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A Clinical Study of Central Corneal Thickness (CCT) in Diabetics in Euglycemic and Hyperglycemic States

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Abstract

Introduction: The central corneal thickness is a sensitive indicator of health of cornea and serves as an index for corneal hydration and metabolism. Normal cornea has a central thickness of 0.52 mm and is thicker paracentrally and peripherally.

Aim: To study if there is a change in central corneal thickness in diabetic individuals in hyperglycemic state in comparison to when the same individuals achieve euglycemic state. To measure among diabetics, the central corneal thickness (by optical coherence tomography) in hyperglycemic state and central corneal thickness in the same patients during euglycemic state after 1 month.

Material and Methods: This study was conducted on total 100 patients (100 eyes) who were hyperglycemic and were evaluated in the Department of Ophthalmology, Government Medical College, Kota, and Rajasthan in year August 2019 to July 2020 after obtaining informed consent. All diabetic patients undergoing blood sugar measurements whose postprandial blood sugar was more than 200 mg/dl (hyperglycemic state) and Central Corneal Thickness (CCT) was measured by Anterior Segment Optical Coherence Tomography (AS-OCT). Subjects were reviewed after 1 month and then 6 months and corneal thickness measured. The CCT values of those patients achieving euglycemic state (postprandial blood sugars <200 mg/dl along with a minimum drop in blood sugar levels of 50 mg/dl from the Previous (hyperglycemic state) were taken for analysis.

Results and Conclusion: A total of 100 diabetic patients (100 eyes) who were hyperglycemic were evaluated between August 2019 to July 2020. Euglycemia at 1 month was achieved by 93 patients among those 100 patients. Seven patients were lost to follow up at 1 month and achieve euglycemia at 2 months, 3 patients & 6 months, 4 patients respectively during the study period. Mean CCT in hyperglycemic state was 540.06 ± 28.61 microns and euglycemic state was 531.74 ± 27.95 microns. P value was 0.038 which was weakly statistically significant. Out of 100 patients 93 patients were achieved euglycemic state at 1 month showing significant reduction in CCT at euglycemic state (p value =0.0001) using Bland-Altman Plot. Poorly controlled diabetic had thicker central cornea than well controlled patients. We found that, CCT, decreases significantly by the control of blood sugar.

Keywords: Central corneal thickness; Hyperglycemic; Euglycemic; Anterior segment OCT; Blood sugar

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Introduction

Diabetes mellitus is a group of metabolic diseases or metabolic syndrome where there is hyperglycemia as a result of defect in the insulin secretion and/or action. In diabetics there is chronic hyperglycemia which is associated with long-term damage, dysfunction, and/or failure of various organs, especially the eyes, kidneys, nerves and blood vessels. DM is a serious & increasingly prevalent health problem worldwide due to sedating lifestyle & population ageing. Limited data from a population based study showed that individuals with diabetes had thicker cornea [8].

Studies [9-20] have looked at the Central Corneal Thickness (CCT) in diabetics. Many studies have shown increased CCT in diabetics [9-18,20] while few others have shown no difference in CCT [18] in diabetics) as compared to normal's. There are very few studies [17] which have looked into changes in CCT in hyperglycemic state in comparison to euglycemic state in the same individual.

Yasim et al. [17] have looked at the variation in CCT in diabetic individuals in euglycemia and hyperglycemia over 6 months. They defined hyperglycemia and euglycemia based on the HbA1c levels. However the actual blood sugar levels at the time of CCT measurements were not recorded/ addressed as a part of the study. This study was conducted to look for any change in the mean

CCT in diabetes patients between hyperglycemic and euglycemic state in the Department of Ophthalmology, Govt. Medical College and Maharao Bhim Singh Hospital, Kota by measuring CCT using Anterior Segment Optical Coherence Tomography (AS-OCT). Cirrus HD-OCT also can image structures within the anterior segment by changing the OCT beam focus, thus it may be advantageous for the posterior segment as well as the anterior segment.

Material and Methods

This cross sectional observational study was conducted on total 100 patients (100 eyes) who were hyperglycemic and were evaluated in the Department of Ophthalmology, Government Medical College, Kota, Rajasthan between 12 months from August 2019 to July 2020. In our study criteria for blood sugar in Hyperglycemic state- postprandial blood sugars >200 mg/dl & in Euglycemic state- postprandial blood sugars <200 mg/dl along with minimum 50 mg/dl reduction of postprandial blood sugars as compared to their hyperglycemic state. Patients satisfying the inclusion and exclusion criteria as given below were enrolled into this study after an informed consent.

