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Original article

Comparative Study of Central Corneal Thickness in Healthy Individuals and Diabetic Patients with and Without Retinopathy using Pentacam

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Abstract:

Background: Precise evaluation of Central Corneal Thickness (CCT) is crucial for both tracking the activity of corneal endothelial cells and detecting corneal disorders including keratoconus and Fuchs Endothelial Corneal Dystrophy. The aim of this work was to use pentacam to measure CCT and generate CCT maps in diabetic patients with and without retinopathy and contrast those with normal subjects. **Patients and methods:** This comparative cross-sectional study was executed on 75 subjects. They were split into three equal groups: (Group A): diabetic patients without diabetic retinopathy; (Group B): diabetic patients with diabetic retinopathy while (Group C): non-diabetic individuals. All groups were subjected to pentacam to measure CCT and generate corneal thickness maps to compare CCT concerning different groups. **Results:** A statistically significant difference was detected in CCT across the groups. Patients with diabetes who did not have retinopathy had CCT that was not significantly different from those who did. It has been demonstrated that patients with diabetes mellitus who have had the condition for more than ten years have a significantly higher mean CCT than those who have had it for less than ten years. CCT showed a positive correlation with age, RBS, haemoglobin A1c (HBA1c) and DM duration. A significant correlation existed between CCT and the DURATION of DM. **Conclusion:** A statistically significant variation was detected in CCT between diabetic patients and normal controls. Age, RBS, HBA1c, and the length of DM can all have positive correlations with CCT.

Keywords: Central Corneal Thickness, Diabetic Patients, Pentacam, Retinopathy

Introduction

Most of the body cells are damaged by hyperglycemia. The cornea and retina are most impacted by hyperglycemia's ocular consequences. When comparing diabetic tear film to control tears, the cornea encounters four times more glucose [1, 2]. All corneal layers are vulnerable to injury in patients with diabetes mellitus (DM). Corneal endothelium is one of the morphological alterations of cornea that is essential for maintaining the stroma dehydrated [3]. Reduced endothelial cell density (ECD), polymorphism, and polymegathism are signs of the injury [4-6]. Clinicians can now use both contact and non-contact devices for CCT estimate, each using a different set of assessment techniques or strategies. However, fewer research has assessed the precision and consistency of various CCT assessment techniques [7-9].

One of the Schiempflug instruments that are sold commercially is the Pentacam (Oculus Inc.). It comes in three models: Basic, Classic, and High Resolution (HR). With the help of the Pentacam's HR rotating Scheimpflug technology, a 1.45 megapixel camera that rotates along the optical axis from 0 to 360 degrees and captures 138.000 real elevation points in a matter of seconds can image the cornea cross-sectionally [10].

It provides pachymetry, anterior chamber angle and depth, anterior and posterior surface topography of cornea, and crystalline lens examination using a blue Light-Emitting Diode (LED) with a wavelength of 475 nm. Various anterior segment metrics can be automatically analyzed by the instrument-based software, which captures 25 photos per measurement in less than two seconds. The Pentacam Scheimpflug camera can be used to evaluate diabetic corneas globally and provide comprehensive data about the effects of DM on human corneas [11].

The goal of this research was to measure CCT and generate CCT maps in diabetic patients with and without retinopathy and contrast those with normal subjects.

Patients and Methods:

Type and setting of research: comparative cross-sectional research was carried out on 75 subjects aged above 18 years old, both sexes and previously diagnosed with DM from September 2022 to August 2023. The study was carried out with permission from Benha University Hospital's Ethical Committee (MS-1-1-2023). The patients gave their informed written consent.

Exclusion criteria include being younger than eighteen years old, having corneal pathologies such as haze, degenerations, and dystrophies, having undergone corneal refractive surgery, having ocular trauma, having glaucoma, wearing contact lenses within a month of the study, and having systemic diseases that affect the eyes, such as inflammatory or autoimmune diseases. Subjects were further split into three equal groups:

Group A: diabetic patients without diabetic retinopathy.

Group B: diabetic patients with diabetic retinopathy.

Group C: non-diabetic individuals.

