A Clinical Study of Central Corneal Thickness (CCT) In Diabetics and Its Correlation with Glycemic Status

Dr. Anita Kumari[1], Dr. Jaishree Singh*, Dr. Ashok Kumar Meena[2]

[1]Resident, Department of Ophthalmology, Govt. Medical College Kota, India
*Senior Professor , Department of Ophthalmology, Govt. Medical College Kota,India
[2]Senior Professor& Head , Department of Ophthalmology, Govt. Medical College Kota,India
* Corresponding author: Dr. Jaishree Singh*

Abstract
Background: The central corneal thickness is a sensitive indicator of health of cornea and serves as an index for corneal hydration and metabolism. It is also important indicator of health of cornea and serves as an index for corneal hydration and metabolism.
Aim & Objective: Aim of this study is to find the impact of diabetes mellitus on central corneal thickness in relation to the duration of the disease and glycaemic control in patients presenting to MBS Hospital, Kota.
MATERIAL & METHODS: - Observational cross-sectional study comprising 94 Consecutive diabetic patients aged 20 years and above was done between September 2019 to August 2020. After obtaining informed consent, complete ocular and medical history was taken, followed by clinical evaluation including visual acuity, refraction, anterior and posterior segment evaluation, intraocular pressure measurement and general examination were done. Relevant laboratory investigations were carried out. Central corneal thickness was measured with anterior segment OCT using anterior segment cornea lens. All the informations were recorded in a precoded Proforma. The study was approved by Ethical Committee of Govt. Medical College, Kota and all patients recruited with informed consent. RESULTS & CONCLUSION: A total 94 right eyes were studied. Group analyses in terms of duration of diabetes and glycaemic control were done. This study showed that diabetic patients with more than 10 years duration and poor glycaemic control had thicker central cornea than that of those who had diabetes less than 10 years duration and good glycaemic control respectively.
Keyword: Diabetes mellitus, Central corneal thickness, Anterior segment OCT

I.   Introduction:

Diabetes Mellitus affects every part of the eye and eventually leads to blindness.

It is the leading cause of irreversible blindness throughout the world [1].In the cornea, diabetes mellitus has a detrimental or harmful effect on the morphology, physiology and the clinical appearance. These changes manifest in almost all the layers of the cornea that is - the corneal epithelium, epithelial basement membrane complexes, stroma, Descemet's membrane and the endothelium. [2,3,4.] Cornea is the most important refractive element in the human ocular system providing 40-45 D of refraction.[5] In frontal view the cornea appears elliptical being 11.7 mm wide horizontally and 10.6mm vertically. The posterior surface appears circular and is about 11.7 mm diameter. Corneal thickness is a sensitive indicator of health of cornea and serves as an index of corneal hydration and metabolism. It is also important indicator of patency of endothelial pump.[6] we will study the relation in the CCT in diabetes patients in the Department of Ophthalmology, Govt. Medical College and Maharao Bhim Singh (MBS) Hospital, Kota by measuring CCT using anterior segment optical coherence tomography (AS-OCT). Current non-contact technologies for CCT evaluation include specular microscopy, scanning slit-beam topography, Scheimpflug technology-based cameras, and Optical Coherence Tomography (OCT). These imaging techniques have several advantages in addition to their non-contact nature of application: ease of use, high-resolution imaging, mapping functions, and comparability/correlation with the gold standard USP [7, 8.]

II.   Material & Methods:

An observational cross-sectional study was conducted on 94 Consecutive diabetic patients aged 20 years and above who attended the Department of Ophthalmology between from September 2019 to August 2020.The study was approved by Ethical Committee of Govt. Medical College, Kota and all patients recruited with informed consent.

Inclusion Criteria:
Diabetic patients aged 20 years and above.
Exclusion Criteria: Patients in whom optical coherence tomography was not possible.Patients who have history of ocular surgery 6 month before. Patients with any corneal pathology, uveitis and glaucoma
Method: A complete history both ocular and medical was taken. Duration of diabetes was noted.
Patients were grouped into different categories based on the following criteria:-Duration of Diabetes:
    Less than 10years.
    More than 10years.
Glycaemic control:
Controlled: -   HbA1c <7.0 %. (Euglycemic)
Poorly controlled: -   HbA1c > 7.0 % (Hyperglycemic)
The following examination and investigations were done:-
Visual acuity. Refraction. External eye examination. Anterior segment evaluation by slit lamp evaluation. Intraocular pressure measurement by Goldmann Applanation tonometer. Posterior segment examination by direct and indirect ophthalmoscopy. Central corneal thickness was measured using AS-OCT.
Investigations: Blood samples were drawn from all diabetic patients for serum glycosylated haemoglobin level (HbA1C) and blood sugar level. Also blood sugar level of all subjects was checked using glucometer.