Inclusion criteria

1. Diabetic patients in hyperglycemic state who were referred from medicine department to our department for fundus examination and those who had a referring physician diagnosis of diabetic mellitus

2. Those who were ready to participate in the study by providing informed consent.

Exclusion criteria

1. Patients with serum creatinine >1.2 mg/dl.

2. Patients in whom optical coherence tomography was not possible.

3. Patients who have undergone previous ocular surgery.

4. Patients who have worn rigid contact lens during the month prior to evaluation and soft contact lenses seven days before.

5. Patients with any corneal pathology (degenerations, keratoconus, collagen- related disorders, glaucoma, intraocular inflammation, ocular surface disorders) including corneal edema.

6. Patients with uveitis.

7. Patients who have undergone procedures such as laser photocoagulation within less than 1 month.

8. Patients less than 18 years of age.

Informed consent was obtained from all participants. The study was approved by the ethical committee of the Institute and this study was conducted as per good clinical practice guidelines.

All diabetic patients undergoing blood sugar measurements whose post prandial blood sugar was more than 200 mg/dl (hyperglycemic state); were screened by the investigator for the study and were enrolled into the study. Central Corneal Thickness (CCT) was measured by Anterior Segment Optical Coherence Tomography (AS-OCT). (Cirrus HD-OCT model 500) As is the routinely followed management protocol/schedule, these patients were called for repeat fasting and post prandial blood sugar estimations at 1 month after changes if any in the antidiabetic medications as advised by treating physician. Subjects were reviewed after 1 month and then 6 months and corneal thickness measured. The CCT values of these patients achieving euglycemic state (postprandial blood sugars <200 mg/dl along with a minimum drop in blood sugar level of 50 mg/dl from the previous hyperglycemic state) were taken for analysis. If the patients failed to achieve the above criteria at 1 month visit, CCT measurements were repeated at the next month follow up and were included for analysis if they achieved the required criteria within the study period. The right eye of the patient was taken for analysis. If the right eye did not fit the inclusion and exclusion criteria, but the left eye fulfilled the criteria, the left eye was taken for analysis (Figure 1).

Statistical analysis

The collected data was fed in MS excel and the analysis was performed using the SPSS version 24. The quantitative variables were measured using mean and standard deviation and qualitative variables were measured using frequency and percentage. Student unpaired t-test was used to compare mean changes in CCT between hyperglycemic and euglycemic states. The Bland-Altman plot (Bland & Altman, 1986 and 1999), or difference plot, was a graphical method to compare two measurements techniques. In this graphical method the differences (or alternatively the ratios) between the two techniques are plotted against the averages of the two techniques. A

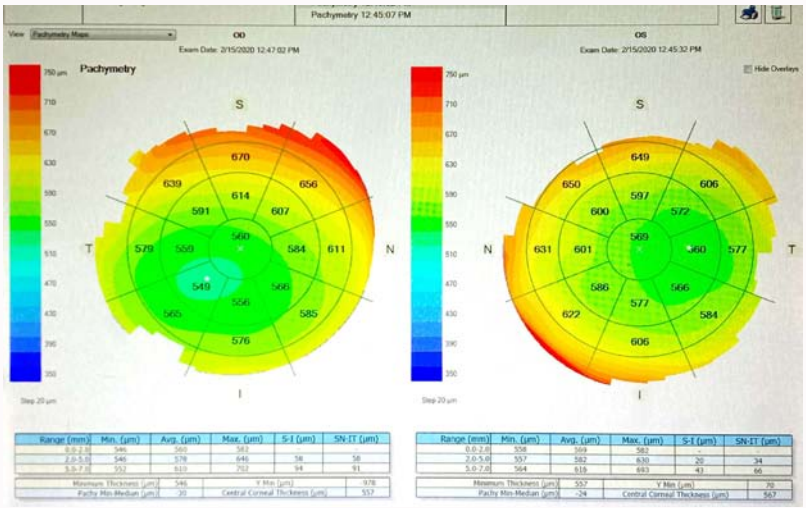

Figure 1: The CIRRUS HD-OCT Pachymetry analysis.

predictive value of less than 0.05 was taken as statistically significantly significant.