All patients were subjected to:

- History: patient information (residence, occupation, sex, and age) medication, any chronic disorder and duration of DM.
- Clinical examination.
- Laboratory investigations: Random blood sugar and HbA1c.
- Visual acuity: unaided and best corrected visual acuity.
- Refraction: refractive errors.
- Slit lamp examination: for corneal state, corneal changes, lid margin examination for meibomian gland dysfunction.
- Intraocular pressure (IOP) assessment utilizing Goldmann applanation tonometer.
- Fundus examination.

- Pentacam was executed for the three groups.

Examinations: Preliminary optometric and ocular health exams were included in the ocular examination. A Snellen visual acuity chart was employed to test the uncorrected distance visual acuity at six meters (m). An auto-refractometer was employed to carry out the objective refraction (Nikon). Subjective refraction was employed to establish the optimal distance optical correction, and the optimal corrected distance visual acuity was noted. The following phase involved an ophthalmologist doing an indirect ophthalmoscopy and utilizing slit-lamp biomicroscopy (Nikon slit-lamp) to examine the anterior and posterior segments in detail. Next, a skilled operator used Pentacam HR (Oculus, Optikgeräte GmbH, Wetzlar, Germany) to image the participants' corneas in low light.

A 1.45-megapixel camera that can record up to 138,000 data points in < 2 seconds was employed to take corneal images using a blue LED with a wavelength of 475 nm as the light source. The equipment was employed in automatic mode to obtain images. Measurements with "OK" quality statement were the only ones considered. Patients were told to blink fully once before imaging to reduce the possibility that the tear film would affect corneal imaging. From Pentacam's maps, information on pachymetry readings was taken out and recorded [13-12].

Definitions:

The central corneal thickness (CCT): was determined by measuring thickness of cornea at its apex.

Refractive errors: were established using manifest refraction's spherical equivalent (SE).

Diabetes mellitus (DM): was determined by comparing HbA1c level of 6.5 % or above with a prior diagnosis.

Method of intraocular pressure (IOP) measurement [14]:

After administering the local anesthetic drops, fluorescein was used. The prism head was exposed to the blue light from the slit lamp and carefully advanced toward the corneal center. The tonometer's calibrated dial was turned clockwise until the two fluorescein semi-circles met at their inner borders. The process was carried out once more for the other eye.

Sample Size estimation:

Utilizing the G*power software version 3.1.9.2, sample size was determined based on an anticipated large effect size (f = 0.4) across the study groups (patients with and without diabetic retinopathy and controls). To find a comparable effect size, a minimum sample size of 75 is required (25 per group). Power and alpha were set at 0.8 and 0.05, respectively.

Statistical analysis

SPSS v25 was utilized for statistical analysis (IBM Inc., Chicago, IL, USA). mean and standard deviation of the numerical values were displayed (SD). Frequency and percentage (%) were employed to present non-numerical facts. The normality of data was evaluated utilizing Shapiro-Wilk test. For parametric variables, the repeated measure ANOVA test was employed. Non-parametric variables were subjected to Kruskal Wallis Test. To contrast non-parametric variables between two research groups, the U test, or Mann Whitney test, was utilized. To investigate how two qualitative variables are related, the Chi-Square test was employed. The degree of correlation between two quantitative variables was determined utilizing Spearman's correlation. A significant two-tailed P value was defined as one < 0.05.

Results:

The current study was carried out on 75 subjects. The mean age for Group A was 55.2±11.4 years, while it was 58.7±10.7 years for Group B and 54.2±11.3 years for Group C. There was no significant variation in age and gender distribution among the groups. The variationn in random blood sugar levels and HbA1c

between study groups was not statistically significant. (Table 1)

Group A had 12 patients (48%) with a DM period of DM less than 10 years, while Group B had 7 patients (28%) in the same duration category. The mean DM duration for Group A was 12.8 years (SD = 5.6), and for Group B it was 14.1 years (SD = 5.7). (Table 2)

The variation in CCT between the groups was statistically significant ($p < 0.001$). The difference in the distribution of examined eyes between the groups was not statistically significant. Patients with diabetes without retinopathy had CCT that was not statistically different from those with retinopathy ($p=0.245$). (Table 3)

Mean CCT for patients with a DM period less than 10 years was 555.1±31.5μm, while it was 574.3±33.4 μm for patients with a period of DM greater than 10 years. A significant higher mean CCT in patients with DM > 10 years in contrast to patients with < 10 years was detected ($p = 0.031$). (Table 4).

