

A study of corneal changes –endothelial cell density (ECD) and central corneal thickness (CCT) in Type -2 DM in relation to HbA_{1c} levels and compare it with healthy individuals

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Abstract

Background: Diabetes in India is very common chronic systemic disease which causes wide range of ocular complications. Besides, diabetic retinopathy, patients with diabetes are prone to developing corneal endothelial damage, corneal oedema, epithelial changes like keratoepitheliopathy in the form of recurrent corneal erosions, persistent epithelial defects, and superficial keratitis.

Objectives: The aim of this study was to measure the central corneal thickness and ECD in type -2 DM in relation to HbA_{1c} levels and compare with healthy individuals of same age group.

Material and Methods: It was a hospital based, prospective case-control study. A total of 120 patients, 50-70 yrs of age, participated in the study, of whom 60 were diabetic type 2 on oral hypoglycemic already established from medicine department and 60 healthy individuals of same age group attended eye OPD were taken after taking Consents from patients at medical college in Uttarakhand, and approval from ethical committee. Study group was divided into two groups – diabetic type 2 (with HbA_{1c} <7 and >7) and healthy individuals. After thorough ocular examination include slit lamp and fundus examination, the central corneal thickness and endothelial cell count (ECD) was measured using specular/ pachymetry nidek machine. Exclusion criteria was any corneal pathology, ocular surgery, trauma any other systemic illness, insulin dependent, on topical drops.

Results: Mean CCT was thicker in diabetic group (575.53µm) when compared to non-diabetic group (560.40µm). The difference between the 2 groups was significant (p<0.001). Mean CCT in diabetic patients was 575.53±7.8µm. Mean duration of diabetes was 9.53±1.9 yrs. The relation between CCT and duration of diabetes was not significant. A statistically significant difference (p=0.001) was found in the endothelial cell density (ECD), between diseased and normal eyes. When the patients were analyzed in terms of HbA_{1c} levels, patients with HbA_{1c} levels over 7% had thicker corneas and lower ECD values than the patients with HbA_{1c} levels under 7% (p=0.031).

Conclusion: In diabetic patients central corneal thickness was more compared to non diabetics. Therefore, diabetes can increase the CCT but there is no significant correlation between duration of diabetes and CCT. A lower ECD was seen in diabetic patients compared to healthy adults which was in turn influenced by poor glycaemic control HbA_{1c}>7 and duration of diabetes.

Keywords: Central Corneal thickness¹, Pachymetry³, Specularmicroscopy⁴, Endothelial Cell Density².

Access this article online	
Quick Response Code:	Website: www.innovativepublication.com
	DOI: 10.5958/2395-1451.2016.00029.9

Introduction

Diabetes mellitus is one of the widely spreading and one amongst the most common non-communicable diseases globally. The ocular complications of diabetes are mainly retinopathy, cataract and glaucoma¹. Diabetic keratopathy is a frequent disease that entails several alterations, especially in the epithelium and endothelium, like punctate epithelial keratopathy, recurrent corneal erosions and persistent epithelial defects. Diabetic keratopathy can cause alterations in all layers of cornea especially the endothelium like

decrease in endothelial cell density and hexagonality, as well as increased polymegathism, pleomorphism and central corneal thickness²⁻³. As the prevalence of type 2 diabetes mellitus rises, so do its, micro vascular 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

Corneal endothelium play a major role in maintaining the optical transparency of the cornea. Extrinsic factors, such as genetics, race, and age,⁸⁻¹³ or intrinsic factors, such as trauma, intraocular surgery, ultraviolet radiation, infection, etc,¹⁴⁻¹⁷ have influence on the structural and functional integrity of the corneal endothelium.

Central corneal thickness is an important measurement for the diagnosis, treatment and management of various ocular conditions and also a sensitive indicator for endothelial physiology and functions.^{18,19}

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 results are variable in type 1 and 2 DM and duration of diabetes²⁰⁻²⁵. Diabetes is a chronic metabolic disease and it is common to have some association between systemic and ocular factors influencing the corneal endothelium. Although the morphology of corneal endothelium, among diabetic patients, has been reported earlier, most of them were from hospital-based studies considering single parameter and with a relatively small sample size.

