



IJCRR  
Section: Healthcare  
Sci. Journal Impact  
Factor: 5.385 (2017)  
ICV: 71.54 (2015)

# Central Corneal Thickness and Diabetes Mellitus - A Study of Correlation in Terms of Duration and Glycemic Control in North Indian Hilly Population

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## ABSTRACT

**Introduction:** Retinopathy is one of major micro vascular complication in long standing diabetes, but diabetic keratopathy has potential to decompensate following stress. The central corneal thickness is a sensitive indicator of health of cornea and may influence outcome in cataract, refractory surgeries and may lead to fallacy in Intraocular pressure measurement. Present study was cross sectional observational study, undertaken to determine the correlation between central corneal thickness (CCT), and diabetes control and duration in hilly north Indian patient.

**Material and Methods:** This is a cross-sectional study conducted in the department of ophthalmology of a tertiary care centre in Kumaon region. 400 subjects from age group 40 to 80 years were studied. An ultrasound pachymeter was used to measure CCT. The subjects were divided into two groups, 200 of them were non-diabetic subjects, and 200 were diabetic patients. The collected data was transformed into variables, coded and entered in Microsoft Excel. Data was analysed and statistically evaluated using SPSS-PC-17 version.

**Results:** The average central corneal thickness in diabetic patients was  $527.01 \pm 25.57$  microns. The average central corneal thickness found in non-diabetic patients was  $513.38 \pm 27.01$  microns. The statistically significant ( $p < 0.001$ ) increase in central corneal thickness found in diabetic patients compared to non-diabetic patients. CCT tends to increase significantly ( $p$  value  $< 0.05$ ) in uncontrolled diabetes (HbA1C level  $> 7\%$ ) and longer duration of diabetes.

**Conclusion:** Diabetic patients had an increased central corneal thickness when compared with non-diabetic patients. And this is more in patient with longer duration of uncontrolled diabetes.

**Key Words:** Central Corneal Thickness, Diabetes

**Key Messages:** Diabetic patients exhibit a greater statistically significant average CCT than non diabetic patients. There was also a positive correlation of thicker cornea with longer duration of diabetes and poorly controlled diabetes signifying that thicker cornea are more likely to be found in advanced stage. Diabetic keratopathy may lead to fallacy in IOP measurement and may decompensate following stress in refractory surgery.

## INTRODUCTION

Type II diabetes mellitus is a major public health concern in this modern day.<sup>[1]</sup>In the year 2000, India had 31.7 million diabetics and became the diabetic capital of the world, with the highest number of people with diabetes mellitus,

followed by China with 20.8 million diabetics and the United States with 17.7 million diabetics, in the second and third places respectively.<sup>[1]</sup>Diabetes mellitus (DM) occurs when the pancreas is not able to produce enough insulin, or the body becomes resistant to insulin, or both, resulting in in-

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ISSN: 2231-2196 (Print)

ISSN: 0975-5241 (Online)

Received: 29.05.2019

Revised: 29.06.2019

Accepted: 03.07.2019

creased blood glucose levels. Although diabetic retinopathy is major concern and may lead to severe vision loss, keratopathy should also be kept in the mind in diabetics as diabetic cornea has higher potential to decompensate following stress. The central corneal thickness is a sensitive indicator of health of cornea and serves as an index for corneal hydration and metabolism. Measurement of CCT is essential to take decisions regarding cataract and refractive surgeries and avoiding fallacy during estimation of IOP in diabetics. There are functional changes in diabetic cornea as a result of increased central corneal thickness. There are two theories behind increased central corneal thickness, firstly in diabetics, sorbitol accumulation within corneal endothelial cells<sup>[2]</sup> and a decrease in Na<sup>+</sup>/K<sup>+</sup> ATPase activity<sup>[3]</sup> induce dysfunction of the corneal endothelium cell layer leading to corneal hydration which translates to increased CCT measurements. Thus, corneal thickness indirectly indicates the functioning of the endothelial layer. Secondly, changes occur in corneal stroma in diabetics, which include structural alterations produced by collagen cross linking. Advanced glycation products accumulate in collagen proteins, resulting in the formation of covalent cross-linking bonds, and may lead to increased corneal thickening and biomechanical changes<sup>[4,5]</sup> Central corneal thickness is an important indicator of patency of corneal endothelium pump and can be objectively measured by variety of techniques like optical pachymetry, ultrasound pachymetry, confocal microscopy, ultrasound biomicroscopy, optical ray path analysis or scanning slit corneal topography and optical coherence tomography.<sup>[6]</sup> Ultrasound pachymetry is the current standard for corneal thickness measurement.<sup>[7]</sup> This study aimed to evaluate the effect of diabetes mellitus on corneal thickness (CCT) by comparing the CCT of diabetic and non-diabetic patients and association of CCT with duration of diabetes mellitus as well as serum level of HbA1c.