CENTRAL CORNEAL THICKNESS MEASUREMENT (μm)-:
        Central Corneal Thickness (CCT) was measured by anterior segment optical coherence tomography (AS-OCT) using anterior segment cornea lens in diabetes mellitus patients. Pachymetry readings were recorded, averaged and used for subsequent CCT analysis. Images were automatically taken as soon as the center of fixation of target on the corneal apex at the pupil plane. Before each measurement, subjects were instructed to blink to create an optically smooth tear film over the cornea, and then to hold their eyes open during the image acquisition process. All measurements taken from scans used for statistical analyses. As there was good correlation between the measurements of both eyes, only the reading of right eye was taken for analysis.

Statistical analysis: The collected data was fed in MS excel and the analysis was performed using the Graph pad instat $3.0\times$ to 3.10 USA software for statistical analysis.The quantitative variable was analyzed using independent sample t test. A predictive value of less than 0.05 was taken as statistically significant.

III.   Observations &Results:
A total of 94 right eyes of 94 patients were studied. Group analyses in terms of duration of diabetes and glycaemic control were done.

Table 1: Age wise distribution of cases

| Age (in years)	Number of cases	Percentage of cases
20 – 30	06	6.38
31 – 40	16	17.02
41 – 50	21	22.34
51 – 60	31	32.98
61 – 70	17	18.09
>70	09	9.57
Total	94	100%
Mean age (in years)	**53.45±13.09**	

Graph 1. : Age distribution of cases
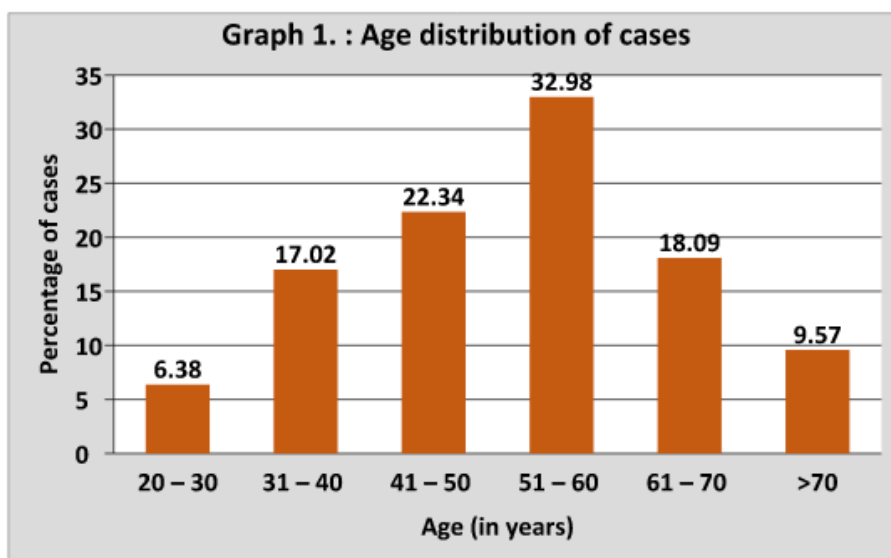
Table 2: MEAN CCT OF DIABETIC PATIENTS ACCORDING TO GLYCOSYLATED HEMOGLOBIN (HbA1C) LEVEL

