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131 CENTRAL CORNEAL THICKNESS AND ITS CORRELATION WITH THE SEVERITY OF DIABETIC RETINOPATHY AND HBA1C LEVELS IN DIABETES MELLITUS

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ABSTRACT

Background: Diabetic retinopathy (DR) is one of the most common causes of preventable blindness in the world. Chronic metabolic stress caused by hyperglycaemia has shown to affect corneal endothelial cells. Central corneal thickness (CCT) is an important indicator of functioning of corneal endothelial pump. It is key parameter for estimation of IOP and in refractive surgeries. Its role in diabetic patients thus needs to be researched upon. **Materials & Methods:** A cross-sectional observational study was conducted between May 2021 to Feb 2022 at the post-graduate department of Ophthalmology, SKIMS Medical college and Hospital after giving clearance by ethical committee of the institute. 100 subjects with type 2 diabetes mellitus & 100 age and sex matched controls were enrolled in the study. The study group was divided into 5 sub-groups according to Early Treatment Diabetic Retinopathy Study (ETDRS) classification. Eyes of subjects with prior history of ocular surface disease, corneal degeneration or dystrophy, ocular surgery, glaucoma, uveitis, on chronic topical medication or contact lens use were excluded. CCT was measured using SD-OCT (Zeiss Cirrus HD-OCT). Fasting blood sugar and HbA1c levels were done in all subjects of the study group. **Results:** Average CCT among the study group was $562\pm21\mu m$ and among the control group was $524\pm22\mu m$. The mean CCT for patients with no diabetic retinopathy was 527.75 ± 7.22. Mean CCT for patients with very mild & mild NPDR was 541.11 ± 7.91, with moderate NPDR was 563.23 ± 8.02, with severe and very severe NPDR was 583.66 ± 7.65 and that with Proliferative diabetic retinopathy was 609.03 ± 16.12 µm. The correlation was significant (p=0.001). Also mean CCT in patients with HbA1c levels between 4-5.6% was 535.64 ± 12.86, in patients with HbA1c levels between 5.61-6.5% was 550.89 ± 13.93 and those with HbA1c levels >6.5% mean CCT was $584.63\pm20.21\mu m$. The correlation was statistically significant(p=0.01). **Conclusion:** This study demonstrates a strong positive correlation between CCT to the severity of DR and HbA1c levels. The corneas of Type 2 diabetics were significantly thicker, indicating that thick corneas are more likely to be found in advanced stage of the disease. Routine assessment of CCT in type 2 diabetic patients along with usual retinopathy assessment should be done. It should be a part of the pre-operative assessment undergoing intra-ocular surgeries like refractive surgery and keratoplasty.

KEYWORDS: Central corneal thickness, Diabetes Mellitus, HbA1c levels, Diabetic retinopathy.

INTRODUCTION

Diabetes mellitus (DM) is the leading cause of blindness worldwide. Type 2 diabetes mellitus accounts for more than 85%-90% of the cases.[1] Diabetic retinopathy (DR) is the most common ophthalmic complication of diabetes, but diabetes can also affect cornea in multitude of ways.[2]

Development of many of the diabetic complications is related to the duration of the disease and degree of metabolic dysregulation.[3] Chronic metabolic stress caused by hyperglycaemia has shown to cause alterations at cellular level affecting the corneal endothelial cells, which are responsible for maintaining stromal hydration by endothelial pump mechanism.[4] Central corneal thickness (CCT) is a sensitive indicator of health of the cornea and serves as index for corneal hydration and metabolism. CCT is an important indicator for the functioning of the corneal endothelial pump. It is also a key parameter of refractive surgery and estimation of IOP.[5]

In clinical practice, CCT is regarded as a static parameter and often measured only once during patient's follow up. However, several studies suggest that diabetic status may affect CCT measurement, thus potentially affecting IOP

measurements. Furthermore, glycated haemoglobin (HbA1c) levels provide adequate information about average serum glucose level for the past 3 months & is a widely accepted indicator of long-term glycaemic control.

Our study aims to correlate CCT with the DR status and HbA1c levels in type 2 diabetes mellitus. This will help us to determine, whether CCT can be used as a screening tool in patients with DR and whether necessary therapeutic interventions to prevent visual morbidity in patients with type 2 diabetes mellitus, needs to be taken.

