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Effect of Central Corneal Thickness in Patients with Type II Diabetes Mellitus in a Tertiary Care Centre

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Abstract

Diabetes mellitus (DM) is a metabolic condition that increases the risk of several ocular problems, including cataracts, diabetic retinopathy and increased Central Corneal Thickness (CCT). Changes in the structure and function of the cornea are linked to diabetes mellitus. DM modifies the function of the sodium potassium ATP-ase activity, which impacts the corneal endothelium and results in functional alterations in diabetic corneas. Changes in CCT are strongly correlated with higher blood glucose and HbA1c levels. To analyse central corneal thickness in subjects with diabetes mellitus and to correlate the association between the duration and severity of diabetes. The current study was a 6-month prospective case control study. A total of 100 people were observed, 50 of whom were diabetic and 50 of whom were not. Every participant had a full ophthalmic examination, which included a slit lamp examination, a fundus examination, an IOP measurement and a CCT. Non-proliferative diabetic retinopathy (NPDR), proliferative diabetic retinopathy (PDR) and diabetics without retinopathy were the three categories into which diabetics were divided. Utilizing ultrasound pachymetry, CCT was determined. Diabetics had their plasma glucose level and glycosylated hemoglobin A1c (HbA1c) measured. The corneal thickness was compared between the diabetic and non-diabetic groups using the Student t test for independent means; a p-value of less than 0.05 was considered statistically significant. Compared to the CCT of healthy controls, which was 511.52±31.65 µm, the mean CCT of diabetics was substantially thicker at 560.04±30.33 µm ($p<0.01$). Although the mean CCT increased in cases where the duration of diabetes increased, this difference was not statistically significant ($p = 0.064$). When compared to patients with HbA1c<7, the mean CCT of subjects with diabetes who had a HbA1c>7 was higher. When the degree of diabetic retinopathy was compared to age, the length of DM, HbA1c and IOP, a statistically significant difference was seen ($p<0.05$). However, there was no discernible correlation seen with CCT. The study found that people with diabetes and those without diabetes had notable variations in central thickness. These findings highlight the impact of diabetes on ocular health and the significance of monitoring corneal parameters in diabetic individuals.

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Key Words

Endothelial cells, central corneal thickness, corneal morphology, diabetes

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INTRODUCTION

Diabetes mellitus(DM) is a metabolic condition characterized by an increase in blood glucose levels, which can cause micro vascular and macro vascular problems[1]. Hyperglycemia can result from insufficient insulin secretion by pancreatic beta cells, a condition that can be influenced by both hereditary and environmental factors. The disorder varies in prevalence between regions. The severity of the condition can be significantly influenced by a number of factors, such as aging, obesity and a lack of physical activity[2].

Ocular problems include corneal abnormalities, iris neovascularization, glaucoma, cataracts and diabetic retinopathy (DR) are common in persons with diabetes. DR is still a major contributor to blindness and visual impairment. It is a significant diabetic microvascular problem that frequently has lipid exudation present[3].

Diabetes patients frequently develop not just DR, but also corneal endothelium damage and kerato-epitheliopathies. A common condition known as diabetic keratopathy involves several changes, particularly to the endothelium and epithelium in diabetics[4]. Corneal hypoesthesia, diminished adhesion to the basal membrane and punctate keratitis are symptoms of corneal epitheliopathy. At the ocular level, the corneal endothelium is critical to maintaining the cornea's optical transparency. The monolayer of corneal endothelial cells appears to be impacted by a persistent metabolic alteration at the cellular level and these cells have a reduced ability for mitosis. Due to its potential to impact corneal transparency and cause fluctuating eyesight, diabetic keratopathy is a serious issue[5].

Central corneal thickness (CCT) is a sensitive indicator of endothelium physiology and functions and a crucial measurement for the diagnosis, treatment and management of a variety of ocular disorders. Intraocular pressure (IOP), as determined by Goldmann Applanation tonometry, exhibits a positive connection with CCT and this relationship may have clinically relevant implications[6,7].

In the event of further corneal injury, CCT can be utilized as a marker to determine endothelium health and to assess corneal edema. There is a postulated correlation between the stages of diabetic retinopathy and corneal thickness. Hyperglycemia-induced metabolic stress modifies ocular endothelial cells, causing a decrease in hexagonality and an increase in variability. Advanced glycosylation end products function as cross-linking agents, causing covalent connections to form and worsening corneal thickness[8]. Furthermore, endothelial cell death can be triggered by matrix metalloproteinases and advanced glycation end products, leading to corneal injury. Elevated blood glucose levels also disrupt the function of Na-K+ATPase, which is an essential constituent of endothelial cells. This leads to morphological alterations that impact the permeability of corneas affected by diabetes[8]. CCT makes precise IOP measurement difficult and error-prone, which affects IOP levels and consequently, glaucoma management[9].

Previous studies had revealed that people with diabetes have higher CCT than non-diabetic control groups; however, other investigations have found no difference in CCT between the diabetic and control groups. Given the growing number of diabetics in India and the dearth of research, particularly in South India, this study was suggested to assess changes in CCT in DM patients.