HbA1C	NO. OF CASES	MEAN CCT (µm)	STANDARD DEVIATION	P - VALUE
<7%	33	559.21	8.02	
≥ 7%	42	564.02	8.97	P=0.018

Graph 2: Mean CCT according to HbA1C level
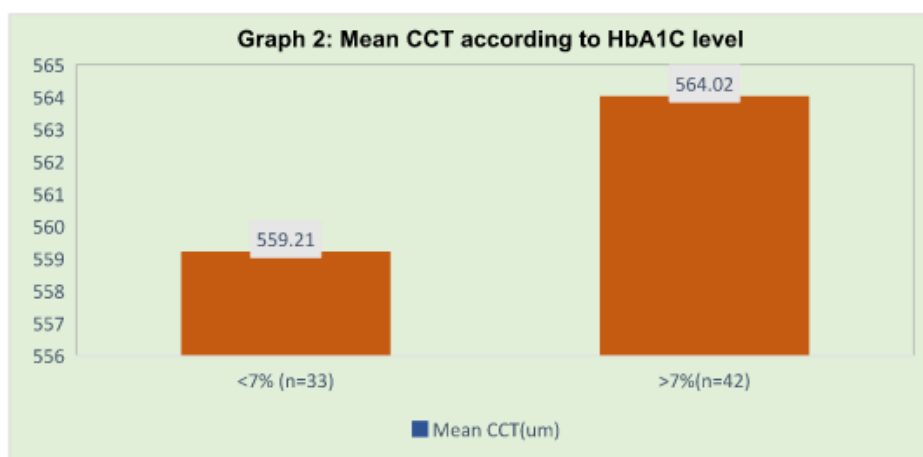
Table 3: MEAN CENTRAL CORNEAL THICKNESS (µm) ACCORDING TO DURATION OF DIABETES

DURATION OF DIABETES IN YEARS	NO. OF CASES	MEAN CCT(µm)	STANDARD DEVIATION	P – VALUE
<10 YEARS	51	560.97	7.25	**P=0.03**
≥ 10 YEARS	43	564.85	9.89	

Graph3: Mean CCT according to Duration of Diabetes
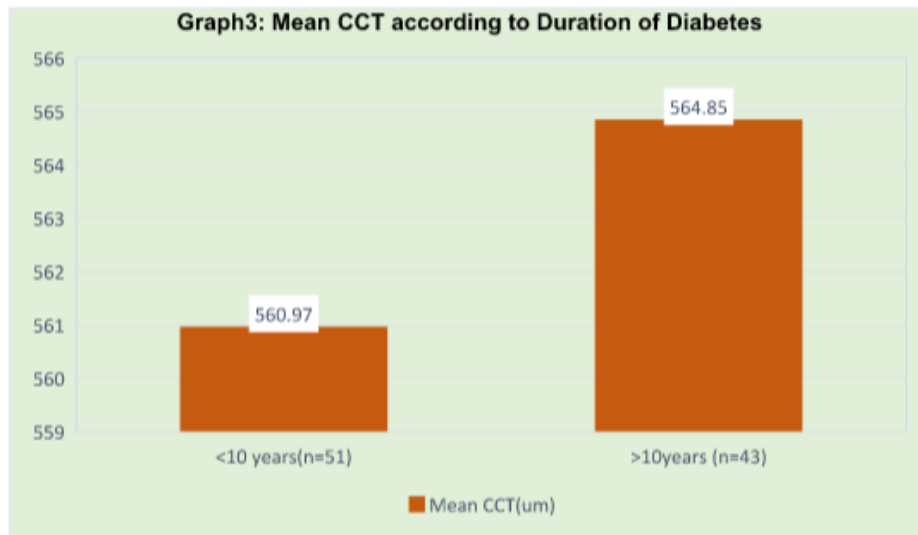
(Table 1, graph 1) The age of all patients in the present study varied from 20 years to 80 years with a mean age of 53.45±13.09 years. The maximum number of patients were in the age group of 51–60 years (32.98%).

(Table 2 and graph2) shows that out of 94 diabetic patients eighty patients were investigated for glycosylated haemoglobin (HbA1C).There were 33 diabetic patients with good metabolic control (HbA1C <7%) and their mean CCT was 559.21±8.02μm. Forty two patients with poor metabolic control(HbA1C≥7) had mean CCT of 564.02±8.97μm. The difference was statistically significant (P=0.018) using unpaired t test.

(Table 3, graph 3) In our study we compared the mean CCT according to duration of diabetes. Mean duration of diabetes was 8.62±5.38 years. Out of 94 diabetic patients fifty one patients had diabetes of less than 10 year duration and the mean central corneal thickness of these patients was 560.97±7.25μm. Fourty three patients had diabetes of more than or equal to 10 years and the mean CCT of these patients was 564.85±9.89μm and the difference between them was statistically significant (P=0.03) using unpaired t test.

