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ORIGINAL ARTICLE

Changes in Corneal Endothelial Cells in Patients with Type II Diabetes Mellitus

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Abstract

Background: Diabetes mellitus has toxic effects on all cells of the body. Cornea is no exception and structural and morphological alterations have been found in endothelial cells in diabetics. ***Purpose:*** To evaluate and compare central corneal thickness, and endothelial cell count and morphological characteristics between diabetics and non-diabetics and to determine the relation of these parameters with the diabetes duration. ***Material and Methods:*** This hospital based analytical observational study included 65 type II diabetics with good glycaemic control and 65 age-matched non-diabetics as control. The diabetics were further divided on the basis of duration of diabetes into two groups: ≤10 years and >10 years. The study parameters included central corneal thickness (CCT), endothelial cell density (ECD), coefficient of variation (CV) and percentage of hexagonal cells (% HEX) using Topcon specular microscope by the same observer. ***Results:*** Mean CCT was observed to be significantly greater in diabetic eyes (516.51 ± 20.83 µm) than in control group (507.42 ± 28.41 µm) (p=0.0391). Mean CV was higher in endothelial cells of diabetic corneas (34.20 ± 4.15) than non-diabetic corneas (32.89 ± 2.98) (p=0.041). The diabetic group had lower mean ECD and percentage of hexagonal cells than the control group, without any statistical significance (p=0.092 & p=0.085, respectively). Of 65 patients with diabetes, 29 were with duration of DM ≤10 years and 36 with duration of DM >10 years. No statistically significant difference was noticed on comparing the corneal parameters among these two diabetic groups. Also, no significant correlation was observed between these endothelial parameters and duration of diabetes. ***Conclusion:*** Diabetics have thicker corneas and increased polymegathism of endothelial cells in comparison to age-matched non diabetics, whereas density and hexagonality of endothelial cells was found to be similar between the two groups. The effect of diabetes duration on these endothelial parameters is insignificant in this study.

Key Words

Central corneal thickness, Coefficient of variation, Endothelial cell density, Hexagonal cells

Introduction

Diabetes is one of the fastest growing health concerns of the 21st century with the number of adults affected being tripled over the past 20 years (1). Diabetic retinopathy is a vision threatening complication of diabetes. Apart from the retina, diabetics have structural and morphological alterations in other parts of the eye including cornea, tear film and crystalline lens leading to alterations in the optical quality of the diabetic eye (2). Apparently, the cornea may be disease free in the diabetic, but it is vulnerable to abnormalities such as endothelial cell dysfunction, punctate epithelial keratopathy, recurrent corneal abrasions, and slow wound healing (3).

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Many studies have demonstrated structural differences in the endothelial cells of the diabetic cornea. These abnormalities comprise of decrease in the endothelial cell count, increase in central corneal thickness and variability in cell shape and size (4-6). Various studies have been conducted to detect any correlation between duration of diabetes and endothelial cell changes and they show contrasting results (6-8). These changes are attributable to the reduced activity of Na^+-K^+ pump in the endothelium of diabetic corneas. This pump action is indispensable for maintaining corneal deturgescence. The parameters to study the endothelial cell function include cell count, coefficient of variation and percentage of hexagonal shaped cells. In-depth analysis of these parameters is required to evaluate the impact of diabetes on corneal endothelium. So, this study was undertaken to assess the morphological features of endothelial cells and central corneal thickness in diabetics in contrast to age-matched non-diabetic controls. The association of these changes with duration of diabetes was also assessed.

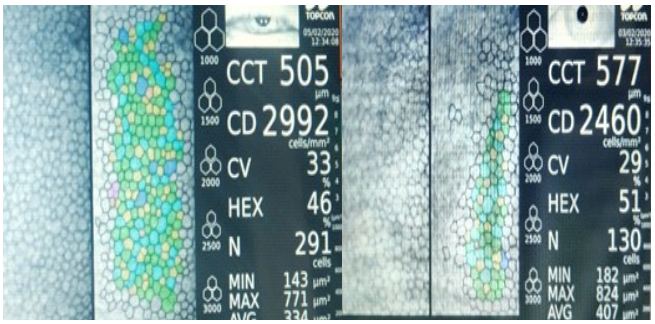
Material and Methods

This hospital based cross-sectional analytical observational study was conducted in the Department of Ophthalmology, Govt Medical College, Jammu, a tertiary care health centre of Northern India. The study was undertaken after obtaining approval from the 'Institutional Ethics Committee' of the College. The study consisted of two groups: Study group comprised of 65 type 2 diabetic patients with good control of blood sugar and control group consisted of 65 non-diabetics. The diabetic group was further divided into 2 groups on the basis of duration of diabetes mellitus (DM): one with a duration of DM ≤10 years and the other with a duration of DM >10 years.