AIM
o To measure the central corneal thickness (CCT) in patients with type 2 diabetes mellitus and assess the relationship of CCT with HbA1c levels.
o To correlate CCT with the severity of diabetic retinopathy.

MATERIALS AND METHODS
A cross-sectional observational study was conducted between May 2021 to Feb 2022 at the post-graduate Department of Ophthalmology SKIMS Medical & Hospital. 100 subjects with type 2 diabetes mellitus & 100 age and sex matched controls were enrolled in the study. The study group was divided into 5 sub-groups.
o Group 1: Type 2 diabetes mellitus patients without retinopathy.
o Group 2: With mild non-proliferative diabetic retinopathy.
o Group 3: With moderate non-proliferative diabetic retinopathy.
o Group 4: With severe non-proliferative diabetic retinopathy.
o Group 5: With proliferative diabetic retinopathy.
ETDRS grades of Very mild & Mild NPDR were grouped together. Also, ETDRS grades of Very severe and severe NPDR were grouped together.

Inclusion Criteria
• Patient with referring-physician diagnosis of type-2 DM (FBS> 126 mg/dl, PPBS >200mg/dl) and who was given antidiabetic medication was defined as diabetic.

Exclusion Criteria
• Prior history of ocular surface disease, corneal degeneration or dystrophy, ocular surgery, glaucoma, or uveitis.
• Prior history of chronic topical medication use.
• Present or past history of contact lens use.

Routine ophthalmological examination was done in all patients which included.
1. Visual acuity.
2. Slit lamp examination.
3. Intraocular pressure with Goldmann Applanation tonometry.
4. Fundus examination using Indirect ophthalmoscopy & 78 D.

Patients were classified according to the "Early Treatment Diabetic Retinopathy (ETDRS) classification". CCT was measured using Spectral Domain Optical Coherence Tomography (Zeiss Cirrus HD-OCT).

Following blood investigations were also done in the study group.
1. Fasting blood sugar level.
2. HbA1c levels.

CCT was measured in all the study subjects and compared with the control group and also among different sub-groups. Levels of HbA1c levels were also correlated among different sub-groups of study population.

STATISTICAL ANALYSIS
At the end of 9 months, all the data were tabulated & statistically analysed. The CCT of diabetic patients and control subjects were compared using *t-test.* ANOVA test was used to test significant difference in HbA1C levels among different sub-groups of study population. Descriptive data was presented as mean and standard deviation. Pearson correlation coefficient test was performed to determine relationship between different variables. A p-value <0.05 was considered to be statistically significant.

RESULTS
For the statistical analysis, mean of two eyes was considered.

Mean age of patients with diabetic retinopathy was 51.5±4 years. Among the study group 54% were males and 46% were females. Average CCT among the study group was 562±21μm and among the control group was 524±22μm. Out of 100 patients, number of patients in different groups were as follows.

No. of patients

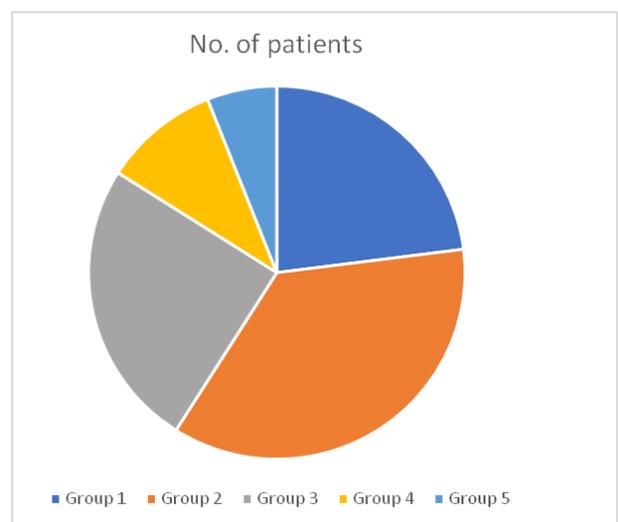Group 1 | Group 2 | Group 3 | Group 4 | Group 5

Table 1: depicts the correlation between Mean CCT (µm) and different study groups (based on severity of diabetic retinopathy). The mean CCT for patients with no diabetic retinopathy was 527.75±7.22. Mean CCT for patients with Very mild & Mild NPDR was 541.11±7.91. Mean CCT for patients with Moderate NPDR was 563.23±8.02. The mean CCT for patients with Severe and Very severe NPDR was 583.66±7.65. Mean CCT of patients with Proliferative diabetic retinopathy was 609.03±16.12 µm.

