Original Article

Comparison of Central Corneal Thickness between Normal Individuals and Primary Open-Angle Glaucoma Patients Using Topical Anti-Glaucoma Therapy

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ABSTRACT

Purpose: To investigate and compare the difference in central corneal thickness among normal individuals and patients with POAG taking long term (>6months) different topical anti-glaucoma medications.

Study Design: Cross-sectional comparative study.

Place and Duration of Study: Civil Hospital Eye OPD from May 2024 to December 2024.

Methods: The study included 170 individuals (85 primary open angle glaucoma patients and 85 normal individuals) after informed consent. The right eye of each patient was selected for central corneal thickness (CCT) measurement using Nidek AL Scan between 10:00am and 02:00pm to avoid diurnal variation in CCT. Frequencies and descriptive statistics were used to calculate mean and standard deviation to assess the general characteristics of study population. Independent T-tests were used to assess differences in mean CCT between distinct groups to find which variables were significantly related to CCT.

Results: The results were analyzed using SPSSv23. Mean age of participants was 54.87±7.55 (range 20-80) years. Individuals with POAG had a lower mean CCT compared to those without glaucoma (p-value <0.001).Use of prostaglandins (p<0.001), beta-blockers, carbonic anhydrase inhibitors and carbonic anhydrase with beta blocker combination was significantly related with decreased CCT compared to control.

Conclusion: Patients with long-standing POAG tend to have thinner CCT compared to healthy individuals. Among glaucoma treatments, prostaglandin analogues are associated with the lowest mean CCT values, highlighting their potential effect on corneal thickness.

Keywords: Primary Open Angle Glaucoma, Latanoprost, Central Corneal Thickness, Beta-Blockers, Carbonic anhydrase Inhibitors.

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INTRODUCTION

The CCT has an essential diagnostic role in the IOP measurement among glaucoma patients.[1] The association of CCT with glaucoma development and progression has long been established.[2,3] A number of factors influencing CCT and IOP have been explored indicating the importance of these factors in diagnosing glaucoma and to see its progression.[4-8]Topical anti glaucoma treatment in the form of prostaglandin analogues, alpha adrenergic agonists, beta blockers and carbonic anhydrase inhibitors are used alone or in combination to lower the IOP. They can affect CCT by either increasing, decreasing, or having no effect depending on the type and duration of treatment. However, limited studies have been done in Pakistan to date to find out the average CCT among POAG patients who are on commonly prescribed

topical anti glaucoma medications.[6]

This study aims to determine the average central corneal thickness (CCT) in patients receiving topical anti-glaucoma treatment. Given that CCT plays a crucial role in intraocular pressure (IOP) measurement and is associated with disease progression, evaluating its average values in treated patients is essential for a better understanding of its clinical implications.

METHODS

This study was conducted in Civil Hospital Eye OPD from 1st May 2024 to 31st December 2024. It was a cross-sectional comparative study in which 168 patients (84 cases and 84 control) were included. Sample size was calculated by using OPEN EPI software v3 with 95% confidential level and taking estimated population as 1 million.[9] The final sample size was rounded off to 170(85 primary open angle glaucoma patients (cases) and 85 normal individuals (control group). Sample was collected through non-probability consecutive sampling. Patients between 40 and 80 years of age, diagnosed with POAG based on clinical findings, OCT, perimetry, gonioscopy and receiving topical anti glaucoma treatment for at least 5 months without gaps were included. Age matched controls were selected from patients who had normal eyes and came with refractive errors or for regular eye checkup. Patients with any corneal disease, scarring, dystrophy, active ocular infection, recent contact lens wear, any retinal disease, history of ocular or refractive surgery, systemic disease other than diabetes mellitus and systemic hypertension, lactation or pregnancy, secondary and angle closure glaucoma, using topical medications other than anti-glaucoma and history of gaps in treatment were excluded.

After approval from the review board **(DUHS/IRB/EXTENSION/2024/364)**, all patients satisfying the inclusion criteria were included. Informed consent was obtained for participation in the study and conducting the procedure. A complete ophthalmologic examination, including slit-lamp examination, IOP measurement, corneal thickness measurement, and fundus examination, was performed. Data was collected in the form of an interview with the patient comprising demographics (age, gender, ethnicity) and history of medications use (type of drug used, number of drops of drugs used per day, monotherapy, or combination therapy) and the details were filled in the form. The right eye of each patient was selected for CCT measurement which was taken using Nidek AL Scan (optical method for biometry and pachymetry) by the same experienced ophthalmology technician. Scanning was done between 10:00am and 02:00pm to avoid diurnal variation in CCT measurement.

The primary outcome measure was to determine whether CCT differed by presence of glaucoma and the type of topical anti-glaucoma medicines used. The secondary outcome was to study correlations between other demographic characteristics and co-morbidities with CCT.

