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Relationship Between Central Corneal Thickness and Type 2 Diabetes: A Case Control Study

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ABSTRACT

The prevalence of diabetes has led to its recognition as a significant global health issue due to its numerous detrimental impacts on ocular tissue. The objective of this study is to examine the impact of diabetes on corneal thickness, specifically in relation to the duration of the disease and the level of glycosylated haemoglobin. A case-control study was conducted at a tertiary eye care centre in central India from May 2019 to April 2020. The study included a total of 200 patients, with 100 individuals diagnosed with type 2 diabetes and 100 individuals without diabetes. In addition to conducting a comprehensive ophthalmic examination, an assessment of the central corneal thickness (CCT) was performed for each eye using an ultrasound pachymeter. A blood analysis was conducted to assess the HbA1c concentration in individuals with diabetes. The average central corneal thickness (CCT) in individuals with diabetes was found to be 564.541±24.56 µ, while in those without diabetes it was 519.453±25.98 µ. The observed difference between the two groups was determined to be clinically significant ($p<0.002$). The average duration of diabetes was 9.478±1.7 years. The central corneal thickness (CCT) was observed to be greater in individuals with diabetes who had a duration of more than 10 years compared to those with a duration of less than 10 years ($p = 0.115$). Similarly, the CCT was found to be higher in individuals with a HbA1c level greater than 6.5% compared to those with a HbA1c level less than 6.5% ($p = 0.231$). However, it is important to note that these differences did not reach statistical significance. There is a notable disparity in corneal thickness between individuals with diabetes and those without the condition. The assessment of central corneal thickness (CCT) is essential in the evaluation of diabetic patients to determine the functional condition of the thickened cornea, as there exists a clear correlation between CCT and diabetes.

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Key Words
Central corneal thickness, pachymeter, diabetes, glycosylated hemoglobin

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INTRODUCTION

Diabetes mellitus is a medical condition characterised by abnormally high levels of glucose in the blood, a condition known as hyperglycemia. This syndrome is typically accompanied by long-term complications affecting both small blood vessels (microvascular) and large blood vessels (macrovascular). Patients with diabetes mellitus frequently develop keratoepitheliopathy, which includes persistent epithelial defects, recurrent corneal erosion and superficial punctate keratitis, in addition to diabetic retinopathy[1,2]. The primary manifestations of diabetes in ocular tissues encompass retinopathy, cataract formation and glaucoma. Diabetic keratopathy, a less extensively investigated pathology, refers to the corneal changes that occur in individuals with Diabetes mellitus[3]. The condition can manifest in various ways, such as reduced corneal sensitivity, epithelial disorders like superficial punctate keratitis and epithelial erosions and a thickened basement membrane[4,5]. Elevated levels of glycosylated haemoglobin in the bloodstream are associated with an increased susceptibility to impaired corneal epithelial barrier function. The utilisation of glucose as a collagen cross-linking agent is facilitated by advanced glycosylation end products. The accumulation of advanced millard products within collagen proteins gives rise to the formation of covalent cross-linking bonds, potentially leading to an increase in corneal thickening and associated biochemical alterations[6]. Elevated concentrations of glycosylated haemoglobin in the bloodstream have been found to potentially contribute to the compromised integrity of the corneal epithelial barrier[3]. Collagen cross-links can be formed by glucose in the presence of advanced glycosylated end products. The authors assert that there is an augmentation of covalent bonding within the corneal stroma, potentially resulting in an elevation of corneal thickness[4]. Corneal hydration is caused by the intracellular accumulation of sorbitol, which functions as an osmotic agent, as indicated by several studies. The inhibition of Na+K+ ATPase activity results in the suppression of the corneal endothelial pump function, which subsequently leads to an elevation in corneal thickness. The corneal endothelium in individuals with diabetes is regarded as a tissue that experiences ongoing metabolic stress. This condition is characterised by an elevated coefficient of variation of endothelial cell area, a reduced percentage of hexagonality and an increased level of corneal autofluorescence[7,8]. The measurement of central corneal thickness is a highly responsive indicator of corneal health, functioning as a valuable metric for assessing corneal hydration and metabolism. Additionally, it is a significant determinant of the functionality of the corneal endothelium pump and its assessment can be conducted through various objective techniques such as optical pachymetry, ultrasound pachymetry, confocal microscopy, ultrasound biomicroscopy, optical ray path analysis, scanning slit corneal topography and optical coherence tomography[9]. The current gold standard for measuring corneal thickness is ultrasound pachymetry[10]. The purpose of this study was to investigate the association between type 2 diabetes mellitus and central corneal thickness in patients seeking medical care at a tertiary care institute in Central ,India.