Aims and Objectives: To analyze the central corneal thickness in patients with diabetes mellitus and to correlate the association between the duration and severity of diabetes.

MATERIALS AND METHODS

This prospective case-control study was conducted from July 2023 to January 2024 in ophthalmology department of Sree Mookambika Institute of Medical Sciences, Kulasekharam.

The Study Included 100 Participants Divided Into Two Groups: 50 with diabetes and 50 without diabetes. These subjects were chosen with care from among those who visited the hospital for medical care during the study period. This study included diabetic individuals (over 30 years old) who visited the outpatient department and willing to participate in the study. These subjects may be newly diagnosed or established instances of diabetes mellitus. Subjects who matched in age and gender and had no prior history of diabetes were chosen as controls. Individuals who already had corneal conditions such trichiasis, pterygium, entropion, or opacities or dystrophy were not suitable. Individuals with a history of contact lens wear, dry eye illness, cataract, pseudophakics, glaucoma, or pterygium were not included in the study. The participants who were not willing or unable to provide informed consent were also excluded from the study.

Written informed consent has been obtained from every individual involved. A general physical examination was conducted first, followed by a thorough ocular and medical examination. A thorough general physical examination, including a systemic and vtal signs assessment, was performed in each instance. All subjects had an examination of their right eye for standardization. Every instance included measurements of visual acuity for both near and far

(using Snellen's chart), Best Corrected Visual Acuity (BCVA) and IOP (using a non-contact tonometer).

A detailed slit lamp biomicroscopy analysis of the anterior region was additionally carried out. A thorough examination was performed on the lids, meibomian glands, conjunctival surface for dryness and congestion and cornea for shine and feeling. A thorough fundus examination was conducted under direct and indirect ophthalmoscopic examination for mydriasis. Non-proliferative diabetic retinopathy (NPDR), proliferative diabetic retinopathy (PDR) and diabetics without retinopathy were the three categories into which diabetics were divided.

Utilizing ultrasound pachymetry, CCT was determined. The investigator aligned the probe perpendicularly on the central cornea to collect a pachymetry reading. The study utilized the mean of the ten values that were obtained, with the greatest and lowest values being eliminated. The ultrasonic pachymetry measurements are dependent on the reflection of ultrasonic waves from both the anterior and posterior ocular surfaces. The measurement is the difference in time (transit time) between the transducer of the probe's ultrasonic signal pulses and the echoes of the reflected signal that reaches the transducer from the cornea's front and rear surfaces. The corneal thickness is measured with an ultrasound pachymeter at 10-20 MHz, with an estimated sound velocity through the cornea of 1630 m/sec.

Using a sterile disposable syringe, a 2-milliliter blood sample was drawn under asepsis from the anterior cubital vein in order to measure blood sugar and hemoglobin A1c (HbA1c). An Excel sheet was used to enter the data. Software for data analysis was SPSS trial version 20.0. Qualitative variables were expressed as percentage and frequency and continuous variables as mean and standard deviation. The student t test was used to perform statistical analysis. A probability value (pvalue) of <0.05 was considered statistically significant.

RESULTS AND DISCUSSIONS

In this study, 50 patients with type II diabetes were compared to 50 healthy controls. The average age of all patients who were recruited was 54.16±8.96 years. The distribution of cases and controls by age, gender, RBS and HbA1C is shown in (Table 1).

Compared to the CCT of healthy controls, which was 511.52±31.65µm, the mean CCT of diabetics was substantially thicker at 560.04±30.33µm (p<0.01). When the duration of diabetes increased the mean CCT increased as well, but this difference was not statistically significant (p = 0.064) as represented in (Table 2 and 3).

When comparing patients with HbA1c<7 to those with HbA1c>7, the former group had higher CCT. With a p value of 0.007, a positive connection between CCT and HbA1c levels was found. (Table 4).

Of the 50 patients with diabetes, 12 (24%) had no diabetic retinopathy, 21 (42%) had NPDR and 17 (34%), PDR. The study showed that the levels of IOP and CCT also increased as the severity of retinal symptoms increased. Regarding age, duration of DM, HbA1c and IOP, there was a statistically significant difference (p<0.05) between the three subgroups. Hhowever, no statistically significant association with CCT was found (Table 5). The PDR group had the greatest IOP and CCT.

Ocular abnormalities in diabetes patients have been widely described. Changes in the corneal epithelium, stroma and endothelium result from prolonged aberrant glucose metabolism. Glycemic status also affects CCT, a measurement of the corneal metabolic state[10].

Several research had shown differing findings about the relationship between CCT and diabetes mellitus. The current study indicated that the CCT measures of the diabetes patients were substantially greater than those of the normal controls. This was in line with study published by Daigavane S[11] who found that there was a significant difference in the mean CCT between the non-diabetic and diabetic groups, with the former having a value of 523.62 µm and the latter 547.91µm. Sarkar P[12] found that CCTs of diabetes patients were thicker than those of normal participants.

