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Study on the effect of diabetes mellitus on corneal thickness

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Abstract
Background: This study was conducted to compare the effect of diabetes mellitus on corneal thickness.
Material and Methods: A total of 100 participants ware observed, among which 50 participants (100 eyes) are diabetes mellitus and 50 non-diabetic participants (100 eyes). The central and paracentral corneal thickness were examined in all eyes using Optical Coherence Tomography. The epithelium thickness was also measured at central and para-central area of cornea.
Results: T-test for independent means was used to compare the corneal thickness between both diabetic and non-diabetic groups and $p<0.05$ was considered statistically significant. The increase in corneal thickness for all the gazes i.e. central, superior, inferior, nasal and temporal found in diabetic participants compared to non-diabetic participants was statistically significant ($p<0.00001$) but the changes in epithelium thickness found in diabetic patients and non-diabetic participants were not statistically significant.
Conclusion: This study documented that there is significantly changes in corneal thickness at all gazes in diabetic participants a comparison to non-diabetic participants. Thicker cornea associated with diabetes mellitus should be taken into consideration while obtaining accurate intraocular pressure measurements in diabetics.

Keywords: corneal thickness, diabetes mellitus, epithelium thickness

Introduction

Diabetes mellitus is a group of metabolic diseases that is caused by high sugar or glucose intake. The main characteristic of diabetes mellitus is because of the hyperglycemia that is resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetics affects body organs and is associated with long-term damage, dysfunction and failure of various organs especially eyes, kidneys, nerves, heart, and blood vessels. Many pathogenic processes occurs due to the development of diabetes. The basis of the abnormalities in carbohydrate, fat, and protein metabolism in diabetes is deficient action of insulin on target tissues. Deficient insulin action results from inadequate insulin secretion and/or diminished tissue responses to insulin at one or more points in the complex pathways of hormone action. The impairment of insulin production and its secretion causes diabetes mellitus [4].

Complications related to diabetes in eye: The primary complications of diabetes due to damage in small blood vessels include damage to the eyes. Damage to the eyes, known as diabetic retinopathy, is caused by damage to the blood vessels in the retina of the eye, and can result in gradual vision loss and eventual blindness. Diabetes also increases the risk of having glaucoma, cataracts, and other eye problems [5].

Cornea: Cornea is a transparent, avascular tissue comprises one-sixth of the anterior eyeball. Cornea and sclera forms outer coat of the eyeball and protects the inner structure of the eye [9]. The tear film present over the cornea provides proper anterior refractive surface for the eye. The cornea has about +43D of refractive power which is around two-third of the total refractive power of eye [3].

Blood Supply of the Cornea: Although the normal human cornea is avascular, it relies on components of the blood to remain healthy. These components are supplied by tiny vessels at the outermost edge of the cornea as well as components supplied by end branches of the facial and ophthalmic arteries via the aqueous humor and tear film.
Nerve Supply of the Cornea: The cornea is one of the most heavily innervated and most sensitive tissues in the body. Corneal nerves and sensation are derived from the nasociliary branch of the first (ophthalmic) division of the trigeminal nerve [8]. In the superficial cornea, the nerves enter the stroma radially in thick trunks forming plexiform arrangements, which eventually perforate Bowman membrane to provide a rich plexus beneath the basal epithelial layer. The cornea also contains autonomic sympathetic nerve fibers [1].

Optical Coherence Tomography (OCT): OCT is a technique that provides two dimensional cross-sectional image of eye that provides imaging of anterior and posterior segments detail of human eyes. This machine uses low coherence, near infrared light with detailed images of anterior and posterior segment with high resolution [6].

Anterior segment imaging: OCT evaluated and measured pre and post operatively after image acquisition, using the analysis mode of the system's software. OCT provide AC depth, anterior chamber angles and anterior chamber diameter. Anterior chamber angle measurement results provide quick and reliable data for narrow angle evaluation [9].

Corneal imaging and Pachymetry: OCT provide high resolution corneal topography images and documentation for anterior segment to support evaluation of ocular health. Rapid acquisition during pachymetry scan ensures an accurate and repeatable pachymetry map result for application in refractive and glaucoma care.