Inclusion criteria were patients of either gender and ≥50 years of age. The diagnosis of type 2 diabetes mellitus was based on the criteria of the World Health Organisation (WHO) (9). Exclusion criteria: a) unwillingness to participate in the study; b) patients under the age of 50 years; c) insulin-dependent (type 1) diabetics; d) uncontrolled noninsulin dependent diabetics (HbA1c >7.5%); e) patients with high myopia (> -6D); f) corneal opacities/dystrophies or any condition that interferes with corneal evaluation by specular microscopy; g) uveitis/or any intraocular inflammation; h) glaucoma; i) previous history of trauma or ocular surgery or contact lens wear.

All the patients were recruited from OPD of the Ophthalmology Department by convenience sampling method and were examined by a senior resident. Each patient was explained about the details of the study and an informed written consent was taken before including them into the study. Age, gender, history of diabetes mellitus, duration of diabetes, most recent fasting blood glucose level, HbA1c value and past and current medical treatment were recorded. General physical examination and detailed local examination of eyes including uncorrected and best corrected visual acuity, slit-lamp examination, fundus examination, and IOP measurement were done.

Corneal endothelial cell density (ECD), morphological assessment [coefficient of variation (CV), percentage of hexagonal cells (% HEX)], and central corneal thickness (CCT) measurement were done using Topcon clinical specular microscope by the same person. The measurements were done three times and the average was taken (*Figure 1*).



a b

Figure 1: Corneal Endothelium Picture Taken by Topcon Clinical Specular Microscope. (a) A 56 Years Old Non-Diabetic Female and (b) 55 Years Old Diabetic Female

The data was entered in MS excel spreadsheet and statistical analysis was done using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp. Released 2017. Armonk, NY, USA). Categorical variables were documented in number and percentage (%) and continuous variables as mean ± SD. Comparison between the two groups for the continuous variables was made using independent-samples *t*-test. Chi-square test was used to analyse nominal categorical variables. Pearson correlation test was performed to detect any relationship between corneal changes and duration of DM. All statistical tests were carried out at 5% level of significance and $p < 0.05$ was considered as statistically significant.

Results

In this study, we compared the corneal endothelial cell parameters in 65 eyes of diabetic corneas with 65 eyes of nondiabetic corneas. In study group, 32 (49.23%) were males and 33 (50.77%) females whereas control group (non-diabetic) consisted of 41 (63.08%) males and 24 (36.92%) females. The mean age of the patients was 61.97 ± 5.54 years (range: 50 to 72 years) in diabetic group and 63.51 ± 7.29 years (range: 50 to 78 years) in non-diabetic group. The difference in age and gender distribution between both the groups was statistically not significant (p=0.178) and p=0.157 respectively). There were 29 patients with duration of DM ≤10 years and 36 with duration of DM >10 years. The mean duration of DM was 12.28 ± 4.59 years (range: 4 - 28 years).

Mean ECD was lesser in the diabetic group (2557.17 ± 243.31 cell/mm^2) than the control group (2630.69 ± 250.99 cell/mm^2) but the difference was not statistically significant (p=0.092). Mean CV was significantly more in the diabetic group (34.20 ± 4.15) than in the control group (32.89 ± 2.98) (p=0.041). Percentage of hexagonal cells was lesser in the diabetic group (56.83 ± 4.93%) than control group (58.23 ± 4.24%) but the difference was not statistically significant (p=0.085). Also, mean CCT was comparatively more in the diabetic group (516.51 ± 20.83 µm) than control group (507.42 ± 28.41 µm), and the difference was statistically significant (p=0.0391) (*Table 1*).

Eyes with duration of DM ≤10 years had higher mean ECD (2581.24 ± 164.58 cell/mm^2) than eyes with duration of DM >10 years (2537.78 ± 292.76 cell/mm^2), and they also had more percentage of hexagonal cells (57.38 ± 3.94%) than those with DM duration of >10 years (56.39 ± 5.61%), but the differences were not statistically significant (p=0.478 and p=0.425 respectively). Also, no significant differences in mean CCT (p=0.535) and CV (p=0.316) were found between the 2 groups (*Table 2*). Pearson correlation analysis showed no significant correlation of duration of diabetes with ECD, CV,

Table 1: Comparison of Mean Values of Corneal Endothelial Parameters Between Diabetics and Non-Diabetics

Corneal Parameters	Diabetics (n=65)			Non-Diabetics (n=65)			*p* value
	Mean ± SD	Min	Max	Mean ± SD	Min	Max	
ECD (cells/mm^2)	2557.17 ± 243.31	1687	2985	2630.69 ± 250.99	1926	3100	0.092
CV	34.20 ± 4.15	27	49	32.89 ± 2.98	24	44	0.041
HEX (%)	56.83 ± 4.93	33	64	58.23 ± 4.24	44	66	0.085
CCT (µm)	516.51 ± 20.83	469	582	507.42 ± 28.41	457	568	0.039

ECD= Endothelial Cell Density or Count; CV= Coefficient of Variation; HEX= Hexagonal Cells; CCT= Central Corneal Thickness; SD= Standard Deviation; Min= Minimum; Max= Maximum; n= Number of Eyes

