A study of correlation between HbA1c level & corneal thickness in diabetes mellitus patients

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Abstract

Introduction: The purpose of this study is to find out the association of duration of diabetes and increased HbA1c level with corneal thickness in patients of DM.

Materials and Methods: After obtaining approval by 'Sumandeep Vidyapeeth Institutional Ethical Committee', a comprised study of 150 type-II DM patients were conducted (only left eye included). All the patients underwent complete ophthalmic examination and all study procedure was performed after obtaining informed consent from all patients and in accordance with declaration of Helsinki.

Result: The mean CCT of patients with DM <7 years was 543.1 (SD - 23.51) and that of patients with duration of DM ≥ 7 years was 546.95 (SD – 25.23). The difference was statistically insignificant (p value = 0.335). The mean CCT of patients with HbA1c <7% was 545.3 (SD – 24.31) and that of patients with HbA1c ≥ 7% was 545.1 (SD – 24.63). The difference was statistically insignificant (p value = 0.96)

Conclusion: In our study we conclude that corneal thickness is not affected by DM, its duration and HbA1c levels.

Keywords: Central Corneal Thickness, Diabetes Mellitus, HbA1c.

Introduction

"Diabetes mellitus is a group of metabolic diseases in which a person has high blood sugar either because the pancreas does not produce enough insulin or because cells do not respond to the insulin produced by it. This high blood sugar produces the classical symptoms of polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger)."[1]

It is a condition primarily defined by the level of hyperglycaemia which give rise to risk of microvascular damage i.e. retinopathy, nephropathy and neuropathy. It is associated with reduced life expectancy, significant morbidity and blindness due to specific diabetes related microvascular complications. There is increased risk of macrovascular complications like ischaemic heart disease, stroke and peripheral vascular disease leading to diminished quality of life.[3]

Eye is affected in many ways in patient with diabetes. It includes deviation in refractive errors, xanthelasma, blepharitis, internal and external hordeolum, acute infectious conjunctivitis, dry eye, superficial punctate keratits, persistent epithelial defect, recurrent corneal erosions, neovascularization of iris, anterior uveitis, cataract, vitreous degeneration, diabetic retinopathy, diabetic papillopathy, oculomotor nerve palsy etc.[4-6]

The morphological changes that develop in the diabetic patients are polymegathism (corneal epithelial cells variation), pleomorphism (cell shape variations), irregular cellular distribution, stunting of surface cell microvilli and corneal epithelial basement membrane thickening. The epithelial barrier function is also altered in the cornea of DM patients. In addition to these, the corneal endothelium also displays an increased incidence of dysfunction such as changes in endothelial cell morphologic features, endothelial cell density and damaged endothelial cell structure that results in persistent postoperative corneal edema and changes in central corneal thickness in diabetic patient.[7,8]

Earliest change in cornea due to DM is change in its thickness & it is associated with increased HbA1c level, blood glucose level & several retinal complications. Corneal endothelial dysfunction because of hyperglycemia in DM may be the responsible factor, which leads to increased corneal thickness.[4,7,8]

This study is done to find out any association of increased HbA1c level with corneal thickness in patients of DM.

Yasser Seddeg Abdulghani et al[9] conducted a cross-sectional study of 160 patients from which 80 patients were diabetic and 80 were non-diabetic and they observed the correlation between central corneal thickness and diabetes. They observed diabetic patients had an increased central corneal thickness when compared with non-diabetic patients.[9]

Another study done by Kenji Inoue et al[10] conducted a study of the corneal endothelium and thickness in type II Diabetes Mellitus in 99 diabetic and 97 non-diabetic eyes. They observed corneal endothelial cell structure was damaged but CCT was not increased in type II diabetic patients.[10]

Mehmet Ozgur ZENGİN et al[11] performed a study on 126 consecutive eyes of diabetic patients to see the effect of HbA1c on corneal thickness and they concluded that Type II diabetic patients have thicker corneas than non-diabetic subjects and a higher HbA1c level may be a marker for predicting the increase in CCT in patients with type II diabetes.[11]

Storr-Paulsen A et al[12] done a study to investigate corneal endothelial cell morphology and corneal thickness in type II diabetic and non-diabetic patients. They concluded that Type II diabetes has no impact on corneal cell density or morphology in subjects with good glycemic status. However, higher HbA1c was associated with lower endothelial cell density. CCT was significantly increased in the diabetic group.