Table 1: Demographic data, random blood sugar and HBA1c among studied groups

		Group A N=25	Group B N=25	Group C N=25	Test	P
Age (years)	Mean ± SD	55.2±11.4	58.7±10.7	54.2±11.3	F=1.103	0.337
	Median(Range)	58(20-70)	57.6(44-79.4)	57(19-69)		
Gender	Male	13(52%)	15(60%)	11(44%)	k=1.282	0.527
	Female	12(48%)	10(40%)	14(56%)		
Random blood sugar(mg/dl)	Mean ± SD	155.4±74.7	159.4±80.5	117±9.6	4.105	0.128
	Median(Range)	125(100-320)	125(102-322)	116(100-130)		
HbA1c (%)	Mean ± SD	6.1±1.6	6.2±1.8	5.1±0.8	6.845	0.063
	Median(Range)	5.8(4.1-10)	5.6(4.3-10.6)	4.8(4.1-6.0)		

F, one way ANOVA test; X^2, Chi square test, Test, Kruskal wallis test; * for significant p value (<0.05)

Table 2: Duration of DM in diseased groups

		Group A N=25	Group B N=25	Test	P
Duration of DM groups	<10 years	12(48%)	7(28%)	X^2=2.122	0.145
	>10 years	13(52%)	18(72%)		
Duration of DM (years)	Mean ± SD	12.8±5.6	14.1±5.7	Z=1.071	0.284
	Median (Range)	11(7-25)	13(5-28)		

X^2, Chi square test; Z, Mann Whitney test

Table 3: Central corneal thickness among studied groups

		Group A N=25	Group B N=25	Group C N=25	Test	p_1
Central corneal thickness(μm)	Mean ± SD	543.8±12.5	594±27.9	505.6±10.9	K=65.724	**<0.001***
	Median(Range)	540(523-564)	587(564-689)	506(485-523)		
Examined eye	Right eye	15(60%)	10(40%)	10(40%)	X^2=2.679	0.262
	Left eye	10(40%)	15(60%)	15(60%)		
Pairwise comparison Group A and B		P_2: 0.245				

p1, Kruskal Wallis test; p2, Mann Whitney test; X^2, Chi square test; * for significant p value (<0.05)

Table 4: Association between central corneal thickness and duration of DM

		Duration of DM		Test	P
		<10 years	**>10 years**		
Central corneal thickness	Mean ± SD	555.1±31.5	574.3±33.4	2.160	**0.031***
	Median (Range)	551(518-630)	565(528-689)		

Test, Mann Whitney test

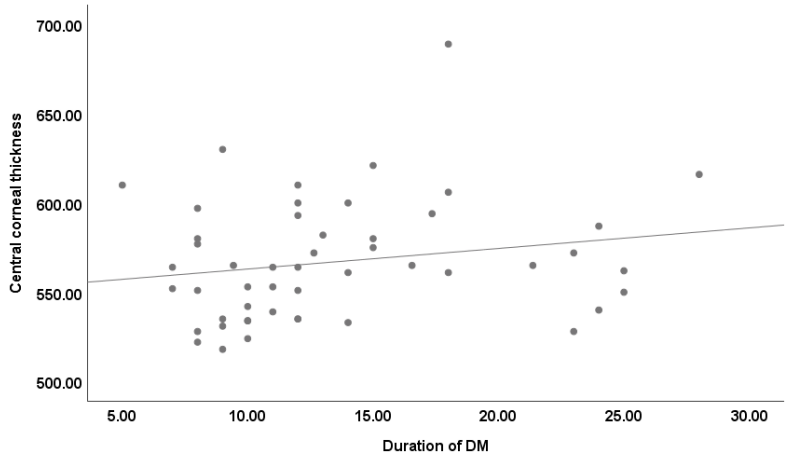

Figure 1: Correlation between central corneal thickness and duration of DM

Discussion

Diabetic patients are more likely to have damage to all layers of cornea. Corneal endothelium has a significant function in preserving dehydrated stroma. The damage shows decreased ECD, polymorphism, and polymegathism [15].

The current investigation found a statistically significant variation in CCT across the groups. There was no discernible variation in CCT between people with diabetic retinopathy and those without retinopathy. DM patients with more than ten years' experience had a significantly higher mean CCT than patients with less than ten years' experience. Positive correlations were seen between CCT and age, RBS, HBA1c, and DM duration. A noteworthy association was discovered between the length of DM and CCT. Numerous investigations that have assessed the CCT in both normal persons and type 2 diabetes patients concur with the current investigation. Most of them stated that there was a statistically significant variation in CCT amongst their patients. They clarified that diabetic individuals' corneal endothelium undergoes morphological alterations [4, 5, 16-19].

