EFFECT OF DIABETES MELLITUS ON CENTRAL CORNEAL THICKNESS AND ENDOTHELIAL CELL COUNT

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ABSTRACT

BACKGROUND

The purpose of this study was to study the corneal endothelial cell density and morphological features in type 2 diabetic patients (cases) and compare it with non-diabetic subjects (Controls) in a population based cross sectional study.

MATERIALS AND METHODS

Patients were recruited from Sarojini Devi Eye Hospital and Corneal endothelial morphological features were recorded in all subjects using noncontact specular microscopy and central corneal thickness was measured using ultrasound pachymeter.

RESULTS

A total of 104 cases and 98 controls were enrolled into the study. The mean corneal endothelial cell density (cells/mm^2) was lower in cases than in controls (2488.88 vs. 2514.25 with $p>0.05$). No difference was observed in the mean pachymetry values, hexagonality%, and coefficient of variation of cell size between cases and controls. Multivariate regression analysis, after adjusting for age, showed the mean cell density to be lesser by 66 cells/mm^2 (95% confidence interval, 6.3–125.9) among diabetic patients compared with non-diabetic subjects.

CONCLUSIONS

The results of this study, from a large population based sample, support the earlier theories of lower endothelial cell counts and increased central corneal thickness among subjects with type 2 diabetes mellitus in comparison with non-diabetic controls.

KEYWORDS

Corneal Endothelium, Type 2 Diabetes, Cross Sectional Study, Population Based Study.

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BACKGROUND

Corneal endothelium plays a major role in maintaining the optical transparency of the cornea. Extrinsic factors such as genetics, race, and age[1] or intrinsic factors such as trauma, intraocular surgery, ultraviolet radiation, infection, etc. are responsible for maintaining the structural and functional integrity of the corneal endothelium. As the prevalence of type 2 diabetes mellitus rises so do its attendant microvascular complications.[4] Besides diabetic retinopathy, patients with diabetes are prone to developing corneal endothelial damage, keratoepitheliopathy in the form of recurrent corneal erosions, persistent epithelial defects, and superficial keratitis.[5–7] Although morphological and physiological changes in the corneal endothelium in patients with diabetes have been documented, most of the studies had small sample size, and no such changes were reported from the large population-based sample. Therefore, the present study was aimed to find out the changes such as mean cell density, coefficient of variation (CV) in the cell area, and hexagonality in the corneal endothelium cells and corneal pachymetry in patients with diabetes (cases) and compare the data with non-diabetic subjects (Controls).

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MATERIALS AND METHODS

All patients diagnosed with diabetes mellitus at Gandhi Hospital and referred to Sarojini Devi Eye Hospital. This was a hospital based clinical study of 104 patients with diabetes and 98 non-diabetic subjects. The age range of diabetic group was 42-75 years (Mean: 58.5) and that of control group was 40-73 years (Mean: 56.5). Ophthalmic examination included a complete medical history, slit-lamp examination and binocular indirect ophthalmoscopic fundus examination. Specular microscopy and pachymetry was done before installation of any mydriatics for fundus examination. Every patient who was included in the study was subjected to investigations related to Diabetic status, like Blood sugars, Glycosylated haemoglobin (HbA1C). Corneal thickness was measured indirectly using the specular microscopy (Tomey EM 3000). Three measurements were completed and averaged to provide a single value for the eye at that session. Then, the average of the reading for both eyes was taken to derive the single value for the patient. Newer generations of ultrasonic pachymeters work by way of Corneal Waveform (CWF).

Patients who had previously undergone intraocular surgery or showed signs of uveitis, trauma, glaucoma, endothelial dystrophies, pseudoexfoliation, other corneal endothelial anomalies, or unreadable images of specular microscopy were excluded.

Corneal Specular Microscopy and Corneal Pachymetry: Noncontact specular microscopy was performed using an autofocus device to assess the corneal endothelial status, and the endothelium was visualised on an incorporated screen. The centres of contiguous cells were marked after which the computer automatically calculated and displayed the endothelial cell density (cells/mm^2), CV (%), hexagonality (%), and analysed the number of cells. The mean cell area and the CV in the cell area (Standard deviation divided by the mean cell area) were used as an index of the extent of variation in the cell area (Polymegathism). The percentage of hexagonal cells in the area analysed was used as an index of variation in the cell shape (Pleomorphism). The central corneal thickness was measured using an ultrasound pachymeter by taking the average of 10 readings.