The data was fed into and analyzed through the IBM Statistical Package for the Social Sciences v23 software. Frequencies and descriptive statistics were used to calculate mean and standard deviation to assess the general characteristics of study population. Independent T-tests were used to assess differences in mean CCT between different groups to find which variables were significantly related to CCT. Linear regression, Analysis of Variance (ANOVA) and Chi-square tests were used where applicable.

RESULTS

Out of these 170 eyes, 85 had POAG and 85 eyes had no history or any evidence of POAG. The mean age of the participants was 54.87±7.55 years (range 20-80). There were 47.6% males (n=81) and 52.4% were females (n=89). The majority were Urdu-speaking (n=135, 79.4%), 58 eyes were pseudophakic, 64 (37.6%) participants had Diabetes Mellitus and 52 (30.6%) were diagnosed with systemic hypertension (Table 1). Females were more likely to have glaucoma than males (p = 0.046).The most frequent anti-glaucoma eye drops used in this study were a combination of Dorzolamide (Carbonic anhydrase inhibitor) and Timolol(Beta blocker).

The age group had a significant relation with CCT, individuals aged 55years or older had mean CCT of 499.32±30.05 um compared to those with less than 55 years age and CCT of 516.31 ± 26.36 um (p value < 0.001). On linear regression, age was significantly associated with thinner CCT measurements (B= -0.638, t=-2.332, p=0.021).Gender, ethnicity, co-morbidities (Diabetes and Hypertension), lens status and intra-ocular pressure did not have significant relation with CCT (Table 3). Individuals with POAG had a lower mean CCT (501.31±24.76 um) compared to those without glaucoma (CCT=519.92 ±26.5; p-value <0.001).

Table 1: *Population characteristics with frequency, percentage, mean and standard deviation.*

Population Characteristics		Frequency N (Percentage %)	Mean	Standard Deviation
Age (years)			54.87	±7.55
Gender	Male	81(47.6%)		
	Female	89(52.4%)		
Ethnicity	Urdu speaking	135 (79.4%)		
	Sindhi	18(10.6%)		
	Pathan	15 (8.8%)		
	Balochi	2(1.2%)		
Status of lens	Pseudophakic	58 (34.1)		
	Phakic ±Cataract	112 (65.9%)		
Diabetes Mellitus	Yes	64(37.6%)		
	No	106(62.4%)		
Systemic Hypertension	Yes	52(30.6)		
	No	118(69.4)		
Intraocular pressure (mmHg)			13.75	±2.88
Central corneal thickness (µm)			510.61	±27.21

Table 2: *Comparison of population characteristics in glaucoma group versus control group.*

Population Characteristics		Frequency (N)	Glaucoma Group	Control Group	p- value
Demographics					
Age (years)	≥ 55	90	44	46	0.759
	< 55	80	41	39	
Gender	Male	81	34	47	0.046
	Female	89	51	38	
Ethnicity	Pathan	15	9	6	0.139
	Sindhi	18	12	6	
	Balochi	2	2	0	
	Urdu	135	62	73	
Systemic Diseases					
Diabetes Mellitus	Yes	64	34	30	0.527
	No	106	51	55	
Hypertension	Yes	52	29	23	0.318
	No	118	56	62	
CCT µm			501.31±24.76	519.92 ±26.5	<0.001

Table 3: *Comparison of mean central corneal thickness among various population characteristics.*

Population Characteristics		Mean CCT(µm)	Std. Deviation	p-value
Demographics				
Age (years)	≥55	499.32	30.05	<0.001
	< 55	516.31	26.36	
Gender	Male	508.88	28.83	0.428
	Female	512.20	25.71	
Ethnicity	Pathan	519.67	30.2	0.542
	Sindhi	512.06	30.6	
	Balochi	518	25.45	
	Urdu	509.31	26.51	
Systemic Diseases				
Diabetes Mellitus		510.98	25.46	0.892
Hypertension		508.46	27.54	0.494

Among topical anti-glaucoma drugs, use of prostaglandins (CCT= 494.2+- 25.43; p <0.001), beta-blockers (CCT= 503.44 +- 24.74; p=0.002), carbonic anhydrase inhibitors (CCT= 504.17 +-23.03; p=0.007) and carbonic anhydrase+ beta blocker combination (p=0.002) was significantly related with decreased CCT compared to control group. Use of 2 or more anti-glaucoma drops per day as compared to single drop and no drop was associated with thinner CCT values (p<0.001). On linear regression, the increased number of drops used per day was significantly associated with thinner CCT values (B=-2.896, t= -2.475, p=0.014). Use of Alpha-adrenergic agonists and other drug combinations did not show significant association with CCT (Table 4).