Materials and Methods

The study was conducted in Department of Ophthalmology at Dhiraj Hospital, SBKS Medical College and Research Centre, Piparia, Vadodara. It is a multispecialty tertiary care centre catering not only to local patients from Vadodara with its neighbouring villages but also patients from other parts of Gujarat and even adjoining regions of Madhya Pradesh, Maharashtra and Rajasthan. This was a clinical, cross-sectional and comparative study. Sample selection was done serially. Patients suffering from diabetes mellitus either in controlled or uncontrolled state, with no history of ocular trauma or previous ocular surgery were included. Patients with ocular surface disorders, pterygium, active ophthalmic infection, corneal dystrophies, and glaucoma were excluded.

After obtaining approval by 'Sumandeep Vidyapeeth Institutional Ethical Committee', a comprised study of 150 type-II DM patients were conducted (only left eye included). All the patients underwent complete ophthalmic examination and all study procedure was performed after obtaining informed consent from all patients and in accordance with declaration of Helsinki.

All individuals underwent a complete ophthalmic examination including a detailed ocular and medical history, Uncorrected Visual Acuity (UCVA) and Best Corrected Visual Acuity (BCVA). Refraction values and Keratometry reading were taken with the help of auto-refracto keratometer. Three consecutive measurements taken with auto-refracto keratometer and the result of three readings were averaged. The steepest and flattest keratometric values were recorded. Detailed Slit-lamp examination was done. Corneal thickness was measured with ultrasonic pachymetry (ACCUTOME Accu Pach VI). Intraocular pressure was measured with Goldmann Applanation Tonometry. Sugar profile (PP_2BS and FBS) and HbA1c levels were measured. Patients were categorised in 2 groups according to the duration of diabetes (longer than 7 years and shorter than 7 years) and HbA1c level (<7% and >7%). Dilated fundus examination of all patients were done with indirect ophthalmoscope. Grading of diabetic retinopathy was done. Measurement of left eye were used for analysis. Statistical analysis was performed with t-test and ANNOVA test.

Results

This study included total 150 eyes of 150 diabetic patients (89 male and 61 female). The age of the patient was from (29-85 years). Mean Age was 60.32 years. Mean duration of DM was 9 years.

The mean CCT of patients with DM <7 years was 543.1 (SD - 23.51) and that of patients with duration of DM ≥ 7 years was 546.95 (SD – 25.23). The difference was statistically insignificant (p value = 0.335) (Table 1)

The mean CCT of patients with HbA1c <7% was 545.3 (SD – 24.31) and that of patients with HbA1c ≥ 7% was 545.1 (SD – 24.63). The difference was statistically insignificant (p value = 0.96) (Table 2)

The mean CCT of the patients divided in five groups on the basis of diabetic retinopathy is calculated and there is no statistical significant difference between them. (p value =) (Table 3)

Table 1: Shows correlation between Central Corneal Thickness (CCT) and duration of DM.

Duration of DM	**N**	**CCT**	
		Mean	SD
<7 Years	80	543.1	23.51
≥7 Years	70	546.95	25.23

*P- Value is 0.335, which is statistically not significant.

Table: 2 Central Corneal Thickness (CCT) of the diabetic patients according to HbA1c levels.

HbA1c level	**N**	**CCT**	
		Mean	SD
<7%	80	545.3	24.31
≥7%	70	545.1	24.63

***P- Value is 0.96, which is statistically not significant.**

Table: 3 Clinical data of study population

	No retinopathy	**Mild NPDR**	**Moderate NPDR**	**Severe NPDR**	**PDR**
Subject (n)	64	22	29	20	15
Mean Age	58.18	62.26	60.27	61.57	56.11
Sex(M\F)	34\30	13\9	19\10	13\7	10\5
CCT	541.67/23.20	538.8/19.26	556.37/27.45	551.5/24.86	535.22/23.16
Flat K	43.78/1.48	42.91/1.48	43.84/1.43	44.32/1.90	43.27/1.72
Steep K	44.76/1.76	44.10/1.15	44.90/1.55	45.16/1.80	44.44/1.73

Discussion

In the present study of 150 eyes we have compared the corneal thickness with the duration of DM. We have also compared the corneal thickness with HbA1c level. It was observed that in type-II DM patients, we have found that there was no change in the CCT with increased duration of DM. Schultz et al[13] conducted the same study in which they compared 46 eyes of 46 patients with type-2 DM (eye randomly selected) with 75 control eyes (non-diabetic patients) and concluded that there was no change in the CCT in the control and diabetic group. There was increased pleomorphism and polymegathism in the diabetic group but no significant difference in endothelial cell density. These results are similar to our study.

