

Central Corneal Thickness and Diabetes – A Study of Correlation in Terms of Duration and Glycemic Control

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ABSTRACT

Introduction: Diabetes has emerged as an important global health concern because of its various adverse effects on the ocular tissue. To study the effect of diabetes on corneal thickness with respect to duration and level of glycosylated haemoglobin.

Material and methods: A case control study with 100 patients, 50 diabetics (type 2) and 50 non diabetics was conducted in our tertiary eye care centre from may 2015-april 2016. Along with complete routine ophthalmic examination, Central corneal thickness (CCT) assessment of each eye was done using ultrasound pachymeter. Blood investigation was done to measure the HbA1c level in diabetics.

Results: The mean CCT in diabetics was $564.541 \pm 24.56 \mu$ and in non diabetic was $519.453 \pm 25.98 \mu$ and the difference between the two groups was clinically significant ($p < 0.002$). Mean duration of diabetes was 9.478 ± 1.7 yrs. The CCT was thicker for diabetics with duration of > 10 years than with < 10 years ($P = 0.115$) and with HbA1c $> 6.5\%$ than HbA1c $< 6.5\%$ ($p = 0.231$) though the difference was not statistically significant.

Conclusion: Diabetic patients have thicker cornea as compared to the non-diabetics. There is a direct correlation of CCT and diabetes so its assessment is must in work up of any diabetic patient to evaluate the functional status of thickened cornea.

Keywords: Central Corneal Thickness, Pachymeter, Diabetes, Glycosylated Hemoglobin

INTRODUCTION

Diabetes mellitus has emerged as an important cause of concern because of its adverse pathological effects on various tissues. India and china have the largest diabetic populations in the world.^{1,2}

Main indicators of diabetes in ocular tissues are retinopathy, cataract and glaucoma. The corneal changes associated with Diabetes mellitus is known as diabetic keratopathy, a lesser studied pathology.³ It can have varied presentations like decreased corneal sensitivity, epithelial disorders like superficial punctate keratitis and epithelial erosions, thickened basement membrane.^{4,5} Increased serum levels of glycosylated hemoglobin increases the predisposition to impaired corneal epithelial barrier function.³ Glucose can act as collagen cross linking agent with the help of advanced glycosylation end products. Advanced millard products accumulate in collagen proteins result in the formation of covalent cross linking bonds and may lead to increased corneal thickening and biochemical changes.⁶

The corneal endothelium in diabetic patients is considered as a tissue under continuous metabolic stress and it has increased coefficient of variation of endothelial cell area, decreased percentage of hexagonality and increased corneal auto fluorescence.^{7,8}

Overall functional status of cornea is dependent on normal

function of all the layers of cornea. 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 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.⁹ Ultrasound pachymetry is the current standard for corneal thickness measurement.¹⁰

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.

MATERIAL AND METHODS

Ethical clearance was obtained from the institutional ethical committee and a case control study was designed in our tertiary eye care centre. Fifty diabetic patients (previously diagnosed by medical practitioners), whether on treatment or not, who gave consent were enrolled irrespective of level of blood sugar. Fifty age matched controls (non diabetic by history and blood sugar level) were also enrolled. Eyes with corneal pathologies like pterygium, corneal dystrophies, contact lens users, receiving treatment for any topical or systemic diseases, any prior history of ocular surgeries were excluded from the study. Complete routine anterior and posterior segment evaluation was done.

The corneal thickness assessment was done for 100 eyes of 50 diabetic and 100 eyes of 50 non diabetic patients with the help of ultrasound pachymeter, Sonomed Pacscan plus, in multiple reading single point mode by a single person. Final reading was the average of 5 readings with standard deviation less than 0.003mm.

STATISTICAL ANALYSIS

Data was analysed using SPSS 16. Comparison between the different parameters was done using student t-test, Pearson correlation coefficient and Chi-square test. p-value < 0.05 was considered significant. 95% confidence limit was used.

