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Research Article

Central Corneal Thickness in Nepalese Glaucoma Patients and Glaucoma Suspects

Abstract

Purpose: To compare central corneal thickness (CCT) among glaucoma patients, glaucoma suspects, and normal subjects and to determine its association with glaucoma severity in Nepalese population.

Methods: This study included 400 eyes (149 glaucoma, 157 glaucoma suspects, 94 controls) of 400 participants examined in a glaucoma clinic and eye OPD in Nepal. CCT was measured by ultrasonic pachymetry.

Results: CCT was significantly different among the study groups (P = 0.05), with the thinnest CCT in normal tension glaucoma (NTG) and thickest in ocular hypertension (OHT). CCT (in µm) was thinner in NTG (519.6 ± 31.6; P = 0.06) and primary open angle glaucoma (POAG) (524.5 ± 35.8; P = 0.026) than controls (536.6 ± 28.9); and it was thinner in POAG compared to primary angle closure glaucoma (PACG) (541.3 ± 50.5; P = 0.028) and OHT (559.8 ± 28.1; P = 0.017). In NTG, CCT was thinner compared to Glaucoma suspects (GS) (531.6 ± 35.0; P = 0.038), PACG (P = 0.008), and OHT (P = 0.008).There was no correlation between CCT and visual field defect and CCT was not statistically different between early, moderate and severe POAG groups.

Conclusions: We report that CCT in glaucoma suspects is similar to normal subjects and POAG, but thicker than NTG. These data will be important in clinically monitoring glaucoma suspects that are at increased risk of glaucoma. Our results may be population specific and further longitudinal studies are warranted to determine influence of CCT on glaucoma progression in this population.

Introduction

Intra Ocular Pressure (IOP) is an important parameter in the detection and monitoring of glaucoma. The Goldmann applanation tonometer (GAT) is the international "gold standard" for IOP measurement [1]. Central corneal thickness (CCT) has been shown to influence the pressure estimate [2], with thin corneas underestimating and thick corneas overestimating the readings [3].

Patients with normal tension glaucoma (NTG) may have thinner corneas than normal individuals resulting in underestimation of their IOP and under diagnosis; and patients with thicker cornea can be misdiagnosed to have glaucoma [4]. Copt et al. have described that many cases of glaucoma were reclassified after evaluating effect of CCT on measured IOP [5]. Thus, CCT should be considered to estimate actual IOP, to decide who requires closer observation or the initiation of treatment before definite damage occurs, and to establish a target IOP.CCT in patients with ocular hypertension (OHT) is greater and in patients with NTG lower compared to controls, with CCT in primary open angle glaucoma (POAG) falling in between OHT and NTG [3,5-13]. CCT in different types of glaucoma has been evaluated, but Glaucoma suspect (GS) excluding OHT has been ignored in this regard. We believe that CCT in glaucoma suspects should also be equally monitored as this group is always at a risk of developing glaucoma and the current study fills this research gap. It has also been shown that lower CCT is associated with visual field defect in glaucoma [11,12,14-18]. However it is controversial if CCT can predict glaucoma progression. Some studies have identified CCT as a risk factor for progression of glaucoma [14,19], and some have determined that CCT is not related to the severity of visual field defect [12,16,17]. Here, we try to address this controversy.

Different races and nationalities might have dissimilarities in CCT, which have been identified in normal population and glaucoma patients as well [13,15,20,21]. Thus, this study aims to compare CCT among glaucomatous, glaucoma suspects and normal individuals, to correlate CCT with severity of visual field loss, and to determine the association of the CCT with age and gender in Nepalese population. We are particularly interested to know the CCT characteristics of Nepalese population because this population has a lower overall prevalence of glaucoma (1.8%) [22] compared to the other south Asian regions (2.6 to 3.3%) [23-25].

Patients and Methods

Glaucoma patients and controls were recruited from glaucoma clinic and eye outpatient department of Tribhuvan University Teaching Hospital, Nepal. The research was approved by Research

Ethics Committee of Tribhuvan University, Nepal. The tenets of the Declaration of Helsinki were followed and informed consent was obtained from the participants after explanation of nature of the study.