Aims and Objectives

The aim of this study was to measure to the central corneal thickness and endothelial cell count in type -2 DM in relation to HbA_{1c} levels and compare with healthy individuals of same age group.

Materials and Methods

This study was designed as a case-control study conducted in Department of Ophthalmology in medical college in Uttarakhand, for duration of 8 months from July 2015 to Feb 2016. Individuals aged 50-70 years attending OPD were included. A total of 120 patients, 50-70 yrs of age, participated in the study, of whom 60 were diabetic type 2 on oral hypoglycemic already established from medicine department and 60 healthy individuals of same age group attended eye OPD were taken, after taking consent from patients at medical college in Uttarakhand, and approval from ethical committee. Exclusion criteria included patients with history of intraocular surgery, trauma, contact lens wear and receiving treatment for any topical or systemic diseases, patients with underlying ocular pathology and on insulin. Duration of diabetes was also reported in study.

Sample size was 120 patients - 60 diabetics type -2 with HbA_{1c} level (<7%; >7%): 60 healthy individuals of same age group. Complete medical history and after thorough ocular examination include slit lamp and

fundus examination, the central corneal thickness(CCT) and endothelial cell density (ECD) was measured using specular/ pachymetry nidek machine (SP-CEM 530) and systemic examination was done. Data was analyzed using SPSS version 23. Comparison between the different parameters was done using student t-test and Chi-square test. p-value of <0.05 was considered significant. 95% confidence interval was used.

Results

Mean CCT of 60 diabetic patients was 575.53 μ m and that of non-diabetics was 560.40 μ m. Mean CCT was thicker in diabetic groups when compared with the non-diabetics. The difference of the mean CCT between the 2 groups was found to be significant (p<0.001). Mean CCT was slightly higher in males (570.67 μ m) than females (556.75 μ m) and the small difference was not statistically significant (p=0.176). No correlation was found between CCT and gender. Mean CCT in diabetic patients were 575.53 μ m. Mean duration of diabetes was 9.53 yrs. We found no correlation between the CCT and duration of diabetes. The patients who had diabetes \geq 10 years had higher CCT compared to those who had diabetes <10 years. This finding was not statistically significant (p=0.095). The evaluated parameters i.e. ECD and mean cell area were also summarized in Table 5. A statistically significant difference (p=0.001) was found in the endothelial cell density (ECD), between diseased and normal eyes. When the patients were analyzed in terms of HbA_{1c} levels, patients with HbA_{1c} levels over 7% had thicker corneas than the patients with HbA_{1c} levels under 7% (p=0.031) (Table 6). The mean corneal endothelial cell density (cells/mm²) was lower in patients having HbA_{1c} > 7 than in patients with HbA_{1c} levels under 7%. (2550 \pm 320 vs. 2510 \pm 290; P = 0.025) (Table 7). Duration of diabetes have a significant impact on the ECD of cornea; the latter being lower in patients with duration of diabetes >10 years compared to the ones who have duration of diabetes <10 years (p=0.007) (Table 8).

Table 1: Mean central corneal thickness (CCT) amongst diabetics and non-diabetics

Groups	Total no. of cases	Mean CCT(μ m)	Std. Deviation	p-value	95% CI
Diabetic	60	575.53	42.33	<0.001	8.5-23.56
Non diabetic	60	560.40	21.56		

Table 2: CCT and duration of Diabetes Mellitus

Variable	No. of cases	Mean	Pearson's correlation	P-value
CCT	60	575.53	0.125	0.158
Duration of diabetes	60	9.53		

Table 3: CCT and Gender variation

Gender	Total no.	Mean CCT	Std deviation	p-value
Males	75	570.67	35.57	0.176
Females	45	556.75	30.68	