Statistical Analysis

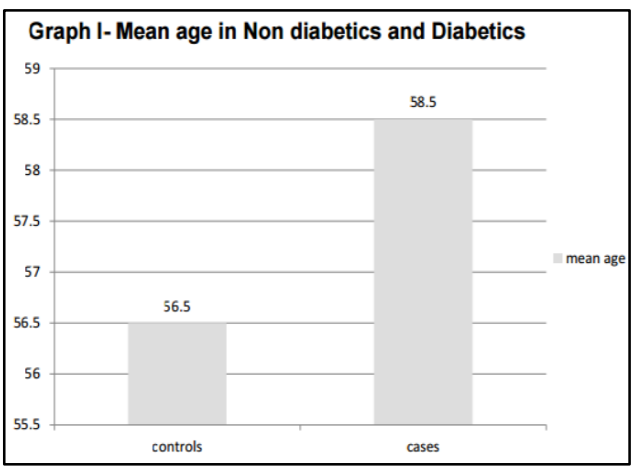
The data were analysed using Stata (Statistical software for professionals, Version 10.1) computer software (StataCorp LP, College Station, TX). The results were expressed as mean±SD. The mean and the proportions were compared using the Student's t test and the X^2 test respectively. Differences among 3 or more groups were identified by the analysis of variance test. A simple linear regression analysis was performed to find the relationship between corneal descriptors and risk factors. Factors found to be significant by simple linear regression were subjected to multiple regression analysis. A value of $P<0.05$ was considered statistically significant.

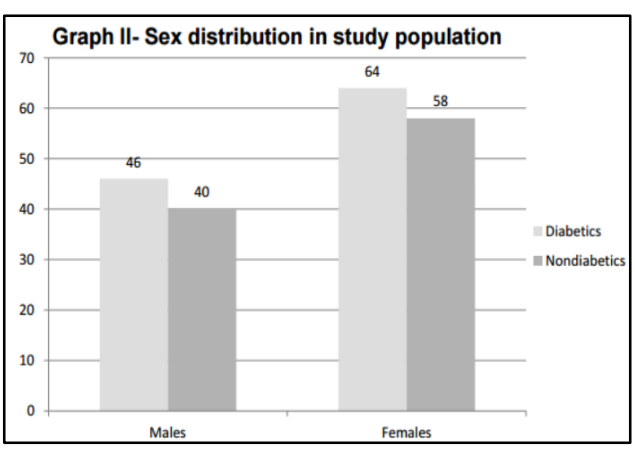
RESULTS

Table 1 describes the demographic profile of cases and controls. The mean CCT in diabetics was 519.98µ, ranged from 433.5µ to 583µ. The mean CCT in non-diabetics was 508.32µ, ranged from 443µ to 595µ. The mean value for endothelial cell density in diabetics was 2488.88 cells/mm^2, ranged from 1378.5 cells/mm^2 to 2824.5 cells/mm^2. The mean value for endothelial cell density in non-diabetics was 2514.25 cells/mm^2, ranged from 2200 cells/mm^2 to 2708 cells/mm^2. There was thicker central thickness and lesser endothelial cell density in the diabetics as compared with the normal persons by numerical data and the difference was not statistically significant ($P>0.05$). The mean corneal endothelial cell density (cells/mm^2) was lower in cases than in controls (2550.96 vs. 2634.44; $P=0.001$). Similar differences were observed across all age groups. No differences were observed between cases and controls with regard to the mean CV of cell size, mean hexagonality percentage, and mean central corneal thickness. However, when groups were stratified by age, some differences were observed: CV and hexagonality percentage were greater in cases than in controls among subjects between 50 and 69 years, and the central corneal thickness was higher in cases than in controls among subjects between 60 and 69 years. On univariate analysis, significant factors influencing endothelium cell density included age (P 0.001), duration of diabetes ($P=0.007$), and diabetic status ($P=0.006$); however, multiple linear regression analysis identified only 2 factors, namely, age (P 0.001) and diabetic status ($P=0.036$). With every increase in age per year (after adjusting for diabetic status), the cell count decreased by 6.4 cells [95% confidence interval (CI), −8.3 to −4.5]; likewise, in those with diabetes (after adjusting age), the cell count was lesser by 66 cells (95% CI, 6.3–125.9) compared with controls. Exponential rate of loss of cells per year was higher among those with diabetes (0.65%; 95% CI, 0.53–0.77) compared with controls (0.28%; 95% CI, 0.19–0.38).

