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A study on central corneal thickness in diabetics and non – diabetics

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ABSTRACT

Background: Diabetes is one of the most leading causes of blindness with complications related to diabetic keratopathy (DK). This chronic metabolic stress makes changes in the endothelial cells of the cornea by loss in pleomorphism, corneal autofluorescence, degeneration of the cells due to stress leads to over hydration of the stroma leads to change in corneal thickness. The central corneal thickness is a sensitive indicator of corneal health and serves as an index for corneal hydration and metabolism. Accurate CCT measurement has diagnostic and therapeutic implications.
Materials and Methods: Cross-sectional comparative study was done with 260 patients divided into two groups. Group 1 included patients with diabetes and group II patients without diabetes (Control group) of age group between 45 to 80 years who are attending Ophthalmology OPD in a time period of 2 months. Thorough history of patients was taken and underwent visual acuity testing, BCVA, IOP, fundus examination, HbA1c and CCT measurement using Optical Coherence Tomography (OCT).
Result: Mean CCT in diabetic population was 560.38±44.51 μm, while in control group was 500.32±39.63 μm with statistically significant p value of <0.001. Correlation analysis shows duration of diabetes and HbA1c shows significant relation and age doesn't show any correlation with CCT.
Conclusion: Our study demonstrates that individuals with diabetes mellitus or increased levels of HbA1c had higher CCT, regardless of age or gender. This signifies that CCT was influenced by prolonged increased levels of blood glucose.

1. Introduction

Diabetes mellitus (DM) is one of the widely spreading non – communicable diseases. It is one of the most leading causes of blindness with complications related to diabetic keratopathy (DK) and diabetic retinopathy (DR). Main indications of DM related to ocular system are retinopathy, cataract, glaucoma. Changes related to cornea are diabetic keratopathy. Corneal pathologies like superficial punctate keratitis, corneal sensitivity seen in diabetic patients.

Corneal in an avascular structure, and it is made up of five layers. Outermost layer is epithelium then bowman's membrane and the stroma inner to it, Descemet's membrane is fourth layer and inner layer is endothelium. Within the stroma collagen fibers are arranged parallelly in one plane and in consecutive plane fibers are arranged perpendicularly, since fibers are arranged regularly transparency of the cornea is maintained.

Since cornea is an avascular structure, it will get its nutrients from the aqueous humor which is produced by the ciliary body. Aqueous humor has all the nutrients required for metabolism and maintenance of cornea. Glucose in the aqueous humor affects the metabolic status of the cornea.

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Endothelial cells of cornea have Na^+- K^+ATPases that are actively pumping out water from the stroma and maintain the stromal integrity and structure. Endothelial cells are monolayer cells present inside the Descemet's membrane. These cells do not have ability to regenerate if the cells are degenerated because of any pathology. These cells are hexagonal in its shape.

In diabetics blood glucose levels are high, such high glucose levels are present in the aqueous humor also. This glucose molecules are taken up by the stroma for its metabolism, water follows glucose to maintain osmolarity. This leads to corneal edema which is one of the complications of the diabetes and structural integrity of the cornea is altered. Since cornea is edematous its thickness increases. In chronic metabolic stress where blood glucose levels are high advanced glycosylated end products (AGE's) are formed, those products enter into the stroma of the cornea and binds to the collagen fibers. These products make cross linking between the fibers leads to changes in the corneal thickness.

This chronic metabolic stress makes changes in the endothelial cells of the cornea by loss in hexagonality, pleomorphism, corneal autofluorescence, degeneration of the cells due to stress leads to over hydration of the stroma leads to change in corneal thickness. DM also decreases the activity of Na^+- K^+ ATPase whose activity is regulated by the insulin. Therefore, insulin resistant diabetics are more prone to develop more complicated corneal changes compare to insulin dependent diabetics. Since the activity of the Na^+ - K^+ATPases is altered corneal over hydration takes place and thickness of the cornea changes. All the parameters finally lead to the changes in the corneal power and visual acuity will be decreased.