TABLE 1. STUDY GROUP	Mean CCT (µm)	P-VALUE
Group 1 (No DR)	527.75±7.22	
Group 2 (Mild NPDR)	541.11±7.91	
Group 3 (Moderate NPDR)	563.23±8.02	0.001
Group 4 (Severe NPDR)	583.66±7.65	
Group 5 (PDR)	609.03±16.12	

Analysis of relationship between severity of diabetic retinopathy and CCT was statistically significant (p=0.001).

Table 2: depicts the correlation between CCT and HbA1c levels. Mean CCT in patients with HbA1c levels between 4-5.6% was 535.64±12.86. Mean CCT in patients with HbA1c levels between 5.61-6.5% was 550.89±13.93 and those with HbA1c levels >6.5% was 584.63±20.21µm.

TABLE 2: HbA1c levels (%)	Mean CCT (µm)	P-Value
4-5.6	535.64±12.86	
5.61-6.5	550.89±13.93	0.001
>6.5	584.63±20.21	

Analysis of the relationship between CCT and HbA1c levels showed statistically significant correlation (p=0.01).

DISCUSSION

Corneal thickening in patients with diabetes mellitus was reported in several studies. The increase in corneal thickness reflects the altered functional status of the corneal endothelium and may lead to falsely high IOP measurements. In the current study, we established age & sex matched groups. According to our results, we found that mean CCT was thicker in diabetic patients than in non-diabetics. Also, CCT was lowest among patients with no diabetic retinopathy and it significantly increased in patients with NPDR and PDR.

In our study we also found that CCT was positively correlated with HbA1c levels. Patients with HbA1c levels >6.5% had a significantly thicker CCT than those with HbA1c levels <5.6%. In a study conducted by Mehmet Ozgur et al, CCT was significantly higher in diabetic patients than non-diabetic subjects. Diabetic patients with HbA1c levels over 7% had thicker corneas. Although severity of retinopathy and disease duration had no apparent effect on CCT.[6]

Similarly, Ozdamar Y et al established that mean CCT in diabetics (564±30µm) was higher compared with control group (538±35µm) (P= 0.001) and explained this finding with mechanisms such as corneal endothelial dysfunction, stromal hydration & swelling of cornea.[7]

In a cross-sectional study of 8846 multi-ethnic Asian adults conducted by Singapore Epidemiology of Eye diseases, association between CCT and HbA1c levels & severity of diabetes mellitus was done. It was found that CCT was thicker in patients with diabetes than those without diabetes. Also, thicker CCT was associated with higher random glucose levels and higher HbA1c levels.[8] which is in congruence to our study. Recently, Storr-

Paulsen et al studied 107 patients with type 2 DM and 128 non-diabetic controls and concluded that CCT was increased among diabetic patients compared to controls.[9] However there are some studies that failed to find a significant association between diabetes & CCT[10][11] The discrepancy may be partly due to different definitions of diabetes.

Similar to our study, S. Guha et al also found a significant positive correlation between mean CCT and severity of diabetic retinopathy, although they found non-positive correlation between CCT and HbA1c levels.[12]

A cross sectional study by Okan et al, also showed that average CCT was significantly higher in diabetic patients than in control group (p=0.04) but CCT in diabetic patients without retinopathy did not significantly differ from that of patients with retinopathy. Similarly, there was no significant difference in CCT between non-proliferative & proliferative diabetic retinopathy.[13]

CONCLUSION

According to our study, patients with type 2 diabetes mellitus were found to have thicker corneas as compared to non-diabetics. This should be taken into consideration while interpreting intraocular pressure and prior to any refractive surgeries or keratoplasty in diabetics. Also, we found that there is a strong positive correlation between CCT to the severity of diabetic retinopathy and HbA1c levels, indicating that patients with thick corneas are more likely to be found in advanced stages of the disease. Routine assessment of CCT may thus may be beneficial in all diabetic patients along with their usual retinopathy assessment to prevent visual disability by early detection and management.

CONFLICTS OF INTEREST
None.

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