Table 4: Association of CCT with duration of diabetes

Duration of Diabetes in years	CCT		χ^2	p-value
	<570 μm	$\geq 570\mu\text{m}$		
<10	15	17	3.96	0.095
≥ 10	13	15		

Table 5: Descriptive parameters of diabetic subjects in relation to their healthy control

Parameters	Diabetic (n=60)	Non-Diabetic (n=60)	p-value
Cell density (cells/mm ²)	2540 \pm 260	2664 \pm 190	0.001
Mean cell area (μm^2)	431 \pm 45	426 \pm 35	0.51
Coefficient of variation	0.44 \pm 0.07	0.44 \pm 0.06	0.61

Table 6: Association of CCT with HbA_{1c} levels

HbA _{1c}	CCT (μm)
<7%	560 \pm 40.33
$\geq 7\%$	575 \pm 20.56
p value	0.031

Table 7: Association of ECD with HbA_{1c} levels

HbA _{1c}	ECD (cells/mm ²)
<7%	2550 \pm 320
$\geq 7\%$	2510 \pm 290
p value	0.025

Table 8: Association of ECD with duration of diabetes

Duration of Diabetes in years	ECD (cells/mm ²)		χ^2	p-value
	<2500 μm	$\geq 2500\mu\text{m}$		
<10	10	22	7.78	0.007
≥ 10	20	08		

Discussion

In our study mean CCT of 60 diabetic patients were 575.53 μm and that of non-diabetics were 560.40 μm . The mean CCT was comparatively thicker in diabetic subjects when compared with the non-diabetics. It is well known that diabetes reduces the activity of Na+K+ATPase of the corneal endothelium and thus causes the morphological and functional changes of diabetic cornea²⁶. The difference between the 2 groups was statistically significant when analysed by t-test (p<0.001). Most studies like the present study showed that diabetic eyes had increased CCT when compared to non-diabetic subjects^{27,28,29,30}. M O Zengin et al postulated that endothelial pump function disturbances are due to reduction of Na+K+ATPase activity which furthermore results in an increase in stromal hydration^{27,31}. N McNamara et al stated that possible CCT changes can be due to hyperglycaemic effect on the cornea which directly inhibits the corneal endothelial pump. Other possible mechanisms that may account for the swelling differences between diabetics

and non-diabetic subjects included reduced corneal lactate production and increased endothelial pump function during corneal hypoxia³². Intracellular accumulation of sorbitol, which acts as an osmotic agent leads to swelling of the endothelial cells.

The results of the present study showed that the mean endothelial cell density was significantly lower in patients with uncontrolled type 2 diabetes mellitus compared with controls/healthy adults which was comparable with the study conducted by Rachapalle. R et al at Sankara Nethralaya (2012). The cell loss rate per year was 0.28% (95% CI, 0.19–0.38) among normal subjects which was similar to previously published studies.^{33,34} Presence of diabetic retinopathy had no influence on the corneal endothelial cell density, and there was no significant difference between various stages of diabetic retinopathy.³⁵ Our study did find a significant association between hemoglobin A1c (a measure of glycemic control) and corneal endothelial changes among diabetes in contrast to the results of earlier studies^{35,36}.

Limitations of study

Further more elaborate study considering corneal changes in Diabetes Mellitus can be done involving multiple parameters and with effect of different factors influencing CCT and ECD on cornea.

Conclusion

In this study it was found that an increase in central corneal thickness is present even in early stages of diabetes. Diabetic patients exhibit a fairly greater statistically significant average central corneal thickness than non-diabetics. A lower ECD was seen in diabetic patients compared to healthy adults which was in turn influenced by poor glycemic control $Hb_{1c} > 7$ and duration of diabetes.

Acknowledgement

We extend our sincere thanks to Dr. Abhishek Arun (MD) for his assistance in medical writing. We are also thankful to junior doctors and staff of Ophthalmology department. Special thanks to everyone who participated in the study.

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