RESULTS

The mean age of the study population was 45.85 years. 54% were males and 46% were females (Figure 1). More than 40% of subjects in both case-control were in the age group of 41-50

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Patients	n	MeanCCT (μ)	SD (\pm)	P-value	95%CI
Diabetic	50	564.541	24.56	<0.002	4.4-8.9
Non-diabetic	50	519.453	25.98		

Table-1: Mean CCT in diabetics (case) and non diabetics control

Gender	n	Mean CCT (μ)	SD (\pm)	P value
Male	35	578.87	30.12	P=0.256
Female	15	551.78	29.11	

Table-2: Gender distribution with mean CCT in diabetic group

Duration of diabetes	n	Mean CCT (μ)	SD (\pm)	X ²	P value
<5 yrs	8	548.76	25.78	2.178	P=0.115
<10 yrs					
5-10 yrs	22				
\geq 10 yrs	20	576.89	16.87		

Table-3: Central corneal thickness with duration of diabetes

HbA1c	n	Mean CCT (μ)	SD (\pm)	P-value	95%CI
<6.5%	37	548.12	21.7	P=0.231	7.8-25.36
>6.5%	13	568.22	18.5		

Table-4: Central corneal thickness with glycemc control

years (Figure 2). The mean CCT for the entire study group was $527.341 \pm 30.56\mu$. For diabetic subjects it was $564.541 \pm 24.56\mu$ and for non diabetic it was $519.453 \pm 25.98\mu$ (Table1). The CCT was higher in diabetic group and the statistical difference was significant (p value<0.002 Mann-Whitney test) as compared to the non diabetics. The mean CCT in male patient in diabetic group ($578.87 \pm 30.12\mu$) was higher as compared to the females ($551.78 \pm 29.11\mu$) the difference being statistically insignificant, p=0.256 (Table 2). Of the 50 diabetic cases, majority had diabetes of 5-10 years duration with mean duration being 9.478 ± 1.7 yrs. Mean CCT in diabetics with duration of disease more than 10 years was higher ($576.89 \pm 16.87\mu$) than those having it for less than 10years ($548.76 \pm 25.78 \mu$) implying positive correlation but the difference was not significant(p=0.115)(Table 3). Diabetics with HbA1c<6.5% had CCT $548.22 \pm 21.7 \mu$ while those having HbA1c>6.5% had higher CCT, that is $568.12 \pm 27.5 \mu$ but again the difference was not significant (p=0.231) (Table 4).

DISCUSSION

Diabetic keratopathy implies spectrum of changes occurring in the cornea of a diabetic patients. In our study we found that Diabetic patients exhibit a greater statistically significant average central corneal thickness than non-diabetics. There are many postulations to explain this. Some studies says reduction of Na+K+ATPase activity directly inhibits the corneal endothelial pump while others explain intracellular accumulation of sorbitol, an osmotic agent causing corneal hydration. Recent studies suggests advanced glycosylated end product act as cross linking agents to increase the covalent bond in corneal stroma and eventually its thickness. The CCT in diabetics signifies overall functional and morphological status of cornea.¹¹ It has been reported as a sensitive indicator of early diabetic keratopathy and a key parameter for refractive surgery