The central corneal thickness is a sensitive indicator of corneal health and serves as an index for corneal hydration and metabolism. It is also an important indicator of patency of corneal endothelium pump and can be objectively measured by variety of techniques. With the advent of precise and better non-invasive measurement tools, central corneal thickness (CCT) measurement has become a vital ocular parameter due to its importance as an indicator of corneal health and integrity. Accurate CCT measurement has diagnostic and therapeutic implications in various conditions like corneal dystrophies (Keratoconus, Pellucid marginal degeneration), contact lens related problems, dry eyes, diabetes mellitus, glaucoma and refractive surgery.

In this cross-sectional comparative study with the basis of HbA1c levels of the diabetic patients of age group 45 to 80 years and age matched controls are taken into consideration for the study.

2. Aim and Objective

To determine the change in thickness of cornea in diabetics and non-diabetics using Optical Coherence Tomography (OCT).

3. Materials and Methods

In this cross-sectional comparative study, a total number of patients 260 were included in this study. Patients were divided into two groups using random sampling. Group 1 included patients with diabetes and group II patients without diabetes (Control group) of age group between 45 to 80 years who are attending Ophthalmology OPD department were considered.

All the diabetic and age matched patients attended to Ophthalmology OPD were included in the study after explaining procedure and taking informed consent. Thorough history of patients was taken. All the patients underwent visual acuity testing, BCVA, intraocular pressure measurement, fundus examination, HbA1c and Optical Coherence Tomography (OCT).

Ethical committee approval was obtained from institutional ethics committee.

3.1. Inclusion criteria

1. Patients with age group 45-80 years was considered.
2. Patients who are willing to give informed consent was considered.

3.2. Exclusion criteria

Patients with history of Intraocular surgeries, Trauma, Retinal lasers, corneal opacities and dystrophies, glaucoma, pseudo-exfoliation, uveitis, usage contact lenses and Use of topical eye drops were excluded

3.3. Statistical analysis

Data was analyzed using IBM SPSS software version 26 (trail version).

Sample size was derived by using 95% of confidence interval Different parameters were compared using Chi-square test, independent samples t-test and Z -test. P value of <0.05 was considered significant.

4. Results

4.1. Difference of two means

Data of 260 (130 diabetic patients and 130 non-diabetic patients) eyes was evaluated. Mean age of diabetic population was 62.95±9.47 years, while mean age of control group was 62.66±9.56 years. Mean HbA1c in diabetic population was 7.86±1.44%, while in control group was 5.40±0.75% with statistically significant p value of < 0.001.

Mean CCT in diabetic population was 560.38±44.51 μm, while in control group was 500.32±39.63 μm with statistically significant p value of < 0.001. Mean CCT with duration of diabetes in <10 years age group

Table 1: Demographic and clinical profile of clinical population

Parameter	Diabetic (n=130)	Non-Diabetic (n=130)	p Value
Gender			
Male	58 (44.615%)	55 (42.307%)	0.7
Female	72 (55.385%)	75 (57.693%)	0.7
Duration of DM			
< 10 years	112(86.154%)	-	
≥ 10 years	18 (13.846%)	-	
HbA1c (%) ≤ 7.5	63 (48.462%)	130 (100%)	<0.0001
> 7.5	67 (51.538%)	0	

Table 2:

Parameter	Diabetic (130)	Non – Diabetic (130)	p value
Age years)	62.95±9.47	62.66±9.56	0.810
HbA1c %)	7.86±1.44	5.40±0.75	<0.001
CCT (μm) mean ± SD	560.38±44.51	500.32±39.63	<0.001