MATERIAL AND METHODS

The researchers obtained ethical clearance from the institutional ethical committee in order to conduct a case control study at their tertiary eye care centre. A total of one hundred individuals with diabetes, previously diagnosed by medical professionals, were included in the study. Participants were enrolled regardless of their current treatment status or blood sugar levels, provided that they provided informed consent. A total of one hundred age-matched individuals without a history of diabetes and with normal blood sugar levels were also included in the study. Participants with corneal pathologies such as pterygium and corneal dystrophies, individuals who use contact lenses, those undergoing treatment for topical or systemic diseases and individuals with a history of ocular surgeries were not included in the study. A comprehensive assessment of both the anterior and posterior segments was conducted.

The assessment of corneal thickness was conducted on a total of 200 eyes, consisting of 100 eyes from diabetic patients and 100 eyes from non-diabetic patients. This evaluation was performed using an ultrasound pachymeter known as Sonomed Pacscan Plus, utilising the multiple reading single point mode. It is important to note that all measurements were taken by a single individual. The final reading was determined by calculating the average of five readings, each with a standard deviation of less than 0.003mm.

RESULTS

The average age of the participants in the study was 45.85 years. Figure illustrates that 54% of the participants were identified as males, while the remaining 46% were identified as females. Over 40% of participants in both the case-control studies belonged to the age bracket of 41-50.

The average CCT for the entire study group was determined to be 527.341±30.56 µ. The mean glucose level for diabetic subjects was 564.541±24.56 µ, while for non-diabetic subjects it was 519.453±25.98 µ

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

Patients	No.	Mean CCT (μ)	SD (±)	p-value	95% CI
Diabetic	100	564.541	24.56	<0.002	4.4-8.9
Non-diabetic	100	519.453	25.98		

Table 2: Gender distribution with mean CCT in diabetic group

Gender	n	Mean CCT (μ)	SD (±)	p-value
Male	70	578.87	30.12	p = 0.256
Female	30	551.78	29.11	

Table 3: Central corneal thickness with duration of diabetes and with glycemic control

Duration of diabetes	No.	Mean CCT (μ)	SD (±)	χ^2	p-value
<10 years					
<5 years	16	548.76	25.78	2.178	p = 0.115
5-10 years	44				
>10 years	40	576.89	16.87		

Table 4: Central corneal thickness with glycemic control

HbA1c	No.	Mean CCT (μ)	SD (±)	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 1). The CCT was found to be significantly higher in the group of individuals with diabetes compared to the control group, as indicated by statistical analysis. 0 31-40 41-50 51-60 61-70 The observed difference in the measured variable between the diabetic group and the non-diabetic group was found to be statistically significant (p<0.002, as determined by the Mann-Whitney test).

Table 2 shows the average corneal cross-linking time (CCT) in male patients within the diabetic group was found to be higher (578.87±30.12 μ) compared to females (551.78±29.11 μ). However, this difference was not statistically significant, as indicated by a p = 0.256 (Table 2). Individuals diagnosed with diabetes and HbA1c levels below 6.5% exhibited a central corneal thickness (CCT) of 548.22±21.7 μ. Conversely, those with HbA1c levels exceeding 6.5% demonstrated a higher CCT of 568.12±27.5 μ. However, it is important to note that this disparity in CCT between the two groups was not found to be statistically significant (p = 0.231) according to Table 2.

Table 3 shows Among the sample of 100 individuals diagnosed with diabetes, a significant proportion exhibited a diabetes duration ranging from 5-10 years, with a mean duration of 9.478±1.7 years. The average central corneal thickness (CCT) in individuals with diabetes who had a disease duration of more than 10 years was found to be higher (576.89±16.87 μ) compared to those with a disease duration of less than 10 years (548.76±25.78 μ), suggesting a positive correlation. However, statistical analysis indicated that this difference was not statistically significant (p = 0.115) (Table 4).