Wiemer et al[14] compared 101 patients of type-II DM with 69 non-diabetic patients for changes in the CCT. Their study showed no difference in the CCT of both groups which is also similar to the results of our study.

However, similar study conducted by Siribunkum et al[15] gave contrary results. In their study, they compared 60 eyes of 30 diabetic patients with the non-diabetic group and concluded that the diabetic corneas tend to be thicker with more pleomorphism and polymegathism.

Lee et al[16] compared 200 diabetic eyes with 100 normal eyes for changes in the corneal thickness with duration of DM. They observed thicker corneas for patients having DM over 10 years. No such correlation with the duration of DM was found in our study. This could be attributed to the lesser time period of our study than that of the aforementioned study, which might be the reason for no such significant change.

The reason postulated for the increased corneal thickness is the disturbance in the endothelial pump function, leading to reduction of Na+/K+ ATPase activity. This disturbance causes stromal hydration which further increases the corneal thickness.[9,11]

Taking other studies into account, we think that the increased CCT in older diabetics, and the lack of a significant correlation between the CCT and other disease related parameters indicate that the CCT changes may be due to the age-related changes in the corneal structure of the diabetic patients rather than any effect of diabetes on the cornea.

Recently, HbA1c levels have been emphasised as a valuable marker of glycaemic control. Haemoglobin is a protein found in the red blood cells to which the glucose gets attached to, forming A1c (HbA1c). Hence raised blood glucose levels cause more glucose to stick to the haemoglobin. Each red blood cell survives for 8-12 weeks and thus, HbA1c levels in blood provide an estimate of the average blood glucose levels for the past 3 months. Thus, regular HbA1c testing determines recent glycaemic control. We investigated HbA1c values and their correlation with corneal thickness. We concluded that CCT has no significant correlation with higher (≥7%) or lower (<7%) HbA1c levels (p value 0.96).

Similiar to our results, Larsson et al[17] and Keoleian et al[18] did not detect any significant correlation between HbA1c and CCT. It is known that abrupt correction of hyperglycaemia results in transient hyperopia. Research on phakic and aphakic diabetic individuals indicate that changes in the function and morphology of the lens are responsible for such refractive changes. It is hypothesised that hyperglycaemia also affects corneal hydration and causes qualitative as well as quantitative corneal changes such as change in refractive index, curvature, and thickness.[11] However, higher HbA1c as a marker of poor glycaemic control was not associated with thicker corneas in our study. One would also expect that disease severity and duration would affect corneal thickness. This might be due to different homeostatic changes during the chronic course of diabetics. Therefore, to ascertain the exact relationship of blood glucose with the corneal thickness longitudinal follow-up studies can be performed.

In our study, to find the correlation between the CCT and the disease severity, patients were classified in 5 groups based on their retinopathy changes. The results demonstrated that severity of retinopathy had no effect on the CCT. Patients with mild to moderate NPDR had higher, but statistically insignificant CCT values than the patients with no diabetes. Mehmet Ozgur et al[11] study, conducted a study on 126 type –II DM patients which showed similar results.

The limitation of our study is that we didn't take endothelial cell count into account. As damage to the endothelium of cornea makes the basis of theory that supports increase in CCT in patients with DM, further studies that compares CCT, duration of DM and endothelial cell count may bring more clarity to the subject. Some such studies have already been done and it has shown a positive correlation but more of similar study has to be done to support it. Moreover this study is a cross sectional study and is less apt than a longitudinal study over a period of time to better determine whether the CCT increases with time in patients with DM.

In our study we conclude that corneal thickness is not affected by DM, its duration and HbA1c levels.

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