	Non Diabetics	Diabetics
Persons (n)	98	104
Mean Age/Range	56.5	58.5
	(40-73 Years)	(42-75 Years)

Table I: Demographic Characteristics of Non-diabetics and Diabetic Patients





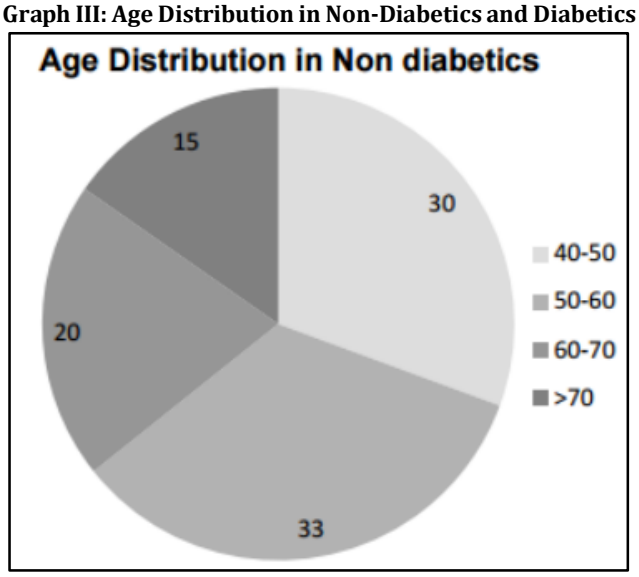
Among 104 diabetics, there were 50 males and females.

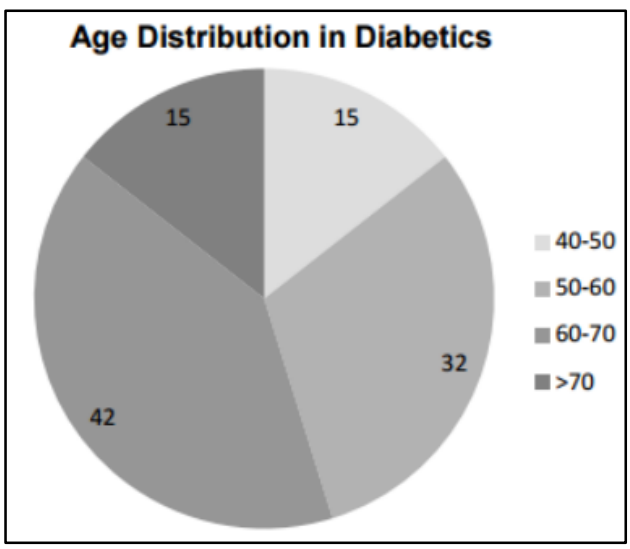
Among 98 non-diabetics, there were 40 males and 58 females.

	Control Group (n)	Diabetics (n)
40-50 Years	30	15
50-60 Years	33	32
60-70 Years	20	42
> 70 Years	12	15