DISCUSSIONS

Diabetic keratopathy refers to a range of corneal changes that occur in individuals with diabetes. Our study revealed that individuals diagnosed with diabetes demonstrate a statistically significant increase in the mean central corneal thickness compared to those without diabetes. There exist numerous hypotheses to elucidate this phenomenon. Several studies have reported that a decrease in the activity of Na+K+ATPase directly hinders the functioning of the corneal endothelial pump. Conversely, other studies have elucidated that the intracellular buildup of sorbitol, an osmotic agent, leads to corneal hydration. Recent studies have indicated that advanced glycosylated end products (AGEs) may serve as cross-linking agents, leading to an augmentation in the covalent bonding within the corneal stroma and subsequently resulting in an increase in its thickness. The corneal confocal microscopy (CCM) technique in individuals with diabetes provides valuable insights into the comprehensive functional and morphological condition of the cornea[11]. The measurement in question has been identified as a reliable indicator of early diabetic keratopathy and is also considered a significant parameter for refractive surgery and the estimation of intraocular pressure (IOP)[12]. In the present investigation, the average central corneal thickness (CCT) of the entire cohort was determined to be 527.341±30.56 μ. This finding exhibits notable disparity when compared to the results obtained in a prior study conducted by Nangia et al on Indian eyes, where the mean CCT was reported as 514±33.0 μ[13]. According to their findings, individuals from rural central India exhibit significantly thinner corneas compared to both Caucasians and Chinese populations. The inclusion of a larger proportion of individuals from urban areas in our study, specifically within a tertiary eye centre, may potentially explain the observed variations in results when compared to previous studies.

The association between CCT and diabetes mellitus has been documented with varying findings across multiple studies[2,14]. In our investigation, the average central corneal thickness (CCT) among individuals with diabetes was determined to be 565.98±30.02 μ, while among those without diabetes it was found to be 514.56±30.02 μ. Notably, a statistically significant difference was observed between the two groups (p = 0.0124, Mann-Whitney test). In a comparable investigation, Claramonte *et al*.[15] demonstrated a noteworthy correlation between diabetes and central corneal thickness (CCT). The average central corneal thickness (CCT) among individuals with diabetes in the conducted study was found to be 571.96 μ, whereas non-diabetic individuals had an average CCT of 544.89 μ. This disparity was determined to be statistically significant[14]. In contrast, Keoleian *et al*.[8] conducted a study aimed at assessing the structural and functional condition of the corneal endothelium in individuals with diabetes. Their findings led them to conclude that,

despite the presence of structural abnormalities, the functional integrity of the corneal endothelium remained unaltered in this population[10]. The researchers observed that there was no statistically significant variation in corneal thickness among individuals diagnosed with diabetes. An additional study conducted in Japan similarly found no significant association between central corneal thickness (CCT) and diabetes[15]. The average central corneal thickness (CCT) for male participants in the diabetic group in this study was found to be higher (528.87±30.12 μ) compared to the female participants (521.78±29.11 μ). Conversely, in the non-diabetic group, the male participants had a lower average CCT (519.65±28.41 μ) compared to their female counterparts (524.89±26.19 μ). There was no statistically significant difference observed in either of the groups, with p = 0.32 and 0.54, respectively. A recent study conducted on Indian individuals has revealed a notable disparity in central corneal thickness (CCT) between males (515.6±33.8 μ) and females (508.0±32.8 μ), with a statistically significant p = 0.001[16]. Lee *et al*.[17] conducted a study to investigate the impact of diabetes duration on corneal thickness. The findings of their research revealed that individuals with a diabetic duration exceeding 10 years exhibited a higher prevalence of corneal morphological abnormalities in comparison to those without diabetes[17]. In our study, we observed that the average central corneal thickness (CCT) in individuals with diabetes lasting more than 10 years was significantly higher (544.64±34.56 μ) compared to those with a duration of less than 10 years (518.98±31.21 μ). McNamara *et al*.[18] (year) conducted a study in which they observed a positive correlation between the level of HbA1c and central corneal thickness (CCT) in individuals with Type 1 diabetes. Additionally, they reported thicker corneas in individuals with diabetes. However, they did not find a direct correlation between HbA1c level and CCT in individuals with Type 2 diabetes, which aligns with the findings of our study[18]. Yasgan *et al*.[19] further substantiated this observation.

CONCLUSION

A notable association was observed between the augmentation of central corneal thickness (CCT) and the presence of diabetes. Moreover, a positive correlation was identified between thicker corneas and the duration of diabetes, suggesting that individuals with thicker corneas are more prone to being diagnosed at an advanced stage of the disease. The mandatory measurement of central corneal thickness (CCT) in diabetic patients is particularly crucial in various clinical scenarios, such as preoperative assessment for refractive surgery, evaluation of donor tissue prior to keratoplasty, individuals suspected of having glaucoma and long-term users of contact lenses. This approach may facilitate the identification of patients who are at an elevated risk of experiencing severe complications, thereby enabling ophthalmologists to administer more precise treatment for their respective conditions. The assessment of central corneal thickness (CCT) in conjunction with the examination of the corneal endothelium can offer additional valuable information for the accurate assessment of patients in terms of their functional outcome. Given that the fundamental histopathological alteration involves the development of covalent bonds within the corneal stroma, it is essential to investigate the potential association between diabetic keratopathy and corneal ectatic conditions.

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