

## CHANGES IN CENTRAL CORNEAL THICKNESS IN DIABETES MELLITUS PATIENTS

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### ABSTRACT

#### BACKGROUND

India has emerged as the diabetes capital of the world. A large percentage of these patients have metabolically uncontrolled Diabetes Mellitus. High glucose level has deleterious effect on corneal endothelial health due to various mechanisms and is associated with changes in central corneal thickness (CCT). We intend to compare the CCT of established DM patients with normal population and correlate its impact with increasing diabetic population.

The objectives of the study were to evaluate the effect of diabetes mellitus on central corneal thickness (CCT) by comparing the CCT of diabetic and non-diabetic patients and association of CCT with duration of diabetes mellitus.

#### MATERIALS AND METHODS

The study group was composed of 53 non-diabetic (29 male and 24 female) and 50 diabetic subjects (15 male and 35 female). Among the diabetic subjects, 27 out of 50 had diabetes of less than 10 years of duration and 23 had diabetes for more than 10 years. The CCT assessment was done for 105 eyes of 53 non-diabetic subjects and 100 eyes of 50 diabetic subjects with Sonomed Pacscan Plus, an ultrasound pachymeter, in the multiple reading single point mode. Each CCT considered in study was the average of 5 readings with standard deviation less than 0.003mm.

#### RESULTS

The statistical difference in the CCT between diabetic (524.264±29.21 microns) and non-diabetic (513.228±30.81 microns) group was significant (two-tailed P value is 0.0167 – Mann-Whitney test). When the CCT of non-diabetic group was compared with those with diabetes of less than 10 years duration, it was not significant (p value 0.13); and those with diabetes of more than 10 years duration, the difference was significant (p value 0.0216). The statistical difference between male and female in either group was not significant.

#### CONCLUSION

With rapid increase in number of diabetic patients, it is necessary to evaluate its effect on cornea, especially in the pre-operative work-up. A thickened cornea in diabetic patients needs to be evaluated for its functional and morphological characteristics.

#### KEYWORDS

Diabetes; Pachymeter; Central Corneal Thickness.

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#### BACKGROUND

Diabetes mellitus has emerged as an important cause of concern because of its adverse pathological effects on various ocular tissues. India and China already have the largest diabetic populations in the world.<sup>1</sup> The corneal changes associated with diabetes mellitus, known as diabetic keratopathy, can present in the form of decreased corneal sensation,<sup>2</sup> epithelial disorders such as superficial

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punctuate keratitis and epithelial erosion,<sup>3</sup> markedly thickened basement membrane of epithelium.<sup>4</sup> Diabetic patients with higher serum HbA1c levels are more predisposed to impaired corneal epithelial barrier function.<sup>3</sup> Glucose can act as a collagen cross-linking agent with the help of advanced glycosylation end products. Advanced Maillard 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>5</sup>

The corneal endothelium in diabetic patients is considered as a tissue under continuous metabolic stress<sup>6</sup> and it has increased coefficient of variation of endothelial cell area, decreased percentage of hexagonality and increased corneal autofluorescence.<sup>7</sup>

The central corneal thickness denotes the overall functional status of cornea as it is dependent on normal function of all the layers of cornea. This study evaluates the

effect of diabetes mellitus on central corneal thickness (CCT) by comparing the CCT of diabetic and non-diabetic patients and association of CCT with duration of diabetes mellitus.

**MATERIALS AND METHODS**

The study group was composed of 53 non-diabetic (29 male and 24 female) and 50 diabetic subjects (15 male and 35 female). Among the diabetic subjects, 27 out of 50 had diabetes of less than 10 year of duration and 23 were diabetic for more than 10yrs.

A thorough anterior and posterior segment evaluation was done. Patients with corneal pathologies example pterygium, keratoconus, corneal degeneration, corneal dystrophies, contact lens users, any prior history of ocular surgeries were excluded from the study.