Different types of glaucoma were defined according to Preferred Practice Pattern Guidelines of American Academy of Ophthalmology [26]. Primary open angle glaucoma (POAG)was defined by typical glaucomatous disc, visual field defect and/or significant loss of retinal nerve fiber layer (RNFL) in the optic nerve head region in Heidelberg Retinal Tomography (HRT) or Optical Coherence Tomography (OCT), IOP > 21 mmHg, and an open anterior chamber angle on gonioscopy. POAG was further divided into early, moderate, and severe on the basis of mean deviation (MD) of Humphrey standard automated perimetry according to Hodapp, Parrish, and Anderson's classification. [27] NTG was defined bytypical glaucomatous disc, visual field defect and/or significant loss of RNFL in the optic nerve head region in HRT or OCT, IOP ≤ 21 mmHg, and an open anterior chamber angle. Primary angle closure glaucoma (PACG) was defined by gonioscopic finding of more than 180° ofirido-trabecular contact, IOP > 21 mmHg, and optic nerve and visual field damage. OHT was defined by IOP > 21 mmHg, but normal disc, field, and angle. Glaucoma suspect (GS) was defined by family history of glaucoma and/or appearance of the optic disc or RNFL that is suspicious for glaucomatous damage including enlarged cup-disc ratio, asymmetric cup-disc ratio, narrowing of the neuroretinal rim, disc hemorrhage, nerve fiber layer defect, but with no visual field defect. For some analysis, OHT was also included in GS group; otherwise they are presented separately to reflect our new findings in GS group (Previous findings in OHT are discussed in introduction and discussion). All eyes with ocular disorders altering CCT, any active ocular disease other than glaucoma, any ocular surgery, corneal astigmatism > 4 D, and history of contact lens wear were excluded from the study. Age and gender matched individuals with healthy eyes were taken as controls.

For diagnosis and classification of glaucoma, detailed history taking, slit lamp examination, IOP measurement, gonioscopy, funduscopy, AVF examination, OCT, and HRT were performed in all cases. Central measurement system of USG Pachymetry (Axis II PR) was used to measure CCT in upright position by same examiner. Five consecutive readings with standard deviation (SD) <5 microns were taken and averaged.

Statistical Analysis

Data were described as mean ± SD and 95% confidence interval; and $p < 0.05$ was considered statistically significant. One-way ANOVA was applied to compute the differences in the CCT among the study groups. The association of CCT with age, IOP, and visual field defect was evaluated with Pearson Correlation and linear regression.

Results

A total of 400 eyes of 400 subjects, comprising 149eyes with glaucoma (72 eyes with POAG, 29 eyes with PACG, and 48 eyes with NTG), 157eyes with GS (6 with OHT) and 94 eyes of control subjects were examined. Among the subjects enrolled in the study, 180(45%) patients were male and 220(55%) patients were female. The mean ± SD age of glaucoma patients, glaucoma suspect, and controls was 45.0 ± 21.1, 45.6 ± 21.5, 45.2 ± 20.8 years respectively and There was no significant difference in mean age among the study groups (P=0.140) (Tables 1-3).

Out of 72 eyes with POAG, 44 eyes had visual field defects; rest of the cases were diagnosed on the basis of disc findings, HRT, and OCT. CCT in POAG eyes with field defect (519.8 ± 37.1) and without field defect (530.1 ± 32.3) was not statistically different (P = 0.241). Table 4 shows CCT in POAG eyes with different severity levels which was not statistically different between the groups (P =0.248). Moreover, CCT showed no correlation (R = 0.144, P = 0.176) with mean deviation in visual field. There was a significant positive correlation between CCT and IOP (r = 0.315, P = 0.019) (Figure 1).