Results

A total of 100 diabetic patients (100 eyes) who were hyperglycemic were evaluated between August 2019 to July 2020. Euglycemia at 1 month was achieved in 93 eyes among those 100 patients. Three patients were achieve euglycemia at 2 month and rest of them (4 patients) achieve euglycemia at 6 month during the study period (Table 1).

Poorly controlled diabetic patients had thicker central corneas (540.06 µm + 28.61 µm) than well controlled patients (531 µm + 27.95 µm) which had statistically significance (p=0.0388) (Table 2).

Out of total 100 patients 85 patients who showed decrease CCT on achieving ES, 9 patients increase CCT on achieving ES while 6 patients had no change in CCT on achieving ES (Figure 2).

Scatter diagram of Bland -Altman analysis showed weaker correlation between these two variable, duration of DM not dependant with CCT difference (Figure 3).

P value was 0.058 which was statistically not significant.

These Bland -Altman plot was showing significant relation between these measurements. Out of 100 patients 93 patients were achieved euglycemic state at 1 month showing significant reduction in CCT at euglycemic state.(p value =0.0001). Poorly controlled diabetics (hyperglycemic state) had thicker central cornea than well controlled patients (euglycemic state) (Figure 4).

Discussion

Diabetes is one of the world's greatest public health problems. The measurement of central corneal thickness has become a very important ocular parameter due to its importance as an indicator of corneal health status, and decisions involving refractive surgery are sometimes dependent on CCT.

Table 1: CCT according to control of diabetes.

Analysis variables	Control of Diabetes		P value
	PPBS>200 mg/dl	PPBS<200 mg/dl	
Central corneal thickness (µm)	540.06 ± 28.61	531.74 ± 27.95	0.0388
Range	446-601	441-591	

Table 2: Total Number of patients showing increased, decreased or no change in CCT in euglycemic and hyperglycemic states.

Total No. of cases	↑ CCT (µm) on achieving state ES	↓ CCT (µm) on achieving state ES	no change in CCT on achieving ES
100	9	85	6

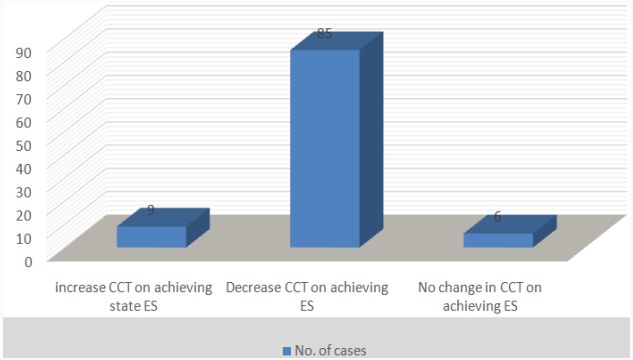

Figure 2: Number of cases.

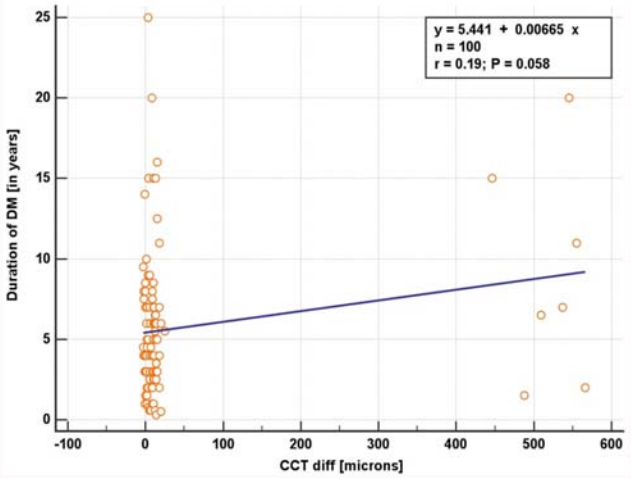

Figure 3: Scatter diagram of Bland -Altman analysis between CCT difference and duration of DM.

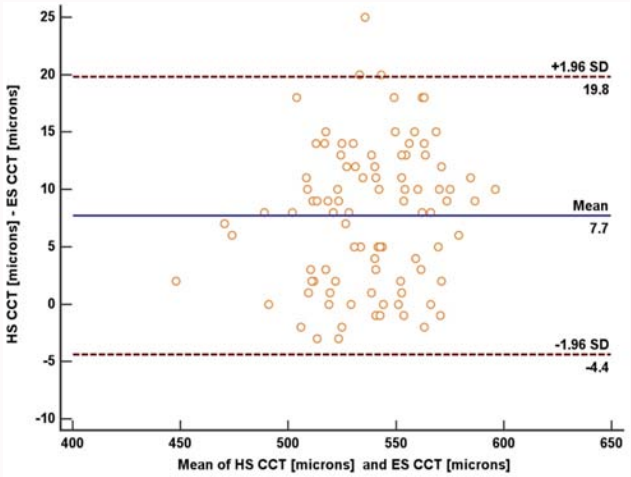

Figure 4: Bland Altman Plot between mean of HS CCT & ES CCT & difference of HS.

