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COMPARATIVE ANALYSIS OF THE CENTRAL CORNEAL THICKNESS IN DIABETIC AND NON-DIABETIC PATIENTS- A CASE-CONTROL STUDY

Ophthalmology

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ABSTRACT

INTRODUCTION- Many ophthalmologic diseases like poor vision, blindness, keratoconjunctivitis sicca, macular edema, cataract, vitreous hemorrhage, glaucoma and diabetic retinopathy are linked with diabetes. Various studies in the past have established that there is a strong association between diabetes and an increase in corneal thickness.

AIMS AND OBJECTIVES- We aimed at conducting a study to compare the effect of Diabetic Mellitus on central corneal thickness in a case-control setting. The impact of disease duration and levels of HbA1c were also evaluated.

MATERIALS AND METHODS- A Prospective observational study was conducted with 50 diabetics (group A) and 50 non-diabetics (groups B). A detailed history taking, along with measurement of blood glucose levels, HbA1c, and a detailed ophthalmologic examination was done in all cases. The mean central corneal thickness was measured using specular pachymetry.

RESULTS- The mean central corneal thickness (CCT) was higher in diabetics (Right eye- 544.45 ± 22.72 µm; 551.01 ± 23.11 µm) as compared to non-diabetics (right eye- 523.27 ± 15.23 µm, left eye 522.13 ± 14.44 µm) ($p<0.05$). The mean central corneal thickness was higher in those having diabetes for >10 years than those having diabetes <10 years. Additionally, the mean central corneal thickness was higher in those having HbA1c >6.5 than those having HbA1c <6.5 ($p=0.0033$).

CONCLUSION- Our study found a significant impact of diabetes, its duration, and its uncontrolled nature on the thickness of the cornea. Corneal thickness can be utilized as a sensitive parameter to assess the uncontrolled nature of diabetes

KEYWORDS

INTRODUCTION

The cornea has the following layers, namely, the outermost corneal epithelium, the Bowman's membrane, stromal layer, the Dua's membrane, the descemet's membrane, and the innermost endothelium layer.[1] There can be loss in the transparency of the vision if any one of these layers is affected.

The reported prevalence of diabetes mellitus in India is 7·3%.[2] Many ophthalmologic diseases like poor vision, blindness, keratocon junctivitis sicca, macular edema, cataract, retinal vasculopathy, hemorrhages in the vitreous and diabetic retinopathy are linked with diabetes.[3] Various studies in the past have established that there is a strong association between diabetes and an increase in corneal thickness. Additionally, diabetics also have higher intraocular pressure, when compared to non-diabetics.[4,5]

Chronically, Raised glucose levels in the blood can cause dysfunction of the epithelium and endothelium along with disruption of the epithelial basement membrane. Electron microscopy of cornea in diabetic epithelium displays thickened basement membrane, reduced anchoring fibrils, loss of stromal adherins, and downregulation of hemidesmosomal proteins.[6,7] Additionally, due to a higher level of **sorbitol** inside the corneal cells, there is the creation of an osmotic gradient which leads to massive intracellular swelling. All these structural changes are responsible for the **reduction in ATP formation**, which leads to the failure of endothelium ATPase pumps. There are irreversible changes in the corneal structure and permeability.[8-10]

We aimed at conducting a study to compare the effect of Diabetic Mellitus on central corneal thickness in a case-control setting. The impact of disease duration and levels of **HbA1c** were also evaluated.

MATERIALS AND METHODS

Study Design:

This was a prospective, observational case-control study conducted in our Ophthalmology outpatient department after obtaining due approval from the institutional ethical board. The study was conducted between May 2021 to November 2021.

Sample Population:

Patients were serially allocated in the study. The study subjects were divided into two groups, namely **"Group A- cases (with diabetes)" and "Group B- controls (without diabetics)". Inclusion criteria** for group A included patients having diabetes diagnosed according to fasting blood glucose level, between the ages of 18-75 years. For group B non-diabetic individuals were recruited. **Exclusion criteria** were the presence of hypertension, thyroid dysfunction, cardiovascular diseases, history of chronic smoking, or any other systemic disorder. Additionally, patients having glaucoma, any corneal or conjunctival disorder, any other ophthalmological disorders like entropion, ectropion, pterygium, trichiasis, refractive error higher than ± 6D spherical and/or ±3D cylindrical were excluded. Patients with a history of any ocular surgeries in the past, contact lens users, and those using any systemic or topical corticosteroids were excluded.

Study Parameters:

The following parameters were compared between the two groups:

1. Central corneal thickness
2. Levels of HbA1c
3. Correlation between central corneal thickness and HbA1c

Detailed data were taken including duration of diabetes mellitus and history of past medication. Levels of HbA1c, fasting, and post-prandial blood glucose levels were recorded on 3 consecutive days and an average was taken.

Central corneal thickness was measured in both groups using specular pachymetry. Additionally, a complete ophthalmologic examination was done for all individuals which included corrected visual acuity, anterior chamber slit-lamp examination, and indirect ophthalmoscopy of the posterior segment using mydriatics to dilate the pupils.

Statistical Analysis:

The data were analyzed using unpaired student T-test and chi-square test. Subgroup analysis was done by stratifying the duration of diabetics and the level of HbA1C. The p-value (2-sided) for significance was set at <0.05.

RESULTS

A total of 100 cases were included in our study. While 50 patients were recruited in group A, 50 were included in group B. There were 31 males

and 19 females in group A. Similarly, in group B there were 33 males and 17 females (p-value- 0.9). The mean age of study participants was 58.8±12.5 years in group A and 59.3±9.7 years in group B. The age was comparable between the two groups (p-value-0.7). The demographic data of patients has been tabulated in table 1.