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.

HYPERGLYCAEMIA ASSESSED BY GLYCOSYLATED HAEMOGLOBIN-With regard to hyperglycaemia assessed by glycosylated haemoglobin (HbA1C). In present study, diabetic patients who had HbA1C level ≥7% has thicker mean CCT (564.02±8.97μm) as compared to those diabetic patients who had HbA1c level <7% (559.21±8.02μm) and this difference was statistically significant (**p=0.018**) using unpaired t test.

Similar conclusion were drawn by **Prempal Kaur et al[9]** in India 2016 on 120 diabetic eyes and found that patient with HbA1C level ≥ 7% have thicker mean CCT (561±9.5μm) than those withHbA1c level <7% (548.4±11.9μm) and this difference was statistically significant (**p<0.00001**). **Mehmet Ozgur ZENZIN et al[10]** (2010) also had drawn similar result with regard to glycosylated haemoglobin (HbA1C). They found thicker mean CCT in those with HbA1C level ≥7% as compared to those with HbA1C level <7% (**570**.61±40.3μm v/s 555.02±32.5μm) and this difference was statistically significant (**p=0.021**) using ANOVA. In contrast to our study **Larsson et al[11]** and **Keoleian et al[12]** did not found any correlation between HbA1C and CCT. What is the effect of glycaemic control on CCT.Haemoglobin is a protein present in red blood cells (RBCs). In the blood, glucose adheres to the red pigment in haemoglobin and form A1C (HbA1c). Life span RBCs in blood is 2-3 month. More the glucose in blood, the more it will stick to the haemoglobin. HbA1c levels reflect the average blood glucose level for the past 2-3 months. Therefore, regular HbA1c testing tracks recent glycaemic control and is a valuable marker of glycaemic control.

CORRELATION WITH DURATION OF DIABETES-In our study, we divided the diabetic patients according to duration of diabetes into two groups, one with duration of diabetes less than 10 years and other had those with duration of diabetes more than or equal to 10 years. The mean CCT in patients with diabetes ≥10 years was thicker than those of less than 10 years duration (564.85±9.89μm v/s 560.97±7.25μm) and the difference between them was statistically significant (**p=0.03**).Similar conclusion was drawn by **Lee et al[13]** (2006). In their clinical study they observed that diabetics with ≥10 year's duration have more corneal morphological abnormalities and the CCT was significantly correlated with diabetic duration. They found

increase in mean CCT who had more than or equal to 10 years of diabetes than those who had less than 10 years of diabetes (595.97±4.2μm v/s 582±27μm) and the difference between them was statistically significant (**p<0.005**). **Ruchi Dabas et al[14]** (2017 India) also conducted cross sectional study and concluded that mean CCT was thicker in patients with more than or equal 10 years of duration compared to those who had diabetes less than 10 years of duration. In contrast to our study, **Mehmet Ozgur ZENZIN et al[10]** (2010) by using Orbscan II topography system measured CCT and found thicker mean CCT in patients who had diabetes of more than or equal to 10 years (565.78±39μm) as compared to those who had diabetes of less than 10 years (561.45±36.20 μm) but the difference was not statistically significant (**p=0.522**).The possible difference may be due to application of different measuring method of CCT. **Busted et al[15]** also reported no significant relation between central corneal thickness of diabetes and the diabetic duration. This difference is probably due to the fact that the mean age of their subjects (34 years) was lower than that (53.45±13.09 years) of our diabetic subjects. The possible explanation of thicker cornea in those who had more than 10 year of diabetes compared to less than 10 year duration is that as the duration of diabetes increases, there is decrease in the ability of corneal endothelial pump to compensate excess turnover of corneal hydration.

IV.   Conclusion:

From this study, we conclude that-

- The mean CCT of diabetic group who had HbA1C level more than or equal to 7% were significantly thicker than those who had HbA1c level less than 7% (564.02±8.97 v/s 559.21±8.02μm) (**p value**= **0.018**).

- Mean duration of diabetes was 8.62±5.38 years and the mean CCT in patients with more than or equal to 10 years duration (564.85±9.89μm) was significantly greater than those with less than 10 years duration (560.97±7.25μm) (**p=0.030**).

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