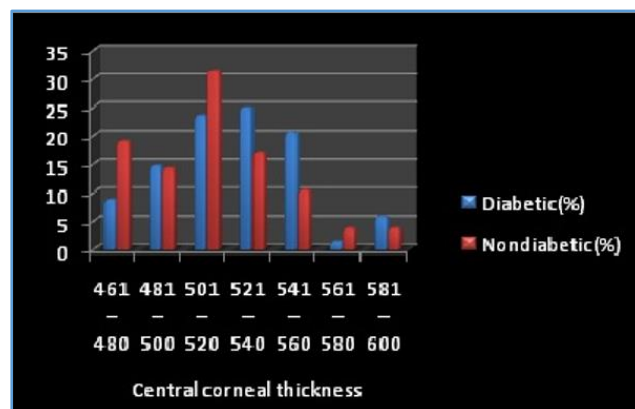
The corneal thickness assessment was done for 105 eyes of 53 non-diabetic subjects and 100 eyes of 50 diabetic subjects with the help Sonomed Pacscan Plus, an ultrasound pachymeter, in the multiple reading single point mode. Each corneal thickness considered in study was the average of 5 readings with standard deviation less than 0.003mm.

**RESULTS**

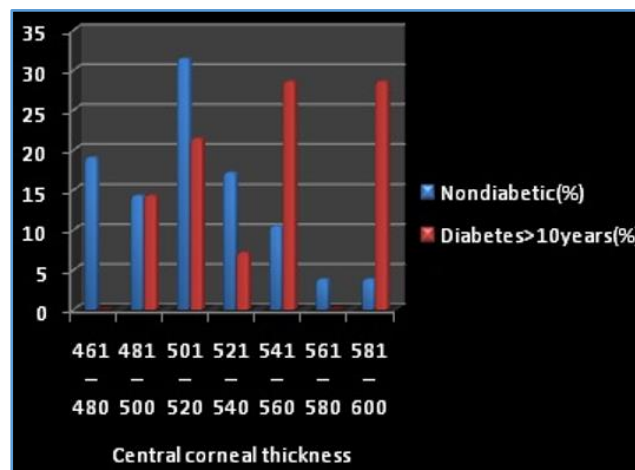
The mean corneal thickness for the entire study group was  $517.56 \pm 30.59$  micron. For non-diabetic subjects, it was  $513.22 \pm 30.81$  micron and for diabetic subjects it was  $524.26 \pm 29.21$ micron as shown in figure 1. The CCT was higher in diabetic group and the statistical difference was significant (two-tailed P value is 0.0167 - Mann-Whitney test) when compared with the non-diabetic group.

Among the diabetic subjects, those who had diabetes for more than 10 years, had higher mean CCT ( $544.64 \pm 34.78$  micron) than those having it for less than 10 years ( $518.98 \pm 25.38$  micron). When the statistical difference was considered between the non-diabetics and the group with diabetes for more than 10year duration as shown in figure 2, it was significant (p value 0.0216).The difference of CCT between non-diabetics ( $513.22 \pm 30.81$  micron) and those who had diabetes for less than 10year duration ( $518.9 \pm 25.38$ ) was not significant (p value 0.13) as shown in figure 3.

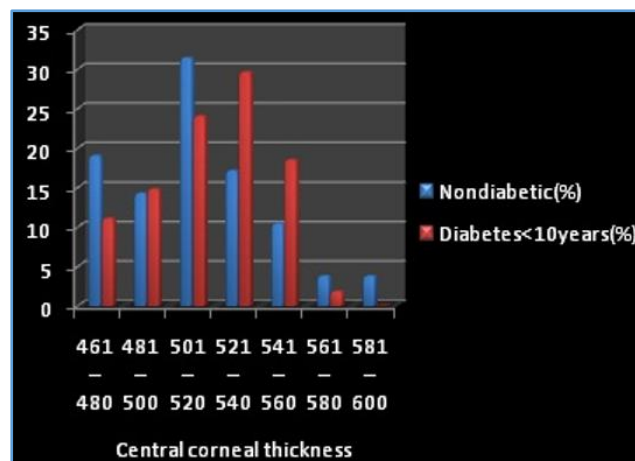
The CCT for male subjects in diabetic group was  $528.433 \pm 30.91$  micron and in non-diabetic group was  $512.21 \pm 29.04$  micron. Female subjects in the diabetic group had central corneal thickness of  $520.97 \pm 27.77$  micron and in non-diabetic group  $514.43 \pm 33.06$  micron. The statistical difference between male and female in either group was not significant.