**Subjects and Methods:** Ethical clearance was obtained from the institutional ethical committee and a cross sectional study was designed in tertiary eye care centre. Two hundred diabetic patients (previously diagnosed by medical practitioners), whether on treatment or not, who gave consent were enrolled irrespective of level of blood sugar. Two hundred age matched controls (non diabetic by history and blood sugar level) were also enrolled. Informed consent was taken from all the participants in the study. After taking detailed history, complete routine anterior and posterior segment evaluation was done. The corneal thickness assessment was done for 400 eyes of 200 diabetic and 400 eyes of 200 non diabetic patients with the help of ultrasound pachymeter, in multiple reading single point mode by a single person between October 2016 to September 2018 at department of ophthalmology Government Medical College, Haldwani.

Exclusion criteria were as followed

- (1) Eyes with corneal pathologies like pterygium, corneal dystrophies
- (2) Any prior history of ocular surgeries
- (3) Active or any previous eye infection or inflammation
- (4) contact lens users

## RESULTS

Four hundred patients included in this study were in age group of 40 to 80 year. Majority of the patients belonged to age group 51-60 years (33.75%) whereas the least common age group was 71 -80 years (9%). Mean Age of diabetic and non-diabetic patients was 58.23±9.77 years and 56.59±9.85 years respectively (Table 1).

**Table 1: Age wise distribution of study subjects (n=400)**

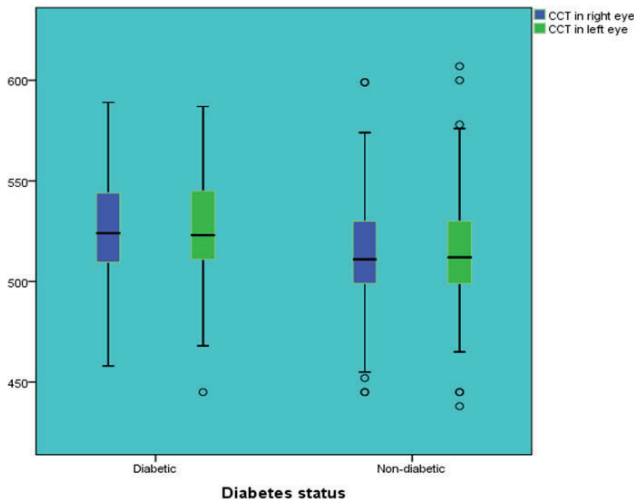
Age	Diabetic		Non-diabetic		Total	
	No	%	No	%	No.	%
40- 50 years	49	24.5	66	33.0	115	27.75
51-60 years	68	34.0	67	33.5	135	33.75
61-70 years	63	31.5	51	25.5	114	28.5
71-80 years	20	10.0	16	8.0	36	9.0
<b>Total</b>	<b>200</b>	<b>50.0</b>	<b>200</b>	<b>50.0</b>	<b>400</b>	<b>100</b>

In non-diabetic group 99 (49.5%) were males and 101 (50.5%) were females with M: F ratio of 0.98. However, in diabetic group, 96 (48.0%) cases were males and 104 (52.0%) were females with M: F ratio of 0.91. Diabetic females had slightly higher preponderance 52.2%.