DISCUSSION

CCT can vary based on age and demographics.[10,11] Generally, it tends to decrease with age, although individual variations exist depending on the refractive errors, axial length and keratometry.[12-14] Compared to

Table 4: *Comparison among anti-glaucoma medications used and central corneal thickness.*

Antiglaucoma Medicines			Mean CCT(um)	Std. Deviation	p- value
Prostaglandins *		30	494.2	25.43	<0.001
Beta Blockers *		77	503.44	24.74	0.002
Alpha adrenergic agonists *		17	500.56	24.34	0.109
Carbonic anhydrase inhibitors		69	504.17	23.03	0.007
Beta Blockers + CAIs		68	503.09	21.35	0.002
Betablockers + PGs		3	524.67	15.53	0.368
Betablockers + AAs		4	511.5	7.37	0.840
Glaucoma	Yes	85	501.31	24.76	<0.001
	No	85	519.92	26.5	
Number of drops	< 2 drops per day	91	517.63	27.17	<0.001
	>= 2 drops per day	79	502.53	25.08	
Duration of treatment	>= 7 months	77	505.05	28.83	0.133
	< 7 months	93	512.39	26.55	

*(alone or combination)

control group, eyes with glaucoma and patients using anti-glaucoma medications had significantly thinner CCT as shown by previous studies.[15-17] Other demographic factors like ethnicity can also influence CCT, with certain groups having thicker corneas on average than others. Additionally, factors such as gender and geographical location may play a role.[18,19]

Thinner CT affects the accuracy of IOP measurements, as CCT is a key determinant of tonometry reliability. In individuals with glaucoma and thinner CCT, clinicians must account for this factor when assessing and managing the condition, as it can influence IOP interpretation and treatment decisions. Additionally, age has shown a significant correlation with CCT, as demonstrated by Hashmani et al, in a study on the normal population of Pakistan.[6] The study demonstrated a linear negative correlation between CCT and age, indicating that CCT decreases with increasing age. This finding aligns with numerous international studies.[19] Age-related corneal thinning is primarily attributed to changes in collagen structure and hydration levels, leading to reduced elasticity. These changes can impact eye health and vision, particularly in conditions like glaucoma, where corneal thinning may affect IOP measurement accuracy and clinical management.[5]

However, gender, other demographic factors, and the presence of systemic diseases showed no significant correlation with CCT. In contrast, the study by Hashmani et al, found that males had significantly thinner CCT than females. This discrepancy may be attributed to differences in study design, as their research was conducted on a normal population with a broader age range.[6] Batawi et al, found no association between CCT and gender or systemic diseases such as diabetes mellitus and hypertension.

This study demonstrated a decrease in CCT with an increased number of daily eye drops, a finding previously reported by Batawi et al.[18] Regular check-ups with an eye care professional are essential for individuals undergoing treatment to monitor changes in corneal health and intraocular pressure. We found thinner CCT values in the prostaglandin group which is in line with previous studies.[20,21] This thinning in CCT is a result of changes in corneal hydration dynamics rather than true tissue loss. It is essential for patients to be monitored regularly by their eye care professionals to ensure the health of their corneas and overall impact of newly reduced corneal thickness upon accuracy of subsequent IOP measurements which can affect management of chronic glaucoma patients.

Our study found that long-term use of beta-blockers and carbonic anhydrase inhibitor combinations was associated with thinner CCT. Additionally, multiple local and international studies have reported a significant reduction in CCT with the use of prostaglandin analogues.[22,23] A longitudinal study in Türkiye observed a significant decline in CCT among patients treated with latanoprost at both the first and third years ($p = 0.039$ and 0.018, respectively).[17]

This study also demonstrated a significant decline in CCT with the combination of latanoprost and a beta-blocker, whereas beta-blocker monotherapy did not show a similar effect. The use of two topical eye drops may lead to greater CCT reduction compared to a single medication, due to their combined effects on

different physiological pathways, resulting in a more comprehensive impact on the corneal structure. A recent quasi-experimental study conducted in Lahore, Pakistan compares the effect of short term (under 6 months) use of topical anti-glaucoma treatments on the central corneal thickness and the results show that use of Prostaglandins is significantly associated with decrease in central corneal thickness under 6 months of usage.[23] Our study aims at long term usage of anti-glaucoma medicines, however, this further backs our findings and adds to the knowledge on this matter.

The study has several limitations. Its cross-sectional design limits the ability to establish causality between anti-glaucoma medications and changes in CCT. Additionally, the findings may not be fully generalizable due to the study's limited sample size and single-center setting. Other factors that could influence CCT, such as ocular diseases, previous surgeries, or genetic predisposition, were not accounted for. The study also measured CCT only once per participant, without long-term follow-up to track progressive changes. Furthermore, variability in medication adherence may have affected the results.

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Patient's Consent: Researchers followed the guidelines set forth in the Declaration of Helsinki.

Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval: The study was approved by the Institutional review board/Ethical review board **(DUHS/IRB/EXTENSION/2024/364).**

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Authors Designation and Contribution

Husna Haroon; Trainee: *Concepts, Design, Literature search, Data acquisition, Data analysis, Statistical analysis, Manuscript preparation, Manuscript editing, Manuscript review.*

Nargis Nizam Ashraf; Assistant Professor: *Concepts, Design, Manuscript editing, Manuscript review.*

Arwa Ismail; Trainee: *Data acquisition, Manuscript preparation, Manuscript editing, Manuscript review.*