**Figure 1. The Number of Diabetic and Non-diabetic Eyes Falling in Different Corneal Thickness Group**



**Figure 2. Comparison of Central Corneal Thickness between Non-diabetic Eyes and Diabetic Eyes of more Than 10 Years Duration**



**Figure 3. Comparison of Central Corneal Thickness between Non-diabetic Eyes and Diabetic Eyes of Less than 10 years Duration**

**DISCUSSION**

Diabetic Keratopathy is a spectrum of changes occurring in cornea of diabetic patients. Glucose with advanced glycosylation end product acts as cross linking agent to increase the covalent bond in corneal stroma and eventually its thickness. The central corneal thickness (CCT) in diabetic patients signifies the overall functional and morphological

status of cornea.<sup>8</sup> It has been reported as a sensitive indicator of early diabetic keratopathy.<sup>9</sup> Measurement of corneal thickness is important for correct measurement of intra-ocular pressure.

CCT of entire study group - The mean CCT for the entire study group was  $517.56 \pm 30.59$  micron, which is in accordance with another study done for Indian eyes by Nangia et al ( $514 \pm 33$  micron).<sup>10</sup> They reported that Indians from rural Central India have markedly thinner corneas than do Caucasians or Chinese.

CCT in males vs. females - In this study, the mean CCT for male subjects was higher in diabetic group ( $528.43 \pm 30.91$  micron) in comparison to female subjects ( $520.97 \pm 27.77$  micron) but it was lower in non-diabetic group ( $512.21 \pm 29.04$  micron for male and  $514.43 \pm 33.063$  micron for female). The statistical difference was not significant (p value 0.29 and 0.71 respectively in diabetic and non-diabetic group) in either of the group. Another study done for Indian eye have reported the mean CCT for the population as  $511.4 \pm 33.5$  micron, and CCT in males ( $515.6 \pm 33.8$  micron) was significantly (P = 0.0001) greater than females ( $508.0 \pm 32.8$  micron).<sup>11</sup>

CCT in diabetics Vs non-diabetics - Study conducted by Claramonte et al<sup>12</sup> to assess the effect of diabetes on CCT, showed a significant relationship between diabetes and CCT. CCT in diabetics in their study was 571.96 microns and in non-diabetics, it was 544.89 microns. In our study, the CCT was higher in diabetic group ( $524.26 \pm 29.21$  micron) than the non-diabetic group ( $513.22 \pm 30.81$  micron) and the statistical difference was significant (two-tailed P value is 0.0167 – Mann-Whitney test) when compared with the non-diabetic group.

The relation between CCT and diabetes mellitus has been reported differently in various studies. The study published by Keoleian<sup>7</sup> et al, to evaluate the structural and functional status of the corneal endothelium in diabetes mellitus, the functional status of corneal endothelium was unaffected despite of their structural abnormality. They reported no significant difference in corneal thickness in diabetic patients. Another study conducted in Japan<sup>13</sup> also reported no relation between CCT and diabetes.

CCT and its relation to duration of diabetes mellitus - Study conducted to assess the relation between corneal thickness and the duration of diabetes conducted by Lee et al<sup>14</sup> reported that patients with diabetic duration of over 10 years have more corneal morphological abnormalities compared with the normal subjects. The CCT was found to be significantly correlated with diabetic duration after controlling for age. In our study also, the mean corneal thickness in subjects with diabetes of more than 10 year duration was higher ( $544.64 \pm 34.78$  micron) than those having it for less than 10 years ( $518.98 \pm 25.38$ ). When the statistical difference was considered between the non-diabetics and the group with diabetes for more than 10yr duration, it was significant (p value 0.0216). The difference of central corneal thickness between non-diabetics ( $513.22 \pm 30.81$  micron) and those who had diabetes for less than 10year duration ( $518.98 \pm 25.38$ ) was not significant (p

value 0.13). The statistical difference of CCT between the diabetics of more than 10 year duration and diabetics of less than 10 year duration was again significant (p value 0.002).

## CONCLUSION

With rapid increase in number of diabetic patients, it is necessary to evaluate its effect on cornea. Unlike diabetic retinopathy, diabetic keratopathy is a lesser studied pathology. A thickened cornea in diabetic patients, especially diabetics of longer duration (more than 10 year), needs to be evaluated for its functional and morphological characteristics. This is especially important in the pre-operative work-up, for donor tissue evaluation prior to keratoplasty, true measurement of intraocular pressure, as coexisting pathology with other corneal conditions, long time contact lens users etc. As the basic histopathological change is formation of covalent bonds in corneal stroma, it would be interesting to study the relation between diabetic keratopathy and corneal ecstatic conditions like keratoconus.

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