New LASIK information: It also provide full thickness pachymetry map that is helpful prior to LASIK surgery, OCT is first non-contact device to image, measure and document both corneal flap thickness and residual stromal thickness immediately follow LASIK surgery [2].

Methodology

Study Site: This study was conducted from Grewal Eye Institute, Chandigarh, India.

Study Design: This is a comparative study which was distributed to 100 participants. OCT cornea has been done of all the diabetic and non-diabetic participants to check the corneal thickness.

Study Duration: The duration of study was about three months (Jan 2020 to March 2020).

***Sample Size*:** A total number of 100 subjects (200 eyes) out of which 50 were diabetics and 50 were non diabetics (general public) were included in the study.

Study Procedure: The main objective of the study was to compare the corneal thickness between diabetic and non-diabetic patients at different gazes i.e. central, superior, inferior, nasal and temporal. Medical history of all the patients was taken regarding diabetes mellitus. Corneal and epithelial thickness of all the participants were collected from Pachymetry Analysis scan using Optical Coherence Tomography Cirrus 5000 machine (Carl Zeiss Meditec Inc., USA).

Statistical Analysis: The quantitative data was coded in Microsoft Excel for data analysis. Frequencies and measures of central tendency (mean) were computed for all the numerical data.

T-test of non-independence was used to compare the corneal thickness between both diabetic and non-diabetic groups. $p<0.05$ was considered statistically significant.

Results

The mean age of diabetic participants was 63 [Range- 40to 80] years and standard deviation (S.D.) was 10.21. In non-diabetic group, the mean age was 65.40 [Range- 40to 80] years and S.D was 8.66. In diabetic group, the ratio between male and female was 34:16 out of 50 diabetic participants and in non-diabetic group, the ratio between male and female was 27:23 out of 50 non-diabetic participants (Table 1).

Table 1: Characteristic of diabetic and non-diabetic groups

Characteristic	Diabetic group (n=100)	Non Diabetic group (n=100)
Age (years)		
Mean	63	65.42
S.D.	10.21603	8.661644
Range	40 to 80	40 to 80
Sex		
Male	34	27
Female	16	23

The mean central corneal thickness in diabetic participants was 544 [Range- 471 to 628] and S.D was 23.60. The average CCT found in non-diabetic participants was 506.45 [Range: 407 to 576] with S.D 29.95. The increase in CCT found in diabetic participants compared to non-diabetic participants was statistically significant ($p<0.00001$) (Table 2).

Table 2: Corneal Thickness of diabetic and non-diabetic participants

Characteristic	Diabetic group (n=100)	Non Diabetic group (n=100)	P value*
Central Corneal Thickness (µm)			
Mean	544	506.45	<0.00001
S.D.	23.60	29.95	
Range	471-628	407 to 576	
Superior Corneal Thickness (µm)			
Mean	586.05	545.06	<0.00001
S.D.	25.52	33.78	
Range	488 to 674	436 to 653	
Inferior Corneal Thickness (µm)			
Mean	548.26	513.37	<0.00001
S.D.	30.63	31.06	
Range	383-639	427 to 588	
Nasal Corneal Thickness (µm)			
Mean	559.49	521.48	<0.00001
S.D.	25.94	34.07	
Range	601 to 567	424 to 604	

*p value less than 0.05 considered significant

The mean superior corneal thickness in diabetic participants was 586.56 [Range-488 to 674] and S.D was 25.52. The

average superior corneal thickness found in non-diabetic participants was 545.06 [Range-436 to 653] and S.D was 33.78.The increase in superior corneal thickness found in diabetic participants compared to non-diabetic participants was statistically significant (p<0.00001) (Table 3).
The mean inferior corneal thickness in diabetic participants was 548.56 [Range-383 to 639] and S.D was 30. The average inferior corneal thickness found in non-diabetic participants was 513.37 [Range-427 to 588] and S.D was 31.06. The increase in Inferior corneal thickness found in diabetic participants compared to non-diabetic participants was statistically significant (p<0.00001) (Table 3).
The mean nasal corneal thickness in diabetic participants was 559.49 [Range-601 to 567] and S.D was 26.18. The average nasal corneal thickness found in non-diabetic participants was 521.16 with a range between of 415 to 624 with S.D value 33.01292064. The increase in Nasal corneal thickness found in diabetic participants compared to non-diabetic participants was statistically significant (p<0.00001) (Table 3).