The mean CCT in 400 eyes of 200 diabetic patients was 527.01µm with SD of 25.57, and in 400 eyes of 200 non-diabetics mean CCT was 513.38 µm with SD 27.09. Mean CCT was significantly higher in diabetics as compared to non- diabetics i.e. p value <0.001. (Table 2 and Figure 1)

**Table 2: Mean central corneal thickness in micro meter of diabetic and non-diabetic patients (n=400)**

Central corneal thickness (µm)	Diabetic		Non-diabetic		P value
	Mean	SD	Mean	SD	
Right eye	527.00	25.09	513.53	27.24	<0.001
Left eye	527.01	26.10	513.24	27.01	<0.001
<b>All eyes (n=800)</b>	<b>527.01</b>	<b>25.57</b>	<b>513.38</b>	<b>27.09</b>	<b>&lt;0.001</b>



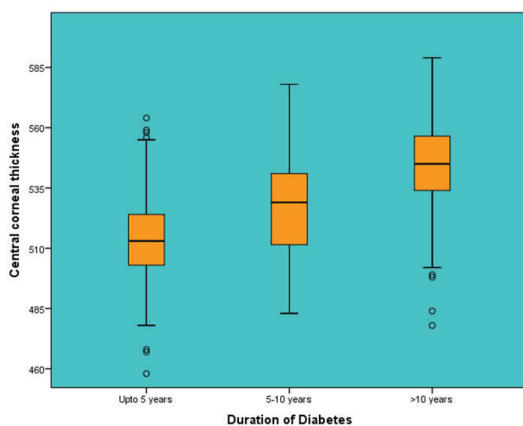
**Figure 1:** Box plot showing comparison of Central corneal thickness (µm) in Diabetic and Non-diabetic patients.

Maximum number of patients had diabetes for less than 5 year i.e. 95(47.5%), followed by patient who had diabetes >10 year i.e. 72 subjects (36.0 %) and least were patients who had diabetes between 5-10 years duration i.e. 33(16.5%).

CCT tends to increase significantly with duration of diabetes (p value <0.001). Highest mean CCT was found in patients with longer duration of diabetes >10 year i.e. 542.92 µm, followed by 5-10-year duration i.e. 528.27 µm and least mean CCT was found among diabetics having duration less than 5 years i.e.514.19 µm.(Table 3 and Figure 2).

**Table 3: Distribution of study subjects as per duration of diabetes and Relation of corneal thickness with diabetic duration**

Duration of diabetes	Total No. (%)	Total Eyes	Mean CCT (µm)	SD	P value
Upto 5 years	95 (47.5)	190	514.19	19.02	<0.001
5-10 years	33(16.5)	66	528.27	22.05	
>10 years	72(36.0)	144	542.92	20.03	



**Figure 2:** Box plot showing Relation of corneal thickness (in microns) with diabetic.

Table 4 depicts that diabetics having HbA1c more than 7% had higher mean CCT i.e. 540.01µm as compared to those having HbA1c upto 7% had mean CCT of 522.46µm. It was significant with p value<0.01(Table 4)

**Table 4: Comparison of central corneal thickness in diabetic patient with HbA1c level**

HbA1c (%)	Mean	SD	p-value
Upto 7	522.46	22.46	<0.01
>7.0	540.01	21.31	

## DISCUSSION

This study elucidates the influence of diabetes on central corneal thickness. Central corneal thickness has become an important indicator of corneal health status and decisions involving refractive surgery and estimation of intraocular pressure. In present study the central corneal thickness was 527.01± 25.57 microns in diabetic patients and 513.38 ± 27.01 microns, in non-diabetic patients, which is similar to another study done on Indian eyes by Nangia et al with average central corneal thickness (514±33.0µ).<sup>[8]</sup> They reported that Indians from rural central India have markedly thinner corneas than do Caucasians or Chinese.

