

Effect of Diabetes Mellitus on Central Corneal Thickness – A Comparative Study

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Purpose: To compare central corneal thickness (CCT) of diabetes Mellitus (DM) patients with age matched subjects without DM and to evaluate the correlation of CCT with glycemic status, duration of DM and severity of diabetic retinopathy (DR).

Study Design: Cross sectional comparative study.

Place and duration of study: Eye Department, PNS Shifa Karachi from March 2016 to February 2017.

Material and Methods: Patients with ages between 20 to 80 years of either gender who were diagnosed to have DM were recruited in the study. Control group comprised of age matched healthy volunteers who did not have DM. CCT was evaluated in each subject with non-contact specular microscope (SP-3000 P, Topcon Corporation, Japan) and all the findings were endorsed on a pre designed performa. SPSS version 13.0 was used for analysis of data.

Result: Two hundred and fifty two eyes (126 diabetic patients and 126 healthy controls) were evaluated. Both groups were age and gender matched ($p > 0.05$). Mean CCT of diabetic population was $512.21 \pm 32.68 \mu\text{m}$ while mean CCT of control group was $498.83 \pm 28.98 \mu\text{m}$ ($p = 0.001$). Difference in CCT values between subgroups of patients with no DR, with NPDR and PDR was statistically non-significant ($p = 0.810$). Pearson's correlation analysis showed that duration of DM ($r = 0.022$, $p = 0.809$), HbA1c ($r = 0.103$, $p = 0.251$), and severity of DR ($r = 0.022$, $p = 0.805$) did not show any significant correlation with CCT.

Conclusion: Significantly thicker CCT was found in patients with DM as compared to healthy age matched controls.

Key words: Specular Microscopy, Central Corneal Thickness, Diabetes Mellitus.

With the advent of precise and better non-invasive measurement tools, central corneal thickness (CCT) measurement has become a vital ocular parameter due to its importance as an indicator of corneal health and integrity. Accurate CCT measurement (Pachymetry) has diagnostic and therapeutic implications in various conditions like ectatic corneal dystrophies (Keratoconus, Pellucid marginal degeneration), contact lens related problems, dry eyes, diabetes mellitus, glaucoma and refractive surgery (LASIK)¹. For years, ultrasound pachymetry remains the gold standard method for measurement of CCT, but newer

non-invasive methods of pachymetry like Scheimpflug system, specular microscopy, spectral domain OCT demonstrated acceptable repeatability and reproducibility. Corneal morphological parameters including CCT vary with age, gender, race and ethnicity. Tayyab et al and Islam et al reported mean CCT of normal Pakistani population using specular microscope as $503.96 \mu\text{m}$ and $505.72 \mu\text{m}$ respectively^{2,3}.

Diabetic keratopathy is a known entity that affects approximately 70% of diabetic population and include decrease in corneal endothelial cell density (CED) and hexagonality, increase in CCT, polymegethism,

pleomorphism, higher corneal auto fluorescence and lower corneal sensitivity^{4,5}. CCT has a positive correlation with intra ocular pressure (IOP) measured by Goldman Applanation tonometry and this effect on measured IOP can be clinically significant⁶. Thicker CCT in diabetes mellitus should be taken into consideration while measuring IOP in diabetics. Several studies had showed variable results while comparing CCT measurements in diabetics with normal subjects. Significantly higher CCT values in diabetic population as compared to healthy age matched controls had been reported by various authors^{4,7-9}. However, there are studies that showed no significant difference in CCT values between diabetics and normal population^{5,10,11}. Available data from Pakistan on the subject is limited. This study was aimed to compare CCT between patients with DM and non-diabetic control subjects and to analyze the correlation of CCT in relation to diabetes duration, glycemic status and severity of DR.

MATERIALS AND METHODS

This was a cross sectional comparative study conducted at Eye Department, PNS Shifa Naval hospital Karachi from March 2016 to February 2017. Patients with ages between 20 to 80 years of either gender who were diagnosed to have DM were recruited in the study through non probability convenience sampling, after approval by ethical review committee of hospital. Written informed consent was obtained from each subject before enrolment and study was conducted in accordance with the declaration of Helsinki¹². Sample size was found to be 126 in each group using power of test as 80, level of significance as 0.5, mean CCT value as 566.7 μm in DR group, and 550 μm in control group and population SD as 35.77. The diagnosis of DM was based on criteria of the American Diabetes Association (ADA) and included all the patients who were already under treatment of physician¹³. Control group comprised of age matched healthy volunteers who did not have DM (subjects with fasting blood sugar of less than 110 mg/dL). Subjects with history of intraocular surgery / trauma / retinal laser, corneal opacity or dystrophy, glaucoma, pseudoexfoliation, uveitis, use of contact lens, and use of topical eye drops were excluded. Sub groups of patients included those with no DR, non-proliferative DR (NPDR) and with proliferative DR (PDR) on the basis of diagnosis by a consultant ophthalmologist. Complete ocular examination including visual acuity assessment, auto