Similar findings were made by Sasalatti N[13] who observed that the mean CCT in diabetics was 531 (±33.42) µm, which was considerably thicker than the CCT in healthy controls, which was 505.70 (±32.19) µm (p<0.01). Cases with diabetes for more than 11 years had higher CCT, although this difference was not statistically significant (P = 0.808). This was similar to the current study. A favorable link was also noted by Elsayed EY[14] between CCT and the occurrence of diabetic retinopathy, HbA1c >7gm% and disease duration ≥10 years. The study additionally found that the duration and degree of severity of the condition considerably increased CCT.

Optical Coherence Tomography was used in the study by Akon M[15] to assess the central and paracentral corneal thickness in each eye. The study observed that while the differences in epithelium thickness between diabetic patients and non-diabetic participants were not statistically significant, the increase in corneal thickness for all gazes-central, superior, inferior, nasal and temporal-found in diabetic participants compared to non-diabetic participants was statistically significant (p<0.001).

Table 1: Demographic and clinical characteristics of cases and controls

	Variable Cases (n = 50)	Controls (n = 50)	p-value
Age (years)	55.157±8.61	52.85±9.89	0.217
Gender (Male/female)	41/9	36/14	0.564
Mean plasma glucose (mg/dL)	182.51±63.19	96.34±11.72	0.041
HbA1c	7.07±1.31	6.11±2.33	0.037

Table 2: Comparison of Mean CCT with diabetics and controls.

	Cases (Mean±SD)	Controls (Mean±SD)	p-value
CCT	560.04±30.33	511.52±31.65	<0.001

Table 3: Mean central corneal thickness with duration of diabetes

Duration	Number (%)	Cases (Mean±SD)	p-value
≤5	24 (48)	524.47±30.98	0.064
6-10	17 (34)	535.05±36.52	
≥11	9 (18)	552.75±38.06	

Table 4: Comparison of Mean CCT in cases with HbA1C

Duration	HbA1c<7	HbA1c>7	p-value
CCT	539.97±27.73	561.46±33.43	0.007

Table 5: Comparison of clinical Profile, CCT and IOP Values according to grade of Diabetic Retinopathy.

Parameter	No DR (n = 12)	NPDR (n = 21)	PDR (n =17)	p-value
Age (years)	50.22±9.54	56.98±8.52	54.34± 8.08	0.001
Mean duration of DM (years)	6.01±3.77	11.0±6.86	14.04±7.15	0.002
Plasma Glucose (mg/dL)	164.55±68.06	177.26±71.74	192.11±73.51	0.553
HbA1c (%)	6.42±1.04	7.08±1.31	7.37±1.28	0.003
CCT (µm) mean ± SD	522.12±32.14	528.92±29.51	531.57±34.35	0.058
IOP (mmHg)	13.81±1.67	14.03±2.12	18.76±2.54	0.017

According to recent studies, advanced glycosylated end products may function as cross-linking agents to strengthen the covalent bonds in the corneal stroma, eventually causing the cornea to become gradually stiffer and affecting the accuracy of IOP measurements[16].

A positive association was seen between the CCT and both the HbA1c and disease duration of ≥7 gm% in the case and control groups. Furthermore, when the grade of retinal symptoms was compared to age, duration of DM, HbA1c and IOP, there was a statistically significant difference in diabetic individuals ($p<0.05$), but not with CCT ($p>0.05$). A correlation analysis by Shifa PN[17] revealed that there was no significant link between CCT and the length of DM, HbA1c, or severity of DR. Additionally, there was a small but significant connection ($r = 0.155$, $p = 0.014$) between plasma glucose level and CCT. This was similar to the current study. In a similar manner El-Mekkawi TF[18] examined the central corneal thickness in persons with and without diabetic retinopathy who were diabetics. With a p value>0.05, the mean CCT for diabetic individuals without diabetic retinopathy was 551.13µ±37.93 and 558.93µ±39.32, respectively, whereas for those with retinopathy.

In their study, Bokhary KA[19] observed that CCT had a significant association ($P = 0.000$, $r = 0.656$) with IOP in type I diabetes mellitus, with or without DR (n = 100) and type II (n = 105). Furthermore, in individuals with DR who had type I and type II diabetes, there was a positive correlation between the length of diabetes mellitus and CCT ($p=0.003$ and p-0.035).

Ahmad I[20] carried out a study on 100 individuals with Type 2 Diabetes. Of them, 19 patients had severe and extremely acute NPDR, 7 patients had PDR, 28 patients had very mild and minor NPDR, 25 patients had average NPDR and 21 patients had no diabetic retinopathy. Furthermore, it became apparent that, in contrast to the present study, there was a statistically significant association between the severity of diabetic retinopathy and CCT. ($p =0.001$).

CONCLUSIONS

Although the consequences of diabetes on the eye have been examined, more thorough research were needed to understand the causes, diagnoses and treatments of diabetes in the eye as its prevalence rises with each generation. This study showed that type-2 DM with retinopathy had high CCT. CCT in diabetics indicates the overall functional and morphological state of the cornea. Given that the duration of the disease and CCT were found to be positively correlated, a straightforward non-invasive test, pachymetry may be able to identify DM patients who may be more likely to experience severe systemic and ocular consequences, allowing for improved disease management.

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