Table 3: Epithelium Thickness of diabetic and non-diabetic participants

Characteristic	Diabetic group (n= 100)	Non-Diabetic group (n=100)	P value*
Central Epithelium thickness (µm)			
Mean	46.86	46.85	<0.49
S.D.	5.56	4.26	
Range	37 to 64	37 to 59	
Superior Epithelium thickness (µm)			
Mean	39.8	40.95	<0.05
S.D.	5.14	4.81	
Range	30 to 66	31 to 53	
Inferior Epithelium thickness (µm)			
Mean	46.7	46.75	<0.47
S.D.	5.77	4.44	
Range	35 to 73	35 to 62	
Nasal Epithelium thickness (µm)			
Mean	43.22	42.87	<0.31
S.D.	5.68	4.46	
Range	32 to 61	34 to 57	
Temporal Epithelium thickness (µm)			
Mean	44.38	43.91	<0.26
S.D.	6.51	3.73	
Range	32 to 81	34 to 51	

*p value less than 0.05 considered significant

The mean central epithelium thickness in diabetic participants was 43.86 [Range-37 to 64] and S.D was 5.56. The average central epithelium thickness found in non-diabetic participants was 46.85 [Range-37 to 59] and S.D was 4.26. The changes in central epithelium thickness found in diabetic participants and non-diabetic participants were not statistically significant (p<0.49) (Table 3).
The mean superior epithelium thickness in diabetic participants was 39.8 [Range-30 to 66] and S.D was 5.14. The average superior epithelium thickness found in non-diabetic participants was 40.95 [Range-31 to 53] and S.D was 4.81. The changes in superior epithelium thickness found in diabetic participants and non-diabetic participants were not statistically significant (p<0.05) (Table 3).
The mean inferior epithelium thickness in diabetic participants was 46.7 [Range-35 to 73] and S.D was 5.68. The average inferior epithelium thickness found in non-diabetic participants was 46.75 [Range-37 to 64] and S.D was 4.44. The changes in inferior epithelium thickness found in diabetic participants and non-diabetic participants were not statistically significant (p<0.47) (Table 3).
The mean nasal epithelium thickness in diabetic participants was 43.22 [Range-32 to 61] and S.D was 5.68. The average nasal epithelium thickness found in non-diabetic participants was 42.87 [Range-34 to 57] and S.D was 4.46. The changes in nasal epithelium thickness found in diabetic participants and non-diabetic participants were not statistically significant (p<0.31) (Table 3).
The mean temporal epithelium thickness in diabetic participants was 44.38 [Range-32 to 81] and S.D was 6.51. The average temporal epithelium thickness found in non-diabetic participants was 43.91 [Range-34 to 51] and S.D was 3.73. The changes in temporal epithelium thickness found in diabetic participants and non-diabetic participants were not statistically significant (p<0.26) (Table 3).

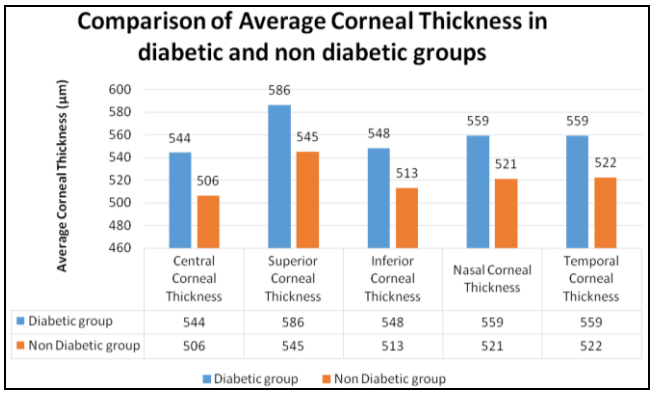

Fig 1: Comparison of average corneal thickness in diabetic and non-diabetic group