refraction, slit lamp bio microscopic examination and non-contact IOP measurement was done in each subject. CCT was evaluated in each subject with non-contact specular microscope (SP-3000 P, Topcon Corporation, Japan) by a single experienced examiner between 09:00 - 11:00 AM. Three images from central cornea of eye with worse retinopathy stage in diabetic group and randomly selected one eye in control group were captured. An average of three readings was used for final analysis. All the findings including demographic data, glycemic status and CCT were endorsed on a pre designed proforma.

SPSS version 13.0 was used for analysis of data that was tested for normality before analysis. For quantitative variables descriptive statistics i.e. means \pm standard deviation (SD) and for qualitative variables frequencies and percentages were used. Chi square test was used to compare frequencies and percentages, while Independent sample 't' test and One way analysis of variance (ANOVA) were used to compare means \pm SD between groups. Association of CCT with DM duration, HbA1c, and severity of DR was analyzed using Pearson's correlation coefficient test. A p value < 0.05 was considered statistically significant.

RESULTS

Data of 252 eyes (126 diabetic patients and 126 healthy controls) was evaluated. Mean age of diabetic population was 54.16 ± 9.70 years (range: 30-75 years), while mean age of control group was 52.00 ± 12.37 years (range: 32 - 80 years). Demographic and clinical profile of both groups is given in table 1. Both groups were matched in terms of age ($p = 0.12$) and gender ($p = 0.30$). Mean fasting plasma glucose level was significantly higher in diabetic group ($p < 0.01$). Mean CCT of diabetic population was $512.21 \pm 32.68 \mu\text{m}$ (range: 403 - 623 μm), while mean CCT of control group was $498.83 \pm 28.98 \mu\text{m}$ (range: 412 - 559 μm) [$p = 0.001$]. Patients with no DR, with NPDR and PDR did not show statistically significant difference in mean CCT values (table 2). However, patients with no DR were significantly younger and had lower HbA1c levels as compared to patients with NPDR and PDR (table 2). Moreover, comparison CCT values between diabetic groups according to duration of DM and/or HbA1c levels did not showed significant difference (table 3). Duration of DM was significantly correlated with type of DR ($r = - 0.421$, $p < 0.01$), HbA1c level ($r = 0.175$, $p = 0.050$), age ($r = 0.305$, $p < 0.01$) and severity of DR ($r = 0.616$, $p < 0.01$). However, Pearson's

Table 1: Demographic and Clinical Profile of Study Population.

Parameter	Diabetic (n = 126)	Control (n = 126)	P value
Age (years)	54.16 ± 9.70	52.00 ± 12.37	0.125
Gender			
Male	76 (60.31%)	67 (53.17%)	0.309
Female	50 (39.68%)	59 (46.82%)	
Type of DM			
Type 1	44 (34.90%)	-	-
Type 2	82 (65.10%)	-	-
Duration of DM			
< 10 years	60 (47.60%)	-	-
> 10 years	66 (52.40%)	-	-
Plasma Glucose (F) mg/dL	184.73 ± 75.90	97.52 ± 12.41	< 0.01
HbA1c Level (%)	6.97 ± 1.12	-	-

Table 2: Clinical Profile and CCT Values according to severity of DR.

Parameter	No DR (n = 42)	NPDR (n = 46)	PDR (n = 38)	P value
Age (years)	49.74 ± 10.76	56.80 ± 8.49	55.84 ± 8.24	0.001
Plasma Glucose (mg/dL)	180.00 ± 83.56	179.76 ± 71.16	196.00 ± 73.33	0.553
HbA1c (%)	6.51 ± 1.07	7.06 ± 1.23	7.36 ± 0.86	0.002
CCT (µm) mean ± SD	512.60 ± 37.01	509.91 ± 28.24	514.55 ± 33.30	0.810

Table 3: Comparison of groups according to DM duration and HbA1c level.