Table II: Age Distribution in Non-diabetic and Diabetic Patients

Graph III: Age Distribution in Non-Diabetics and Diabetics



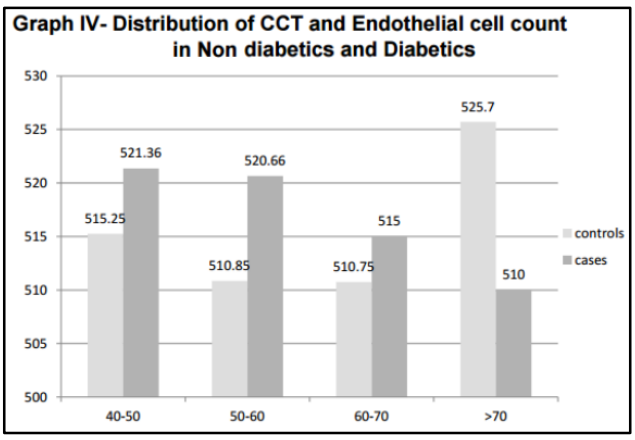


Among 104 diabetics, 15% were in age group of 40-50 years, 32% in 50-60 years, 42% in 60-70 years and 15% in more than 70 years. Among 98 non-diabetics, 30.61% are in the age group of 40-50 years, 33.67% are in 50-60 years, 20.4% are in 60-70 years and 15.3% in > 70 years.

Age Group	Non Diabetics		Diabetics	
	Central Corneal Thickness	Endothelial Cell Density	Central Corneal Thickness	Endothelial Cell Density
40-50 Years	515.25	2525.8	521.36	2516
50-60 Years	510.75	2554.5	520.66	2424.85
60-70 Years	510.75	2510.67	515	2420.35
> 70 Years	525.7	2257.31	510	2400

Table III: Distribution of Central Corneal Thickness and Endothelial Cell Density in Non-diabetic and Diabetic Patients

Graph IV- Distribution of CCT and Endothelial cell count in Non diabetics and Diabetics



	Central Corneal Thickness	Endothelial Cell Density
Control	508.327	2514.245
Diabetics	519.980	2488.880

Table IV: A Comparison of Mean Value between Non-diabetic and Diabetic Patients

DISCUSSION

Central corneal thickness has become a very important ocular parameter of study due to its importance as an indicator of corneal health status, its effect on applanation tonometry.

This study was attempted to determine the effect of diabetes on corneal thickness and endothelial cell count. In our study of 404 eyes of 202 patients, 104 (58.5) were diabetics and 98 (56.5) were non-diabetics. The average corneal thickness in diabetics was 519.980µ and in non-diabetics it was 508.327µ (P=0.07). The mean endothelial cell count in diabetics was 2488.880 cells/mm^2 and in non-diabetics was 2514.245 cells/mm^2 (P=0.06).

According to our results, diabetic patients showed significant differences compared with normal persons in terms of central corneal thickness and morphological changes in corneal endothelium. The study suggests that diabetes leads to decrease in corneal endothelial count and increase in central corneal thickness and warrants for minimal invasive procedures for surgery and prompt treatment of other compounding endothelial insults in diabetic patients.

Hyperglycaemia is thought to be a major factor in the pathogenesis of diabetes and several hyperglycaemia-induced biochemical processes have been implicated. Of particular interest is recent evidence linking elevated glucose to reduced Na+, K+- ATP-ase activity in corneal endothelial cells. In vitro studies show that polyhydroxyl compounds (glucose, galactose, galactitol, sorbitol, or xylitol) inhibit Na+, K+-ATP-ase activity in cultured bovine corneal endothelial cells whereas in vivo studies show reduced Na+, K+-ATP-ase activity in the corneal endothelium of diabetic rabbits after only 10 weeks of alloxan-induced hyperglycaemia. Because this enzyme is a major component of the endothelial fluid pump, it is not surprising that these same diabetic rabbits also showed greater baseline corneal thickness, decreased corneal swelling response, and slower recovery from hypoxic oedema than did non-diabetic rabbits.

The morphometry of corneal endothelial cells and central corneal thickness value in diabetics were not appreciably different from those found in normal persons. In fact, the central corneal thickness of diabetics is thicker than that of

normal persons, and diabetic corneal endothelial morphology shows distinct differences compared to normal cornea. These morphological changes of the diabetic cornea were revealed by some experimental studies using mice or dogs that reported a decrease in the corneal endothelium density, a decrease in hexagonality, and an increase in the coefficient of variation for cell size in the case of diabetes.

CONCLUSIONS

In conclusion, there was no statistically significant relationship between CCT in diabetics and non-diabetics observed. There was no statistically significant relationship between endothelial cell count in diabetics and non-diabetics.

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