Table 1: Demographic data of study participants

Parameter	Group A	Group B	P value
Total number of patients	50	50	
Male: female	31:19	33:17	0.9
Mean age ± standard deviation	58.8±12.5 years	59.3±9.7 years	0.8

Table-2: Mean central corneal thickness (CCT) in group A (diabetics) and group B (non-diabetics)

	Group A	Group B	P-value
Mean CCT ± standard deviation (in µm)			
Right eye	544.45 ± 22.72	523.27 ± 15.23	<0.0001
Left eye	551.01 ± 23.11	522.13 ± 14.44	<0.0001

The mean central corneal thickness (CCT) was higher in diabetics (Right eye- 544.45 ± 22.72 µm; left eye- 551.02 ± 23.11 µm) as compared to non-diabetics (right eye- 523.27 ± 15.23 µm, left eye- 522.13 ± 14.44 µm) (table 2). The difference between the two groups was highly statistically significant (right eye group A vs B: standard error 5.511; 95% confidence interval -34.6704 to -12.9696; t-statistic 4.388; P < 0.0001; left eye group A vs group B: standard error 5.402; 95% confidence interval -41.5121 to -19.8855; t-statistic -5.561; P < 0.0001).

Table-3: Mean central corneal thickness (CCT) in diabetic patients with relation to the duration of diabetes and HbA1c levels

	Duration >10 years	Duration <10 years	P-value
Number of patients	37	13	
Mean CCT ± standard deviation (in µm)			
Right eye	552.34 ± 24.66	543.28 ± 15.21	0.21
Left eye	557.08 ± 25.27	544.31 ± 14.31	0.25
	HbA1c >6.5%	HbA1c <6.5%	P-value
Number of patients	39	11	
Mean CCT ± standard deviation (in µm)			
Right eye	559.36 ± 25.11	521.49 ± 21.25	<0.0001
Left eye	557.05 ± 24.49	532.41 ± 18.95	0.003

Additionally, in group A while 37 patients had diabetes mellitus for more than 10 years, the remaining 13 had diabetes for less than 10 years. The mean central corneal thickness was higher in those having diabetes for >10 years (Right eye: 552.34 ± 24.66 µm; Left eye: 543.28 ± 25.27 µm) than those having diabetes <10 years (543.28 ± 15.21 µm; 544.31 ± 14.31µm) (table 3).

In group A while 39 patients had HbA1c >6.5, the remaining 11 had HbA1c <6.5. The mean central corneal thickness was higher in those having HbA1c >6.5 (Right eye: 559.36 ± 25.11 µm; Left eye: 557.05 ± 24.49 µm) than those having HbA1c <6.5 (521.49 ± 21.25 µm; 532.41 ± 18.95 µm) (table 3). The difference between the two subgroups was highly statistically significant (right eye: standard error 8.235; 95% confidence interval -54.5140 to -21.2260; t-statistic -4.599; P < 0.0001; left eye: standard error 7.890; 95% confidence interval -40.5861 to -8.6939; t-statistic -3.123; P = 0.0033)

DISCUSSION

All the compartments of the eye can be affected in the case of diabetes mellitus. The most significantly reported change is **diabetic retinopathy**. Other changes like corneal defects, recurrent corneal erosions, and punctate epithelial keratopathy are also frequently observed. **Sorbitol accumulation** in the cornea can lead to delayed healing after a cataract or refractive surgery. Our study observed that there was a significantly greater thickness in diabetics compared to non-diabetic cases. Additionally, we observed that the mean CCT was higher in diabetic individuals having the disease for more than 10 years than those who had a shorter duration of diabetes. Similarly, amongst group A, the mean central corneal thickness was higher in those patients who had HbA1c levels >6.5% when compared to those diabetic patients who had HbA1c <6.5%.

According to the results **of Ozdama et al** the mean CCT has a statistically significantly higher value in diabetics compared to non-diabetics (cases: 564±30 µm vs controls: 538±35 µm; p=0.001.[11] Another study conducted by **Sorokhaibam et al** also found mean CCT to be significantly higher in diabetics (574.359µm) than non-diabetics (557.76µm) (p=0.0001).[12] Our findings were fairly similar.

Another such study conducted **by Su et al**.has also made similar observations.[13] However, unlike their study which had an exceedingly higher number of patients (748 cases) our study had a small sample size with 42 cases. However, the results of our study were in close approximation with their work. Su et al had concluded that diabetics have an average of 6.5 µm thicker cornea than non-diabetics (p < 0.001). Moreover, just like our observations even they had found a significant correlation between mean CCT and higher levels of HbA1c.[13]

In fact, even when cut-off HbA1c levels were kept as high as 7% in **Dabas et al** work, there was a significantly higher (p<0.009) thickness of the cornea in those patients who had uncontrolled diabetes.[14] **Claramonte et al**[15] and **Math et al**[1] have also made similar observations.

The influence of the disease duration of diabetes with the mean CCT has been studied by Lee et al[16] and Math et al[1] Both studies have reported that there is a positive correlation between the thickness of the cornea and the duration of diabetes. Just like our study, both studies have found that patients having diabetes for more than 10 years have a higher degree of corneal thickness.

CONCLUSION

Our study data add to the pre-existing data on the significant impact of diabetes, its duration, and its uncontrolled nature on the thickness of the cornea. This study has shown that the mean CCT can be utilized as a sensitive parameter to assess the uncontrolled nature of diabetes (which depends upon HbA1c levels). The assessment of mean CCT must be done in all cases as part of a routine workup before any ophthalmological surgery, especially in patients having hyperglycaemia, which could significantly reduce the postoperative complications and long-term sequelae in old patients.

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