%) but there was no significant difference ($p=0.528$). The proportion of glaucoma group with history of diabetes was 8.2% compared to 2.9% of non glaucoma group and this difference was statistically significant ($p=0.034$).

Further comparisons revealed that a positive family history of glaucoma was less common in the non-glaucoma group ($p<0.001$); a higher proportion of the non-glaucoma group had visual acuity $\geq 6/18$ ($p<0.001$) and that IOP was lower in the non glaucoma group ($p<0.001$) see Table 1.

Table 1: Demographic and clinical characteristics of glaucoma and non glaucoma groups

	Glaucoma group		Non Glaucoma group		Both groups	
Age group	Male (%)	Female (%)	Male (%)	Female (%)	Male (%)	Female (%)

40-49	32(40.0)	19(21.1)	28(37.8)	34(35.4)	60(39.0)	53(28.5)
50-59	22(27.5)	30(33.3)	27(36.5)	37(38.5)	49(31.8)	67(34.1)
60-69	24(30.0)	26(28.9)	13(17.6)	20(20.9)	37(24.0)	46(25.0)
70 and above	2(2.5)	15(16.7)	6(8.1)	5(5.2)	8(5.2)	20(7.6)

	Glaucoma Group (%)	Non Glaucoma Group (%)	P value
Gender			
	80(47.1)	74(43.5)	0.513
Male	90(52.9)	96(56.5)	
Female			
Hypertension			
Yes	44(25.9)	39(22.9)	0.528
No	126(74.1)	131(77.1)	
Diabetes			
Yes	14(8.2)	5(2.9)	0.034
No	156(91.8)	195(97.1)	
Family history of glaucoma			
Yes			
	38(19.5)	7(4.1)	<0.001
No	132 (77.6)	163(95.9)	

Visual acuity in the better eye			
≥ 6/18	137(80.5)	156(91.8)	<0.001
6/24 - 3/60	25(14.7)	14(8.3)	
< 3/60	8(4.7)	0(0.0)	
Mean IOP (mmHg)			
Right eye	18.0±7.4	13.3±2.8	<0.001
Left eye	18.5±8.4	12.9±2.8	<0.001
Both eyes	18.3±7.9	13.1±2.8	<0.001

The commonest diagnosis type among glaucoma patients was POAG, found in 137 cases (80.6%) and NTG was found in 33 cases (19.4%). The distribution of diagnoses by gender is shown in Table 2. Similar proportions of males and females had POAG and NTG (Table 2).

There were no significant differences between glaucoma and non glaucoma in the CCT measurements. The mean for both groups was 530µm for both eyes. The p values for the comparisons for right and left eyes were 0.620 and 0.857 respectively.

Table 2: Association between gender and diagnosis among glaucoma group

Diagnosis	POAG	NTG	P value
Gender			

Male	65(81.3)	15(18.7)	0.847
Female	72(80.0)	18(20.0)	

Table 3: Comparison of central cornea thickness between glaucoma and non glaucoma cases

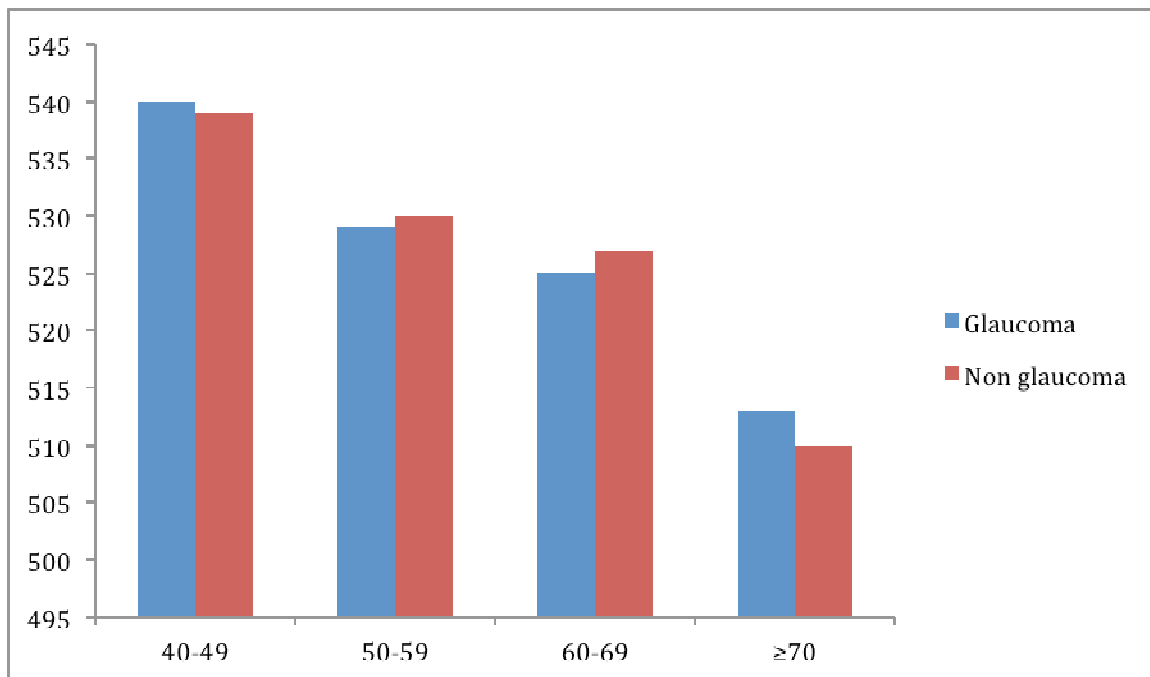
	Glaucoma CCT (μm)	Non glaucoma CCT (μm)	P value
Right eye	530±0.035	531±0.032	0.620
Left eye	530±0.037	530±0.032	0.857
Mean eyes)	(both 530±0.037	530±0.032	0.731

The CCT was also compared between the types of glaucoma. There was no significant difference between POAG and NTG though it was higher among those with POAG (p = 0.196).