There are two different hypothesis suggesting higher CCT in diabetics

- Glucose can act as collagen cross linking agent with the help of advanced glycosylation end products. Advanced glycation products accumulate in collagen proteins result in the formation of covalent cross-linking bonds and may lead to increased corneal thickening and biochemical changes.<sup>[9]</sup>
- In addition to this there is decrease in Na<sup>+</sup>/K<sup>+</sup> activity in corneal endothelium.

Rashmi Kumari et al <sup>[10]</sup> conducted case control study in Max Eye Hospital, Patna,( from May 2015 to April 2016) measured Central corneal thickness in 100 patients out of which 50 were diabetic and 50 were non-diabetic and concluded that the Diabetic patients had thicker cornea as compared to the non-diabetics.

Prem pal Kaur et al <sup>[11]</sup> conducted cross sectional study at Amritsar on 240 eyes, in which 120 eyes of diabetic patient and 120 eyes of non -diabetic patient taken at Government Medical College, Amritsar, and found that in the diabetic group, the mean CCT and mean endothelial cell density varies significantly from non diabetic controls . They also concluded that CCT was significantly thicker for diabetics with duration of >10 years and HbA1c >7.

In contrast Kenji Inoue et al<sup>[12]</sup> in Japan, compared the endothelial structure and thickness of the cornea in diabetic and non diabetic patients. They found no significant difference between CCT in the diabetic group to non-diabetic individuals. Corneal endothelial cell structure was damaged, but CCT was not increased in type II diabetic patients however, Allan Storr-Paulsen et al<sup>[13]</sup> establish that Type II diabetic subjects did not differ from the non-diabetic control subjects with regards to endothelial cell density, hexagonality or variation in CV, but showed a significant increase in CCT.

Su et al.<sup>[14]</sup> also observed that among 3280 Malay adults aged 40 to 80 years, those with diabetes and hyperglycemia showed significantly thicker central corneas, which was independent of age and IOP levels.

Abdul ghani et al<sup>[15]</sup> in Sudanese population and Busted et al<sup>[16]</sup>, reported similar results as present study.

Central corneal thickness was observed higher in diabetic patient having duration more than 10 year that was  $541 \pm 22.41 \mu\text{m}$  as compared with diabetics having duration <5 year that was  $514.71 \pm 19.61 \mu\text{m}$  this is positively correlated with the study done by Rashmi Kumari et al<sup>[10]</sup>, Lee et al<sup>[17]</sup> where they found positive relation of higher CCT with longer duration of diabetes.

The present study depicts that patient having HbA1c more than 7% have significantly higher CCT [i.e.  $540.01 \mu\text{m}$ ] as compared to the non diabetic subjects [i.e.  $522.46 \mu\text{m}$ ].

This study correlates with other studies done by Rashmi et al<sup>[10]</sup> Su et al<sup>[14]</sup> Stella Briggs et al<sup>[18]</sup> where they found association of higher CCT with uncontrolled hyperglycemic level.

Possible limitations of this study are that corneal endothelial density and hexagonality associated with the hypertension and dyslipidemia were not measured. Ultrasound pachymetry is most common and gold standard for central corneal thickness measurement but it has its own disadvantages like it yields slightly thinner measurements as a result of tissue indentation. Mild patient discomfort and risk of infection are some additional concerns with this method.

However, newer non-contact technologies for the measurement of corneal thickness allows better repeatability and reproducibility.<sup>[19]</sup> These include the Pentacam, the Orbscan and optical coherence tomography.

## CONCLUSION

Retinopathy is one of major microvascular complication in long standing diabetes, but diabetic keratopathy has potential to decompensate following stress. Diabetic patients had an increased central corneal thickness when compared with non-diabetic patients. And this is more in patient with longer duration of uncontrolled diabetes. The central corneal

thickness is a sensitive indicator of health of cornea and may influence outcome in cataract, refractory surgeries and may lead to fallacy in Intraocular pressure measurement.

## ACKNOWLEDGEMENT

Authors acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript. The authors are also grateful to authors / editors / publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

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