The mean CCT in the 100 patients studied was 540.06 µm ± 28.61 µm (range: 446 µm to 601 µm) in the hyperglycemic state and 531.74 µm ± 27.95 µm (range: 446 µm to 606 µm) in the euglycemic state, achieved at 1 month in 93 patients and 3 patients at 2 month and rest of them at 6 month. CCT of euglycemic state is lower than hyperglycemic and there was statistically significant difference was found in the CCT between hyperglycemic and euglycemic state. (P value - 0.038) using unpaired -t test (<0.05).

Out of 100 patients 93 patients were achieved euglycemic state at 1 month showing significant reduction in CCT at euglycemic state (p value =0.0001) using Bland -Altman plot.

Poorly controlled diabetic patients had thicker central cornea as compared to well controlled patients. In present study mean age of diabetics was 52.77 + 12.55 years.

Mean age (52.77 ± 12.55) was similar to Ozdamar et al. [7], (57.3 years ± 4.7 years), and contrast to Busted et al. [10], (34 years). There are few studies which have looked into corneal changes in CCT in

hyperglycaemic and euglycemic state in same individuals.

Larsson et al. [25], did a study to find central corneal thickness was thicker in type I diabetes (580) than control (550 micron). In our study, we demonstrated that hyperglycemia were associated with thicker CCT. Although the basis of association of diabetes and hyperglycemia remains unknown, we postulate that excess glucose in the cornea of patients with diabetes leads to intracellular accumulation of sorbitol, which act as an osmotic agent and results in the swelling of endothelial cells. In our study we did not find any relation between duration of diabetes and CCT difference (p value=0.058) using Bland Altman analysis.

Huntjens B et al. [100], studied the effect of short-term fluctuation (12 hour) of blood sugar levels on refractive error, ocular aberration as well as other anterior biometric parameters including CCT measured every 2 hours between 8:00 hours and 20:00 hours. They found that short term fluctuations of sugar of up to 108 mg/dl on a time scale of few hours caused no changes in CCT in both well controlled and poorly controlled patients. CCT variation of around 5 μm was seen in both diabetics and controls, though the CCT was thicker in diabetics compared to controls. The present study results were similar, though the CCT measurements in this study were not done over a single day but a month later. CCT variation <15 μm between euglycemic state was seen in most patients. Most studies have not shown any changes [7,9,10], according to severity of retinopathy though some have reported variation of corneal thickness according to the grade of retinopathy. We did not assess retinopathy during the study. It is unlikely that this would have affected the results, However all patients seen in the MBS Hospital are regularly screened for retinopathy as a part of their regular management protocol and appropriately managed for retinopathy if found.

Summary and Conclusions

1. Male (59%) and female (41%) both were included in our study. The mean age in our study was 52.77 years, male- 54.96 years and female 48.87 years.

2. Mean duration of DM (in years) was in male (5.46 ± 4.65) and in female was (6.64 ± 5.11), (p=0.233).

3. Out of 100 patients 95 right eye and 5 left eyes was taken for analysis in our study.

4. Mean CCT in hyperglycemic state was 540.06 ± 28.61 microns and euglycemic state was 531.74 ± 27.95 microns. P value was 0.038 which was weakly statistically significant.

5. Out of 100 patients 93 patients were achieved euglycemic state at 1 month showing significant reduction in CCT at euglycemic state (p value =0.0001) using Bland- Altman Plot.

6. Poorly controlled diabetic had thicker central cornea than well controlled patients. We found that, even though mean hyperglycemic and euglycemic CCT measurements were in normal range, CCT decreases significantly by the control of blood sugar.

7. There was no relation found between duration of DM and CCT difference in our study.

Limitations

1. Our study did not find any relation between diabetic retinopathy and CCT.

2. We did not perform confocal microscopy of corneal endothelium.

3. Duration of follow up was short.

4. CCT was measured within half an hour of the documented time of blood sugar measurements.

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