Discussion

IOP is an important risk factor and has a significant influence on diagnosis and management of glaucoma. GAT is used worldwide for IOP measurement because of its accuracy but its results may be affected by CCT. We measured CCT in different types of glaucoma and glaucoma suspects and evaluated the relationship between CCT and severity of glaucoma. CCT was significantly different between the study groups, with thinnest CCT in NTG and thickest CCT in OHT. CCT in PACG was thicker than in NTG and POAG, NTG and

Table 1: Gender and CCT in different study groups. Table shows that CCT in females was significantly thinner than in males in controls and glaucoma patients, but not in glaucoma suspects.

	Gender	n	Mean CCT(μm)	p-value
Control	M	48	542.6 ± 31.4	0.040
	F	46	530.4 ± 25.0	
Glaucoma	M	66	533.5 ± 34.0	0.037
	F	83	520.3 ± 40.8	
Glaucoma suspect	M	66	535.7 ± 35.4	0.368
	F	91	530.6 ± 35.0	

Table 2: Age and CCT in different study groups. Table shows that CCT in different age groups among the study groups. There was no significant correlation between age and CCT in controls (R=-0.194, P =0.061) and glaucoma patients (R=0.008, P=0.927). However, in glaucoma suspects, CCT was negatively correlated with age (R=-0.216, P=0.007) (Figure 1). Multiple linear regression was done to evaluate how age and gender interact to affect CCT. The interaction was significant [$F_{(2,91)}$ = 4.9, P = 0.010] in controls and glaucoma suspects [$F_{(2,154)}$ = 3.8, P = 0.024], but not in glaucoma patients [$F_{(2,146)}$ = 2.5, P = 0.085].

Age Range	Control		Glaucoma		Glaucoma suspect	
	n	Mean CCT (μm)	n	Mean CCT (μm)	n	Mean CCT (μm)
11-20	6	534.2 ± 14.5	8	504.4 ± 35.9	14	544.0 ± 28.4
21-30	6	554.2 ± 32.0	13	524.6 ± 39.0	37	541.6 ± 35.6
31-40	16	548.9 ± 37.4	23	532.6 ± 24.3	25	545.6 ± 35.7
41-50	30	528.4 ± 23.8	33	539.5 ± 43.9	21	512.0 ± 30.5
51-60	16	545.8 ± 28.9	28	521.0 ± 44.0	32	526.1 ± 29.3
61-70	12	537.6 ± 15.8	32	511.8 ± 34.1	22	526.7 ± 43.7
71-80	8	511.8 ± 30.0	12	544.0 ± 23.6	6	525.5 ± 10.8

POAG did not differ in CCT; and CCT in GS was thicker than NTG. There was no relationship between CCT and severity of POAG. CCT in females was thinner than males in controls and glaucoma patients and CCT decreased with age in glaucoma suspects.

This study confirms the evidences that CCT in NTG is thinner than normal subjects. [3,5,8,10] Majority of studies on CCT in OHT show that CCT in OHT is thicker than normal subjects, NTG, and POAG [3,4,6,8,10,12,13]. Though CCT in OHT was thicker than NTG and POAG in the current study, we found no significant difference between OHT and controls; this finding is in concert with a study in Spanish population [11]. Our results on OHT might not be conclusive due to small number of eyes with OHT and need further investigation with larger sample size in Nepalese population.

Table 3: CCT in controls, patients with different types of glaucoma, and glaucoma suspects. Table shows that CCT was lowest in NTG and highest in OHT among the study groups. The comparison of CCT between the study groups showed significant difference (P = 0.05). CCT was thinner in NTG (P = 0.006) and POAG (P = 0.026) than controls; and it was thinner in POAG compared to PACG (P = 0.028) and OHT (P = 0.017). CCT in NTG was thinner compared to GS (P = 0.038), PACG (P = 0.008), and OHT (P = 0.008).

Type	n	Mean CCT (µm)
Control	94	536.6 ± 28.9
NTG	48	519.6 ± 31.6
PACG	29	541.3 ± 50.5
POAG	72	524.5 ± 35.8
OHT	6	559.8 ± 28.1
GS	151	531.6 ± 35.0

Table 4: CCT and severity of POAG. Table shows CCT in POAG eyes with different severity levels which was not statistically different between the groups (P =0.248). Moreover, CCT showed no correlation (R = 0.144, P = 0.176) with mean deviation in visual field. There was a significant positive correlation between CCT and IOP (r = 0.315, P = 0.019).

