Study of impact of diabetes mellitus on corneal central thickness and endothelial parameters in Indian eyes

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Abstract

Aim: The purpose of the study is to find the impact of diabetes mellitus on central thickness and endothelial parameters of cornea when compared with non diabetic patients and in relation to duration of disease and glycaemic control.

Study Design: Prospective, Observational and quantitative study.

Materials and Methods: Study included 125 patients (125 eyes) with diabetes mellitus and 143 controls (143 eyes). Tomey specular non-contact microscope (EM 3000) was used to measure central corneal thickness (CCT), endothelial cell density (ECD), coefficient of variation of cell size (CV) and percentage of hexagonal endothelial cells (6A).

Results: Comparison of age matched controls with diabetics did not show any statistical significance with respect to CCT, ECD and CV. 6A showed some significant change (p value= 0.02) between controls and diabetics. There was no significant correlation with respect to the duration of diabetes and glycaemic control.

Conclusion: Corneal endothelial parameters and thickness did not show any statistical significance between diabetics and controls except hexagonality of endothelial cells which was significant. Moreover there was statistically no difference based on duration of the disease, glycaemic control and presence or absence of retinopathy.

Keywords: Central corneal thickness, Endothelial cell density, Diabetes mellitus.

Introduction

Diabetes mellitus is a major systemic disease in our society and its prevalence is increasing day by day significantly. At the ocular level, main indicators for diabetes are diabetic retinopathy, cataract and glaucoma. Diabetic retinopathy is the 5th leading cause of blindness globally, while it is the first leading cause of blindness in the developed countries in adults at working age. Though the cornea appears normal, significant biochemical changes occur which alter the function of cornea. Advanced glycation end products (AGEs)[1-4] and matrix metalloproteinases (MMP) have been proposed to be the cause for corneal damage. The accumulation of AGEs enhanced the apoptosis of retinal pericytes, corneal endothelial cells, neuronal cells, and renal mesangial cells. AGEs is seen in the corneal stroma, Descemet's membrane and basement membrane of the corneal epithelium. The accumulation of the AGEs in diabetic corneas provided evidence that nuclear oxidative DNA damage caused by AGEs is responsible for the apoptotic damage of cornea in diabetic patients[5] Na-K ATPase of cornea endothelium is also affected which causes change in permeability of cornea.[6]

Corneal thickness increases in diabetic patients possibly due to inhibition of endothelial pump, increased endothelial permeability and increased swelling pressure of corneal stroma.[6] The purpose of the study is to find the impact of diabetes mellitus on central corneal thickness (CCT), endothelial count (ECD), CV and hexagonality in relation to duration of disease and glycaemic control.

Materials and Methods

This is a prospective, observational quantitative study done in Chettinad Hospital and Research institute. It adhered to the tenants of Declaration of Helsinki. Comprehensive consent was obtained after explaining the study. The study included 125 diabetic patients (Male- 66, Female- 59) and 143 controls (Male- 61, Female- 82).

Inclusion Criteria: All diabetic patients aged 30 years and above consented for the study were included.

Exclusion Criteria: All patients with any history of ocular surgery, trauma, corneal diseases, congenital anomalies of eye, previous eye infection or inflammation, glaucoma, ocular laser procedures, pterygium, lid anomalies, regular usage of contact lens, eye drops, systemic drugs interfering with tear film were excluded. Patients with systemic illness interfering with tear film like rheumatoid arthritis, systemic lupus erythematosis were also excluded.

A complete ophthalmic examination and relevant laboratory investigations were done. Tomey non-contact specular microscope (EM 3000) was used to evaluate corneal parameters. Average of three readings were taken after instilling lubricant eye drops. CCT, ECD, polymegathism (CV) and % of hexagonal cells (6A) were taken for study. All the information were recorded in a precoded format.

Fig. 1: Measurement of corneal central thickness and endothelial parameters

The diabetics were divided into two groups each based on

1. Duration of disease i.e Less than 5 years and greater than 5 years
2. Glycemic control i.e HbA1c less than 7gm/dl and greater than 7gm/dl,
3. Age of the diabetics i.e less than 50 years old and above 50 years
4. With and without retinopathy.

Statistical Analysis: Unpaired t test was used for statistical analysis to compare controls with diabetics first and then comparison among diabetic subgroups were done.

Results

Mean age of diabetic patients was 53.84±10.80 years and controls 53±9.29 years.

Table 1 shows the comparison of age matched controls with diabetics which did not show any statistical significance with respect to CCT, ECD and CV. Hexagonality of endothelial cell showed statistically significant change (p value= 0.02) between controls and diabetics.

Table 1: Control Vs diabetic patients

Corneal parameters	Controls (n=143)	Diabetics (n=125)	P value
CCT	521.57+48.78	518.1±43.15	0.584
ECD	2504.41+305.25	2529.4±365.30	0.542
CV	40.14+10.74	40.48±10.89	0.820
6A	45.4±7.81	43.5±5.92	0.020
CCT-Central corneal thickness, ECD-Endothelial cell density, CV-Co-efficient of variation, 6A-Percentage of hexagonal cells			

Comparison of controls with duration of diabetes greater than 5 years did not show any statistical significance (Table-2).