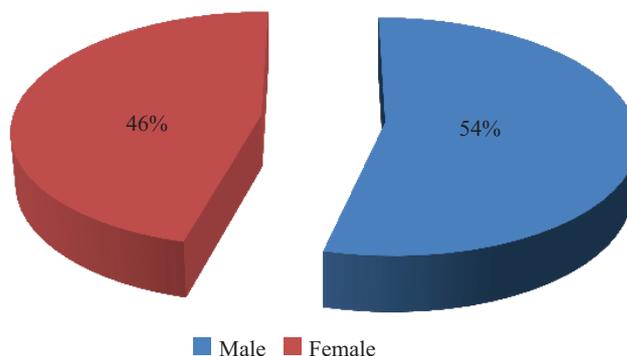


Figure-1: Sex distribution in study population

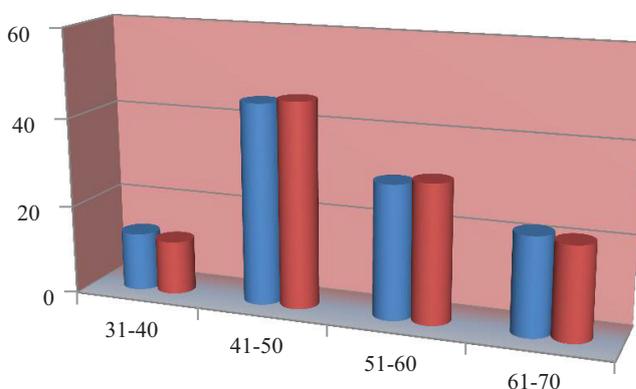


Figure-2: Age distribution in case (blue) and control (red) groups

and estimation of IOP.¹² In our study, the mean CCT of the entire group was $527.341 \pm 30.56\mu$ which is quite different from another study done on Indian eyes by Nangia et al ($514 \pm 33.0\mu$).¹³ They reported that Indians from rural central India have markedly thinner corneas than do caucasians or chinese. Our study included more of urban population in tertiary eye centre may account for the difference in results from other studies.

The relation between CCT and diabetes mellitus has been reported differently in various studies.^{14,15} In our study the mean CCT in diabetics was $565.98 \pm 30.02\mu$ and in non diabetics was $514.56 \pm 30.02\mu$ and the difference between the two groups was statistically significant (pvalue 0.0124-Man whitney test). Claramonte et al in a similar study showed significant relationship between diabetes and CCT. The mean CCT in diabetics in their study was 571.96μ as compared to 544.89μ in non diabetics with statistically significant difference.¹⁵ On the other hand Keoleian et al in a study to evaluate structural and functional status of corneal endothelium in diabetics concluded that the functional status of corneal endothelium was unaffected despite their structural abnormality.⁸ They reported no significant difference in corneal thickness in diabetics. Another study feom Japan also reported no relation between CCT and diabetes.¹⁶ The mean CCT for male subjects in diabetic group in present study($528.87 \pm 30.12\mu$) was higher as compared to the females ($521.78 \pm 29.11\mu$) while in non diabetics the male subjects had lower mean CCT ($519.65 \pm 28.41\mu$) as compared to the

female counterparts ($524.89 \pm 26.19 \mu$). The difference was not significant in either groups (p value 0.32 and 0.54 respectively). Another study done for Indian eyes have reported significantly higher CCT in males ($515.6 \pm 33.8 \mu$) than females ($508.0 \pm 32.8 \mu$) with p value 0.001.¹⁷ The effect of duration of diabetes on corneal thickness was studied by Lee et al who reported that diabetic duration of over 10 years have more corneal morphological abnormalities as compared with normal ones.¹⁸ In our study also the mean CCT in subjects with diabetes of more than 10 years duration was higher ($544.64 \pm 34.56 \mu$) than those having it for less than 10 years ($518.98 \pm 31.21 \mu$). McNamara et al observed positive correlation between HbA1c level and CCT in Type 1 diabetics but reported thicker corneas in diabetics but found no direct correlation with HbA1c level in type 2 diabetes similar to our study.¹⁹ This observation was reinforced by Yazgan S et al.²⁰

CONCLUSION

A significant correlation was found between increase CCT and diabetes, with positive correlation between thick cornea and the duration of the diabetes, indicating that patients with thick corneas are more likely to be found in an advanced stage of the disease. Measuring CCT in diabetic patients should be mandatory especially in preoperative work up of refractive surgery, for donor tissue evaluation prior to keratoplasty, glaucoma suspects, long term contact lens users etc. This may help to identify patients at higher risk of developing severe complications thus enabling the ophthalmologist to treat their disease more accurately. Measurement of CCT complemented with study of the corneal endothelium can provide further insight for the proper evaluation of these patient regarding their functional outcome. As the basic histopathological change is formation of covalent bonds in corneal stroma, study of relation between diabetic keratopathy and corneal ectatic condition is warranted.

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