Severity (in terms of MD*)	n	Mean CCT(µm)
Early	29	523.4 ± 36.5
Moderate	12	506.2 ± 33.9
Severe	3	540.7 ± 52.6

*MD = mean deviation

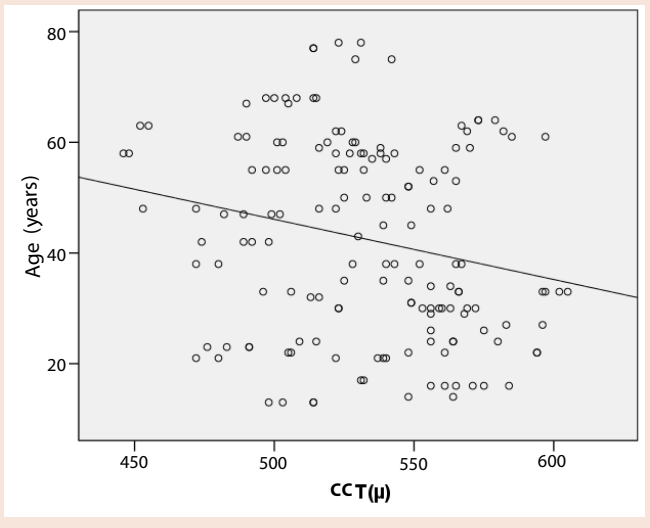

Figure 1: Correlation between age and CCT in glaucoma suspects ((R=-0.216, P=0.007).

CCT in POAG has been found to be equivalent to normal subjects in many studies [3-6,10,12,22], but there is also evidence of reduced CCT in POAG [11]. We observed that CCT in POAG is thinner compared to normal subjects. Difference in CCT between POAG and NTG is controversial, with some studies reporting equivalent CCT in POAG and NTG [5,6], and some reporting higher CCT in POAG than NTG [3,7,12]. We determined that POAG and NTG show similar CCT. We present one of the early reports on CCT in PACG that it is similar to controls supporting a report in similar population [22], but it is thicker than POAG and NTG. We are the first to report that CCT in GS is similar to controls and POAG, but thicker than NTG.

POAG eyes with visual field defect have been shown to have thinner CCT than those without field defect [16-18], but we show no significant difference in CCT between these subgroups. Some studies show thin CCT in patients with advanced glaucoma [11,15] and association of thin CCT with glaucoma progression [14], but we observed no difference in CCT among POAG eyes with different severity levels and this is consistent with the findings of Sullivan-Mee et al. [16,17]. However, our results on severe glaucoma are not conclusive due to small sample size (n = 3).

There are variable findings on effect of gender on CCT, with one study [13] showing thicker CCT in females than in males and three studies [10,12,28] showing no effect of gender on CCT. We found thinner CCT in females than males in control and glaucoma group, but no difference in glaucoma suspects. Thapa et al. [28], Hornova et al. [7], and Lee et al. [10] report decreased CCT with age, while Jonas et al. [12] report CCT is age independent; we found that CCT is independent of age in glaucoma and normal subjects, but decreases with age in glaucoma suspects.

In conclusion, we present the novel findings that CCT in glaucoma suspects is similar to normal subjects and POAG, but thicker than NTG. These data will be important in monitoring glaucoma suspects clinically that are at increased risk of glaucoma. CCT is thinnest in NTG and thickest in OHT among glaucoma subtypes, but it is not associated with severity of visual field loss in POAG. Females with glaucoma show thinner CCT than their male counterparts. Our results might have been affected by the choice of ultrasound pachymetry which may be less accurate than optical pachymetry to measure CCT. The overall findings may be population specific and further longitudinal studies will be helpful to determine influence of CCT on glaucoma progression in this population.

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