Table 4: Mean CCT between the types of glaucoma among group

Diagnosis	Mean CCT (μm)	P value
POAG	531±0.037	0.196
NTG	522±0.027	

Figure 1: Comparison of mean CCT between glaucoma and non glaucoma cases by age group



This figure shows the mean CCT among glaucoma and non glaucoma group by age group. The CCT decreased with age in both groups.

DISCUSSION

A total of 780 eyes were studied - 340 eyes in each group. The higher proportion of patients with visual acuity better than 6/18 in the non-glaucoma group is not unexpected as the eyes in glaucoma group are more likely to have poorer vision from the disease.

There was a higher proportion of glaucoma cases with self reported hypertension which was not statistically significant. The proportion of glaucoma cases with self reported history of diabetes was significantly higher in the glaucoma group. This finding was also documented in the Barbados Eye Study[11] which found that diabetes was highly prevalent among glaucoma patients.

The commonest type of glaucoma was POAG, and similar proportions of males and females had POAG and NTG. POAG is the most prevalent type of glaucoma affecting 1 in 100 of the general population over the age of 40 years and it affects both sexes equally.[3]

The mean CCT in the non-glaucoma group in this study is $530 \pm 0.032\mu\text{m}$ (Table 3). This is lower than findings in studies by Mercieca [12], ($535 \pm 38\mu\text{m}$) in southern Nigeria, $533.34\mu\text{m}$ in Ghanaians [13], $552 \pm 35\mu\text{m}$ in the European Caucasians in Switzerland [14] , $548.1\mu\text{m}$ in Hispanics [15] , $550.4\mu\text{m}$ in Caucasians[15] and $555.6\mu\text{m}$ in the Chinese [15]. The mean CCT in the glaucoma group was also $530 \pm 0.037\mu\text{m}$. There was no difference between the two groups. This value is similar to a study by La Rosa [16] in which he compared CCT of whites and African Americans in glaucoma

and non glaucoma population with a mean CCT of $531 \pm 37\mu\text{m}$ for the 82 African American in the study. The mean CCT in this study is higher than the mean CCT in the study by Aghaian et al [15] in a glaucoma clinic. The mean CCT was $521\mu\text{m}$ in 107 African Americans who were enrolled in the study although a higher mean of the age groups was said to be probably responsible for this. Herndon [17] studied one hundred and nine subjects (184 eyes). Forty-eight patients (74 eyes) had glaucoma, 28 patients (51 eyes) had ocular hypertension, and 33 patients (59 eyes) were normal. The CCT of glaucomatous eyes was $554 \pm 0.022\mu\text{m}$ and normal control was $561 \pm 0.026\mu\text{m}$. There was no significant difference in CCT between normal and glaucomatous eyes ($P = 0.40$). Argus [18] also studied thirty-six patients with OHT compared with 29 control subjects and 31 patients with glaucoma. The mean CCT in patients with glaucoma was $557 \pm 0.039\mu\text{m}$ and control subject was $567 \pm 0.036\mu\text{m}$. This was not statistically significant. In the European glaucoma prevention study [19] CCT was measured in eight hundred fifty-four of 1077 ocular hypertensive participants. The mean CCT was $572.6 \pm 37.4\mu\text{m}$ which is higher than the value of this study. Various other studies [1,20,21] have shown that there were no statistically significant difference between glaucoma patients and controls. However, Rotterdam study found CCT was thinner in POAG than control. [22]

Table 4 presents comparison of mean CCT between POAG and NTG. The mean CCT in POAG patients was $531 \pm 0.037\mu\text{m}$ and $522 \pm 0.027\mu\text{m}$ among NTG patients. Although, the CCT was thinner in the NTG patients, it was not significant ($p = 0.196$). This is similar to the study by Copt [14] et al which also revealed a thinner CCT in NTG than POAG and there was no significant difference between normal controls and POAG.

Figure 1 presents mean CCT among glaucoma and non glaucoma by age group. CCT findings were significantly related to old age. CCT decreases with increasing age in both groups. However, there have been contradictory reports concerning the relationship between age and CCT. Some studies reported no significant association, [22,23,24] whereas the Barbados Eye Study [11], European glaucoma prevention study [19] and others found a definite inverse relationship [25,26]. This is probably due to the decrease in inter-fibrillary spacing in the proteoglycan composition of the inter-fibrillar matrix of the stroma microstructure with increasing age.

4. CONCLUSION

There was no difference in the mean central cornea thickness of glaucoma and non glaucoma group. The study also confirms that primary open angle glaucoma is the commonest type of glaucoma in our clinic population and that there was no significant relationship between central cornea thickness and specific open angle glaucoma. Central cornea thickness was also shown to decrease with age.

LIMITATION

Data for keratometry was not collected in this study. Keratometer was not readily available at the time of the study.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration between all authors. Author ASA designed the study, provided clinical care for the patient, collected and analysed the data and wrote the first draft of the manuscript. Authors AGBK, AAO, BCO and OBA provided clinical care for the patient participated in the writing of the manuscript and literature searches. All authors critically reviewed the manuscript and approved the final version.

CONSENT

Informed consent was obtained from each patient.

ETHICAL APPROVAL

Study approval was obtained from the ethical committee of the University College Hospital, Ibadan and the Head of GOPD.

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