Table 3: Difference of two means

Parameters	Age (years)	CCT (μm)
Duration(years)		
<10 years	62.77±9.54	526.85±50.07
≥10 years	63.39±9.22	577.39±51.81
p value	0.789	<0.001
HbA1c (%)		
≤7.5	63.06±9.57	517±48.04
>7.5	62.09±9.33	568.66±42.14
p value	0.4715	<0.001

was 526.85±50.07 μm, while in control group was 577.39±51.81 μm with statistically significant p value of < 0.001. Mean CCT with HbA1c levels of ≤ 7.5% was 517±48.04 μm, while in control group was 568.66±42.14 μm with statistically significant p value of <0.001. Duration of diabetes and is significantly correlated with CCT. HbA1c levels also significantly correlated with CCT. Correlation analysis showed that duration of diabetes and HbA1c shows significant correlation with CCT. However, age did not show any significant correlation with CCT.

5. Discussion

The majority of studies, including the current study, revealed that diabetic eyes exhibited higher CCT than non-diabetic eyes.[1–5]

Why does the corneal thickness in diabetic eyes increase? It is hypothesised that an increase in stromal hydration is caused by an endothelial pump function disfunction brought on by a decrease in Na+/K+ ATPase activity, despite the fact that the reason is unknown.[4–6]

What impact does glycaemic control have on CCT? Recently, emphasis has been placed on HbA1c level as a crucial indicator of glycaemic management. A protein contained in RBC is called haemoglobin. A1c is created in the bloodstream when glucose binds to the red pigment of haemoglobin (HbA1c). Red blood cells have a lifespan of 8 to 12 weeks.

One may anticipate that hyperglycaemia would also have an impact on corneal moisture and result in both qualitative and quantitative alterations to the cornea, including adjustments to its refractive index, curvature of the cornea, and corneal thickness.[7,8] In our study, a higher HbA1c, a measure of poor glycaemic management, was linked to thicker corneas.

Additionally, one may anticipate that disease duration and severity would both have an impact on corneal thickness. However, there was no way to tell if these characteristics ha any impact on corneal thickness. This may be a result of several homeostatic modifications that diabetics experience during the course of their chronic condition. Therefore, in order to determine the precise association between blood glucose and the cornea, longitudinal follow-up investigations must be carried out.

Therefore, more glucose in the blood at this period, more it will adhere to the haemoglobin. Blood HbA1c readings give insight into the past two to three months' typical blood glucose levels. As a result, routine HbA1c testing monitors recent glycemic management. We looked into HbA1c numbers and how they related to CCT. Patients who had greater HbA1c levels (7%) had increased CCT than those who had lower HbA1c levels (7%).[1]

Larsson et al.[3] and Keoleian et al.[9] found no association between HbA1c and CCT. Keoleian et al. found that despite the anatomical abnormalities of the corneal endothelium in diabetes patients, the endothelium's functional state was unaltered. They stated that there was no discernible change in the corneal thickness of diabetics.

In a related study, Claramonte et al.[10] found a strong correlation between diabetes mellitus and CCT. In their study, diabetics' mean CCT was 571.96, compared to non-diabetics' 544.89, with a statistically significant difference.

In a study by Mehmet Özgür ZENGİN et al[1] they found correlation between HbA1C and CCT.

In another study by Kumari et al., the mean CCT was likewise greater in people with diabetes who had it for more than 10 years (544.6434.56) than it was in those who had it for shorter than 10 years (518.9831.21).[11]

McNamara et al[12] discovered no direct link between HbA1c level and CCT in type 2 diabetes but identified a favourable correlation between HbA1c level and CCT in type 1 diabetics who also had thicker corneas.[7]

Table 4:

Study	Cohort	Results
Srećković S, et al. (2022) [13]	49- type 2 Diabetics 47- non diabetic control group	CCT was not statistically significantly impacted by the presence of retinopathy.
Yoo Jin Kim & TaeGi Kim (2021) [14]	511 (1022 eyes) type 2 diabetes patients 900 (1799 eyes) non-diabetic patients.	Age-related diabetes and chronic diabetes with greater HbA1c have an impact on ocular endothelial cells.
C VReddy,*, and M H Reddy [15]	168 subjects divided into 3 groups: 40 diabetics duration >10 yrs, 46 diabetics duration ≤10 yrs, 82 controls.	Compared to people without diabetes, those who have type 2 diabetes mellitus have corneas that are thicker.
Handan Canan*, et al, [16]	47 patients in Group I with diabetic retinopathy changes and 49 patients in Group II without diabetic retinopathy changes	The CCT was not much impacted by the duration of DM or the existence of diabetic retinopathy.
Rajni Sethia et al [17]	150 type-II DM patients were conducted (only left eye included)	DM duration, HbA1c levels, and corneal thickness are unaffected
Qamar-ul-Islam et al [18]	252 eyes 126 diabetic patients 126 healthy controls	In comparison to age-matched healthy controls, patients with DM had significantly thicker CCT.
Kumari et al [11]	The corneal thickness assessment was done for 100 eyes of 50 diabetic and 100 eyes of 50 non diabetic patients	Patients with diabetes have thicker corneas than people without diabetes. Diabetes and CCT are related in a direct manner.
Mehmet Ozgür ZENGİN et al [1]	136 type II diabetic patients and 36 non-diabetic healthy subjects	Contrary to healthy individuals, type II diabetic patients have thicker corneas.
Lee et al. [2]	200 insulin dependent diabetics and 100 controls	CCT and disease duration were associated
Keoleian et al. [9]	14 type I diabetics, 14 control subjects	CCT [560 m] compared favourably to controls [560 m].
Larsson et al [3]	49 type 1 diabetics, 60 type 2 diabetics, 62 control subjects	CCT was similar in diabetics with type I (580 m) and type II (570 m) diabetes.
Roszkowska et al. [5]	30 type I diabetics 45 type 2 diabetics 62 controls	When compared to controls, CCT was greater in both type I (580 m) and type II (570 m) diabetics (540 m for type I controls). For class II controls, 550 m

In our study duration of diabetes data is as follows ‹10 years 112(86.154%) and ≥ 10 years 18 (13.846%). In our study the mean CCT in diabetics was 560.38±44.51 and in non-diabetics was 500.32±39.63 and the difference between the two groups was statistically significant (p value 0.001).

In our study, the mean CCT value in diabetics < 10 years duration was 526.85±50.07 and in diabetics >10 years of duration it was 577.39±51.81. This shows a correlation between duration and diabetes and CCT with significant p value <0.001).

Mean of HbA1C levels of ≤7.5 was 517±48.04 when compared to patients with HbA1C levels of >7.5 was 568.66±42.14. In our study a correlation between HbA1C levels and CCT was noted with a statistically significance (p value <0.001).

6. Limitations of this Study

Confocal microscopy which is more appropriate method of evaluating changes in corneal thickness was not used. Many other systemic diseases which effect central corneal thickness like Hypertension hyperlipidemia were not considered.

7. Conclusion

Our study demonstrates that individuals with diabetes mellitus or higher levels of glycosylated haemoglobin had higher CCT, regardless of age or gender. These findings imply that chronic hyperglycemia may influence CCT measures, and they, along with results from subsequent studies, may contribute to our understanding of the pathophysiological mechanisms behind diabetes. Increased CCT and diabetes were shown to be significantly correlated, and thick corneas were positively correlated with the length of diabetes, suggesting that people with thick corneas are more likely to have the disease at an advanced stage.

The correct assessment of these patients with regard to their functional result can be made more reliable by the measurement of CCT in conjunction with research on the corneal endothelium. The creation of covalent bonds in the corneal stroma is the primary histological change, hence research into the relationship between diabetic keratopathy and corneal ectatic state is necessary.

8. Source of Funding

None.

9. Conflict of Interest

None.

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