According to a study done previously [20] it was shown that, diabetics possessed thicker corneas, while in another previous study [21] it was discovered that the cell densities of type 2 diabetic patients were noticeably lower.

Patients with type 2 diabetes similarly exhibited a significant decline in corneal ECD and hexagonality and a rise in CCT in other investigations conducted some studies [22, 23].

In contrary, it was found that no difference was noticed between the CCT and ECDs of diabetics and normal subjects [24].

In a recent study it was proved that there were significant variations in ECD, CV, hexagonality, and CCT between individuals with long-term diabetes (those with a duration of ≥10 years) and controls of all ages, which aligns with the findings

of the current study. Only CV and CCT, however, revealed a discernible difference between the control group and those with diabetes for shorter than 10 years. Furthermore, individuals with high haemoglobin A1c (≥7%) demonstrated variations in ECD, CV, and CCT, while those with low haemoglobin A1c (<7%) only displayed variations in CV and CCT [25].

It was therefore hypothesized that long-term diabetic patients had a higher influence on corneal endothelium alteration than did patients with high Hb1Ac. Additionally, they discovered that the length of DM is related to alterations in ECD, CV, and CCT, with individuals with DM for more than ten years showing more notable alterations [22, 26].

The claim that HbA1c indicates short-term DM management was disproved, and it has been noted that CCT can vary quickly based on HbA1c levels. This shows that chronic corneal endothelium damage is more significantly linked with the duration of diabetes than with HbA1c [22].

HbA1c did not significantly connect with corneal metrics in Kim et al correlation's investigation, however DM duration did correlate with ECD and CCT. This is since HbA1c indicates short-term diabetes management rather than long-term damage to ocular endothelial cells. For the purpose of forecasting corneal endothelial cell damage, the length of diabetes is thus advised over HbA1c [25].

Furthermore, was demonstrated that long-term exposure to hyperglycemic environments might result in diabetic neuropathy from nerve injury as well as microvascular problems. Trigeminal nerve anomalies and diabetic corneal neuropathies, which can impact the cornea, are caused by diabetic nerve injury. Previous research suggests that in early stages of diabetes, corneal nerve length and central corneal sensitivity may diminish [27].

Moreover, it was noted that trigeminal neuropathy results in abnormalities related to reflex lacrimation, which in turn leads to instability in the tear film and dry eye syndrome. Additionally, it was noted that there was a strong association between the length of DM and CCT [28].

Some scientists claimed that the difference between neuropathy, an early alteration in diabetes, and ocular endothelial cell failure, a persistent alteration, explains these results [29, 30].

A positive association between CCT and age was observed. This is consistent with our findings. ECD, hexagonality, and CCT declined when the groups were categorized by age, although CV tended to rise with ageing [31].

A few studies have used age groupings to compare diabetic individuals. According to Sudhir et al., diabetes patients had higher CV and hexagonality than 50–69 year old controls, and their CCT was thicker than that of 60–69 year old controls [16].

In patients with long-standing diabetes (≥10 years), CCT revealed a significant difference after 50 years, and ECD, CV, and hexagonality exhibited significant variations following 60 years when Kim et al. evaluated DM period and HbA1c of the DM and control groups stratified by age. High HbA1c group (≥7%) revealed similar trends; at 40 years of age, CCT indicated a difference, while at 60 years of age, ECD, CV, and hexagonality exhibited significant variations. The short-term effect of increased HbA1c on CCT may be the cause of variations in CCT in patients with elevated HbA1c at the early age of 40 [25].

Conclusion and Recommendations:

Hyperglycemia's ocular consequences are particularly severe in the cornea and retina. A statistically significant variation existed in CCT between normal volunteers and diabetic patients. CCT can be positively correlated with age, RBS, HBA1c and duration of DM. It is recommended to consider the assessment of CCT as a tool to achieve early detection of ophthalmic complications of hyperglycemia and to pay attention to this fact while outlining the

recent guidelines for diagnosis and management of diabetic eye. In addition, further studies must be done to analyze all aspects of this issue.

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