Parameter	Age (Years)	Glucose (mg/dL)	CCT (µm)
Duration (years)			
< 10 years	52.08 ± 10.91	181.06 ± 73.71	513.99 ± 33.20
> 10 years	56.05 ± 8.08	188.07 ± 78.25	510.59 ± 32.38
p value	0.021	0.607	0.563
HbA1c (%)			
≤ 7.5	53.78 ± 9.79	158.03 ± 57.95	510.98 ± 31.74
> 7.5	54.98 ± 9.57	242.15 ± 78.68	514.85 ± 34.89
p value	0.522	< 0.01	0.538

Correlation analysis showed that duration of DM, HbA1c, and severity of DR did not show any significant correlation with CCT. Moreover, plasma glucose level showed weak but significant correlation with CCT ($r = 0.155$, $p = 0.014$).

DISCUSSION

The relationship between DM and CCT is very important as the current burden of DM in Pakistan is approximately 7.0 million people and this figure is expected to rise by the year 2040 to an alarming 14.4

million making Pakistan the 8th highest country in terms of burden of DM¹⁴. It is postulated that hyperglycemia may cause endothelial dysfunction with resultant stromal hydration and swelling of cornea that leads to higher CCT values in diabetic population¹⁵. Evaluation of corneal morphological parameters including CCT has been done worldwide with conflicting reports. Corneal morphological parameters do differ among various races and ethnic groups with age being the major confounding factor. In this study, both groups were age matched to eliminate the age related bias in CCT measurement among groups. In our study, Mean CCT of diabetic population was significantly higher as compared to normal controls ($512.21 \pm 32.68 \mu\text{m}$ vs. 498.83 ± 28.98 ; $p = 0.001$). Significantly Thicker CCT values in diabetic population as compared to healthy controls had been reported in various other studies^{4,7-9,15-19}. Modis et al in their study found significantly higher CCT values in type I diabetics as compared to controls, whereas in type II diabetics the difference was not statistically significant²⁰. Roszkowska et al reported that pachymetric values were significantly altered in both type 1 and type 2 diabetic groups, with values being higher in type 1 diabetics²¹. On the contrary, there are studies which documented that diabetic subjects did not differ from non-diabetic controls with regard to CCT^{5,10,11,22,23}. Habib et al in their study found no significant difference in pachymetry values between diabetic and non-diabetics in Pakistani population²⁴.

In our study, severity of DR did not have a significant effect on CCT. Ozdamar et al⁸, Inoue et al¹⁰ and El-Agamy et al²² also reported that all diabetic groups (No DR, NPDR and PDR) had no significant difference in pachymetry values. Whereas, Parekh et al reported that CCT values were significantly higher in patients with moderate to severe NPDR and PDR as compared to patients with no or mild DR²³. Regarding comparison of CCT values in patients with DM duration of ≤ 10 years and those with DM duration of > 10 years, no statistically significant difference was detected. Briggs et al and Habib et al reported thicker corneas in patients with > 10 years of DM but the difference was statistically non significant^{18,24}. However, Lee et al and Urban et al reported significantly higher CCT in diabetics with > 10 years of duration^{4,25}. In our study, comparison of the mean values of CCT in diabetic patients with HbA1c $\leq 7.5\%$ and those with HbA1c $> 7.5\%$ showed no significant difference. Similar results are quoted by El-Agamy et al²² in their work, whereas, Gupta et al¹⁹ in their study

reported significantly thicker corneas in patients with HbA1c levels of $> 7.0\%$.

Correlation between CCT and various systemic and ocular variables such as duration of DM, plasma glucose level, HbA1c level and severity of DR had been extensively evaluated worldwide. In our study, duration of DM, HbA1c, and severity of DR did not showed any significant correlation with CCT. Non-significant correlation of duration of DM, HbA1c, and severity of DR with corneal endothelial parameters had been found in various studies worldwide^{5,7,22}. However, there are studies that showed significant correlation of CCT with duration of DM, HbA1c level and severity of DR^{4,23,25}

The strength of this study was the appropriate sample size, age matched groups, and prospective data collection. Limitations of the study include lack of multivariate analysis, not performing gold standard test (glucose tolerance test) to exclude diabetes in controls and not taking into account possible confounding factors like smoking, IOP and corneal diameter. Results of this study provide a greater insight into the understanding of corneal morphology in diabetic population especially in the context of pre-operative evaluation and glaucoma diagnosis. In fact, Blue Mountains eye study showed persons with diabetes are thought to be at higher risk of glaucoma²⁶. Therefore it is recommended that thicker CCT associated with DM must be taken into consideration while measuring IOP in diabetics.

CONCLUSION

Mean pachymetry values were found to be significantly thicker in diabetic population as compared to healthy controls. However, duration of DM, HbA1c, and severity of DR did not showed any significant correlation with CCT.

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Role of Author

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