Table 2: Comparison of Mean Values of Corneal Endothelial Parameters According to Duration of Diabetes in Diabetic Groups (Mean ± SD)

Corneal Parameters	Duration of Diabetes Mellites		*p* value
	≤10 Years (n=29)	>10 Years (n=36)	
ECD (cells/mm^2)	2581.24 ± 164.58	2537.78 ± 292.76	0.478
CV	33.62 ± 4.04	34.67 ± 4.24	0.316
HEX (%)	57.38 ± 3.94	56.39 ± 5.61	0.425
CCT (µm)	515.06 ± 21.56	518.31 ± 20.10	0.535

ECD= Endothelial Cell Density or Count; CV= Coefficient of Variation; HEX= Hexagonal Cells; CCT= Central Corneal Thickness; SD= Standard Deviation; n= Number of Eyes

Table 3: Correlation Between Corneal Changes and Duration of Diabetes

Corneal Parameters	Duration of Diabetes Mellites (Years)	
	Pearson Correlation	
	(*r* value)	(*p* value)
ECD (cells/mm^2)	-0.033	0.793
CV	0.047	0.710
HEX (%)	-0.101	0.425
CCT (µm)	0.053	0.673

ECD= Endothelial Cell Density or Count; CV= Coefficient of Variation; HEX= Hexagonal Cells; CCT= Central Corneal Thickness

hexagonality, or CCT (*Table 3*).

Discussion

The ocular complications of diabetes are most profound in the cornea and retina. 70% of diabetics have impaired corneal function described as diabetic keratopathy (10). The toxic effects of hyperglycaemia on the corneal endothelium hampers its ability to keep the cornea clear and increases its susceptibility to any form of stress. Multiple studies have been conducted to assess the morphological features of diabetic cornea with conflicting results. Our study provides data from diabetic population of North-India which will further aid in detecting the association of diabetes mellitus with endothelial cell characteristics.

In present study, we found increase in mean CCT of the cornea in diabetic group (516.51 ± 20.83 μm) as compared to controls (507.42 ± 28.41 μm) with the difference being statistically significant (p=0.03). Similar findings have been reported in many other studies. Kudva *et al.* (11), reported a mean CCT of 509.89 ± 30.32μm in diabetic cornea and 492.25 ± 19.41μm in non-diabetics and concluded that diabetics have a significantly thicker cornea than non-diabetics. Similarly, in a study conducted by Lee *et al.* (6), the mean central corneal thickness in the diabetic eyes was 588.2 ± 2.7 μm and in the non-diabetic eyes was 567.8 ± 3.8 μm (p<0.05). However, El-Agamy *et al.* (8) concluded that difference in CCT between diabetics and non-diabetics is insignificant.

Our study showed lower mean ECD in the diabetic group (2557.17 ± 243.31 cells/mm^2) as compared to non-diabetics (2630.69 ± 250.99 cell/mm^2) but the difference was of no significance (p=0.09). Like our study, Storr-Paulsen *et al.* (12) demonstrated that the mean ECD in diabetic subjects was 2578 ± 77 cells/mm^2 and in non-diabetics was 2605 ± 66 cell/mm^2 and the two groups did not differ with regard to ECD. On the contrary, studies conducted by Choo *et al.* (3) and Islam *et al.* (7) showed significantly lesser density in diabetic endothelial cells as compared to non-diabetics.

In our study, mean CV of diabetic patients was 34.20 ± 4.15 and non-diabetic patients was 32.89 ± 2.98. This difference was statistically significant (p=0.04) which suggests increased polymegathism in diabetic cornea. Similarly, study conducted by Choo *et al.* (3) also found significantly increased CV in diabetic corneal endothelium (67.2 ± 47.2) as compared to non-diabetics (58.2 ± 43.0). Lee *et al.* (6) also reported higher CV in diabetic group as compared to non-diabetics (p<0.05). However, study by Kudva *et al.* (11), showed that CV among these two groups was alike. Our study revealed insignificant difference in hexagonality on comparing the diabetic and non-diabetic groups (p=0.085). These results were supported by many other studies (8,13,14).

We also compared all these corneal endothelial parameters (CCT, ECD, CV and HEX) in diabetics ≤10 years duration with diabetics of >10 years duration. All these parameters showed no significant difference among these two diabetic groups. On conducting Pearson correlation analysis, the duration of DM had no significant correlations with CCT or any of the studied endothelial cell parameters. Like our study, many studies (8,14,15) have also reported no significant relation between duration of diabetes mellitus and corneal endothelial parameters.

Conclusion

Our study revealed that diabetics have increased baseline thickness of central cornea and increased polymegathism as compared to non-diabetics whereas the count and percentage of hexagonality of endothelial cells found to be similar between diabetics and non-diabetics. However, the time span of diabetes has no significant effect on these endothelial parameters.

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Conflicts of Interest

There are no conflicts of interest.

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