Table 2: Control Vs Duration of diabetes >5 yrs

Corneal parameters	Controls (n=143)	Diabetes more than 5yrs (n=60)	P value
CCT	521.57+48.78	513.7±49.2	0.301
ECD	2504.41+305.25	2574.6±253.3	0.119
CV	40.14+10.74	40.1±8.7	1.00
6A	45.4±7.81	43.8±6.2	0.303
CCT-Central corneal thickness, ECD-Endothelial cell density, CV-Co-efficient of variation, 6A-Percentage of hexagonal cells			

Comparison of the parameters with controls and diabetics with HbA1c >7 did not show any significance (Table 3). Comparison with controls and diabetic with retinopathy also showed no significance (Table 4).

Table 3: Control Vs HbA1c >7

Corneal parameters	Controls (n=143)	HbA1c >7 (n=108)	P value
CCT	521.57+48.78	518.1±44.6	0.571
ECD	2504.41+305.25	2524.2±382.5	0.645
CV	40.14+10.74	39.5±8.84	0.694
6A	45.4±7.81	43.4±6.1	0.079
CCT-Central corneal thickness, ECD-Endothelial cell density, CV-Co-efficient of variation, 6A-Percentage of hexagonal cells			

Table 4: Control Vs diabetic retinopathy

Corneal parameters	Controls (n=143)	Diabetic patients with retinopathy (n=29)	P value
CCT	521.57+48.78	515.3±38.3	0.500
ECD	2504.41+305.25	2539.2±219.3	0.558
CV	40.14+10.74	40.3±7.0	1.000
6A	45.4±7.81	42.6±5.9	0.119
CCT-Central corneal thickness, ECD-Endothelial cell density, CV-Co-efficient of variation, 6A-Percentage of hexagonal cells			

After comparison of diabetics with controls, the corneal parameters were compared within the diabetic group (Table 5). Among diabetic patients, CV alone showed significance when they were compared in terms of age less than 50 years and more than 50 years and the glycemic control. Other parameters did not show any significance.

Table 5: Comparison of corneal parameters within diabetic group

Diabetic sub groups	CCT	ECD	CV	6A
Age <50yrs (n=52)	522.75±35.45	2517.71±384.37	41.89±13.72	44.00±6.44
Age >50yrs (n=73)	514.8±47.86	2537.75±353.56	39.48±8.3	43.29±5.55
P value	0.383	0.779	0.012	0.323
Duration < 5yrs (n=65)	522.14±36.56	2487.66±442.39	40.82±12.64	43.35±5.63
Duration > 5yrs (n=60)	513.73±49.26	2574.65±253.31	40.12±8.71	43.83±6.26
P value	0.525	0.436	0.380	0.651
HbA1C <7gm% (n=17)	517.655±33.64	2562.24±233.9	46.65±18.71	44.58±4.58
HbA1C >7gm% (n=108)	518.18±44.6	2524.25±382.45	39.50±8.85	43.42±6.11
P value	0.431	0.601	0.001	0.266
Retinopathy-No (n=29)	515.34±38.30	2539.28±219.30	40.31±7.08	42.55±5.94
Retinopathy-Yes (n=96)	518.94±44.67	2526.44±399.96	40.53±11.84	43.9±5.91
P value	0.917	0.362	0.645	0.801
CCT-Central corneal thickness, ECD-Endothelial cell density, CV-Co-efficient of variation, 6A- Percentage of hexagonal cells				

Discussion

Corneal endothelial parameters change in diabetics is well observed in literature and articles, showing reduced endothelial density, increased polymegathism (CV), decrease in hexagonality of cells and increased corneal thickness.[7,8] According to our study this was not the observation, ECD, CV and corneal thickness did not show any significant change between diabetics and controls. Hexagonality of cells alone had significant difference (p= 0.02). This is similar to a study done by Sudhir et al[9] and Shashi et al[10] who showed that there was no difference observed in CCT, CV and hexagonality between diabetics and controls, but they showed reduced ECD in diabetics. In our study ECD was not statistically different from control, this could be due to increased deviation of cell count between diabetics and controls. (SD in diabetics is 365 compared to 305 in controls).

Corneal endothelial parameters were also compared with age of patient, duration of diabetes, glycaemic control and presence of diabetic retinopathy. JS Lee et al[7] has shown that patients with diabetes of more than 10 years showed significant difference in ECD, CV, CCT and hexagonality. In our study there was no significant difference in CCT, CV, ECD and hexagonality. This was similar to a study done by Stella et al[11] who showed there was no correlation with disease duration. In our study comparison was between less than 5 years and above 5 years, but most of the studies compared 10 years of diabetes.

Comparison of glycaemic control in relation with HbA1c below and above 7 showed no significant correlation with respect to CCT, ECD and hexagonality but CV showed significance. This is similar to Vineetha et al[12] who showed HbA1c had negative correlation with ECD and hexagonality of cells. However studies by Allanstor et al[13] and Manish Gupta et al[14] showed increase in HbA1c greater than 7gm/dl was associated with changes in CCT and endothelial parameters. The variation in our study could be due to the number of patients compared. (Patients with HbA1c less than 7 was 17 and above 7 was 108). Neither age nor the presence or absence of retinopathy showed any significant correlation.

Conclusion

In conclusion corneal endothelial parameters and thickness did not show any statistical significant difference between diabetics and controls except hexagonality of endothelial cells which was significant. Moreover there was statistically no difference based on duration of the disease, glycaemic control and presence

or absence of retinopathy.

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