Figure 1 indicates the comparison of average corneal thickness in diabetic and non-diabetic groups. The average CCT in diabetic group is more i.e. 544µm as comparison to non-diabetic group i.e. 506µm. The superior corneal thickness in diabetic is 586µm and in non-diabetic group is 545µm so the superior corneal thickness is also higher than non-diabetic group. 548µm is inferior corneal thickness is measured in diabetic group which is also greater than non-

diabetic groups i.e. 513µm. Nasal corneal thickness in diabetic group is 559µm and in non-diabetic group was 521µm. The temporal corneal thickness is also greater in diabetic group i.e. 559µm and in non-diabetic group it was 522µm.

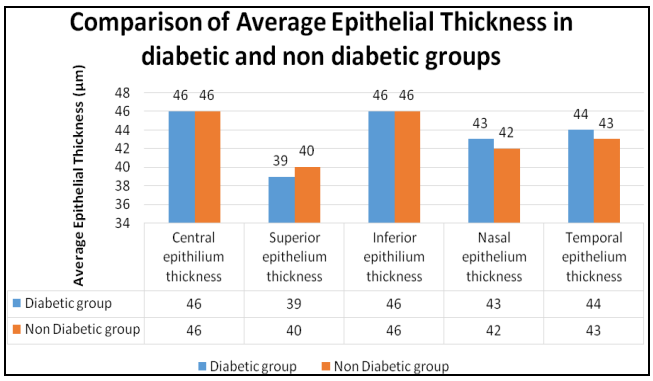

Fig 2: Comparison of average epithelium thickness in diabetic and non-diabetic group

The comparison of average epithelium thickness in diabetic and non-diabetic groups is shown in Figure 2. In both the diabetic and non-diabetic groups, the average epithelium thickness is 46µm. The superior epithelium thickness in diabetic group is 39µm and in non-diabetic group is 40µm. In both diabetic and non-diabetic group the inferior corneal thickness is also same i.e. 46µm. The nasal epithelium thickness in diabetic group is 43µm and in non-diabetic group, the nasal epithelium thickness is 42µm. The temporal epithelium thickness in diabetic group is 44µm and in non-diabetic group it is 43µm.

Discussion

In this study, the corneal thickness in both diabetic and non-diabetic groups were observed at central and paracentral area that included superior, inferior, nasal, temporal and central thickness. The epithelium thickness all measure in both groups at all gazes. It is concluded that corneal thickness of all the diabetic participants is thicker than that of non-diabetic participants but there was no significant changes in epithelium thickness in comparison to both groups. As increase in corneal thickness leads to high IOP and thin cornea may lead to low IOP, keratoconnus, keratoglobus. Corneal thickness is highly indication for high IOP and if IOP increases then there are the chances of glaucoma. Lee *et al*. measured CCT of diabetic patients with normal fundus and background diabetic retinopathy and found higher CCT values in patients with DM compared with control group. They also found that CCT correlated with diabetes duration. They reported that older diabetic patients had thicker corneas than younger diabetics owing to corneal endothelial pump dysfunction and increased hydration of cornea.

Conclusion

In conclusion, a significant correlation was found between increase CCT and diabetes, with positive correlation between thick cornea so it is mandatory to check the corneal thickness of diabetic patients so that it will help to identify the patient with high risk of developing severe complications. Sometimes thick cornea leads to glaucoma so it's necessary to every diabetic patient to take the opinion with glaucoma consultant. Diabetic mellitus leads to so many ocular diseases like diabetic retinopathy, diabetic macular edema, and cataract. Glaucoma is one of the main causes that occur in diabetic patients. As this study shows that imbalance level of glucose in diabetic patients leads to high corneal thickness that can cause glaucoma. It is very important to every diabetic person that their diabetes should be under control and always undergo to the retina checkup as well as glaucoma opinion once in a year if diabetes is under control. In any case, if diabetes is not in under control its mandatory to consult an ophthalmologist.

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