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STUDY OF RELATION BETWEEN HBA1C LEVELS AND CORNEAL ENDOTHELIUM IN TYPE 2 DIABETES MELLITUS PATIENTS

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Abstract:

Introduction:

The corneal endothelium plays an important role in the corneal transparency. Lower endothelial cell density (ECD) in type 2 diabetes mellitus is due to glycaemic stress. The evaluation of cornea is important in diabetics, as the outcome of various intraocular surgeries depend on the status of cornea. In our study, we studied the association of type 2 diabetes mellitus and HbA1c levels on the corneal endothelium.

Materials And Methods:

A case control study was conducted in the department of Ophthalmology. 130 study subjects were included and the patients were enrolled into two groups, 65 known case of type 2 diabetes mellitus and 65 non-diabetic age matched controls. All patients underwent complete ophthalmic evaluation along with endothelial cell parameters using Specular Microscope.HbA1c levels of all the study population was tested.

Results:

There was significant reduction in mean endothelial cell density (ECD) and hexagonal cells among patients with HbA1C >7% compared to subjects with HbA1C ≤7%. A significant difference in mean ECD was correlated with duration of diabetes (p=0.048).

Conclusion:

We found correlation between HbA1C levels of ≤7% and >7% with ECD and Hexagonal cells and the differences were found to be statistically significant. Thus, it is important to access the corneal endothelium in all type 2 Diabetes Mellitus. It should be a part of assessment in

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all diabetes mellitus patients so that a high-risk cornea prone for early decompensation can be identified.

Keywords: Diabetes Mellitus; HbA1c; Endothelial Cell Density; Hexgonal cells.

Introduction:

Type 2 diabetes mellitus (T2DM) is a metabolic disease characterised by hyperglycemia and the disease is triggered by insulin resistance and decreased insulin release. [1] By the year of 2025, it is estimated that >75% of people with diabetes will be residing in developing countries, as compared with 62% in 1995.[2] Corneal endothelium has an important role in maintaining the optical transparency of the cornea. [3] The control of corneal hydration pump and leak mechanism is by the endothelial cells which, acts as a barrier to the movement of solute and fluid into the stroma from the aqueous humor and as an active pump of solute out of the stroma into the aqueous humor.[4]

The evaluation of thickness and density of this layer is important in a wide range of disorders such as glaucoma, dry eyes, contact lens related complications and diabetes mellitus. The corneal status is also affected by various intraocular surgeries including cataract, keratoplasty, vitrectomy and refractive surgeries. [2] The endothelial changes seen in diabetic patients are similar to the changes which are caused due to aging process with a high rate of endothelial cell loss. The endothelium of diabetic patients is under stress and there is higher propensity for it decompensate. [5] Specular microscopy (SM) is a non-invasive technique for visualizing the structure and function of the corneal endothelium. [6] The intracellular accumulation of sorbitol, causes swelling of the endothelial cells in the cornea of diabetic patients and slows down the Krebs cycle leading to consequent reduction in production of ATP which is necessary for normal functioning of endothelial pump. This results in increased permeability and morphological changes in the cornea. [7]

Diabetic keratopathy affects approximately 70% of diabetic population and the features are decrease in corneal endothelial cell density (CED) and hexagonality, increase in CCT, polymegethism, pleomorphism, higher corneal auto fluorescence and lower corneal sensitivity. [4] Thus, it is important to access the corneal endothelium in all type 2 Diabetes Mellitus using Specular Microscopy. This study was done to compare endothelial cell changes in type 2 DM patients with HbA1C levels of >7% and ≤7%.

Methodology:

A case control study of 130 eyes of 130 patients attending the ophthalmology department was enrolled for this study. Institutional ethical committee clearance was obtained and informed consent was taken from the study group. Group A (n=65) included age, sex matched, non diabetic healthy controls, Group B (n=65) included type 2 diabetes mellitus patients (American Diabetic Association criteria), [8] 50 years and above and of either sex.

Group A: Controls: Age matched nondiabetic, normal subjects.
Group B: Cases: Type 2 Diabetes Mellitus.

Patients with history of past intraocular surgeries, type 1 diabetes mellitus, corneal diseases, contact lens users, active eye infections or inflammations, pterygium and glaucoma were excluded from the study. Ophthalmological examination included Visual acuity (best corrected) using Snellen`s Chart, refraction, slit lamp biomicroscopy examination, IOP with Goldman's applanation tonometery, fundus examination with direct and Indirect

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Ophthalmoscope. Corneal endothelial cell count was assessed by Non-contact Topcon SP 3000P Specular Microscope.

Procedure of Specular microscopy:

Corneal endothelial cell morphology and endothelial cell density was examined in all eyes by Non - contact specular microscope (TOPCON SP 3000P). The endothelial structure was studied by measuring endothelial cell density and percentage of hexagonal cells.

HbA1c levels was tested in all the study subjects including diabetics and non diabetic study groups.

Sample Size Estimation:

Sample size calculation was done with reference study conducted by El-agamy A. [9]

Sample size calculated was 63 in each group.

Stastistical Analysis:

Chi square test and student's 't' test was used to compare corneal endothelial cell density and cell morphology between diabetic and non-diabetic patients. Odds ratio with 95% confidence interval was calculated and p value less than 0.05 was considered as significant.

Results:

65 type 2 diabetic patients and 65 non-diabetic patients were included in the study.

Demography and Epidemiology:

In the current study, mean age group of controls was 61.59±5.38 years and mean age group of cases was 61.79±5.08 years. The study included 71 (54.6%) males and 59 (45.4%) females. In non- diabetic (control) group, 13 (47.7%) were males and 34 (52.3%) were females. In diabetic group, 40 (61.5%) were males and 25 (38.5%) were females.

Table 1: Comparison of mean HbA1C (%) between two groups:

	Group A	Group B	Unpaired t test P value
HbA1C	5.90 ± 0.35	7.01 ± 0.95	< 0.001

In group A the mean HbA1C was 5.90±0.35 and in group B the mean HbA1C was 7.01±0.95.There is increased HbA1C in diabetic group than in non-diabetic group which is statistically significant (P value <0.001)

Table 2: Descriptive analysis of HbA1C in study population (N=130)

HbA1C	Frequency(N)	Percentage (%)
>7	29	22.3%
≤7	101	77.7%
Total	130	100%

In Our study, 22.3% of the total population had HbA1C of more than 7% and remaining 77.7% had HbA1C of less than or equal to 7%.

Table 3: Endothelial Cell Density (ECD) and HbA1C levels:

HbA1C	>7(N=29)	≤7(N=101)	Unpaired t test P value
ECD	2306.38 ± 254.21	2432.56 ± 256.38	0.021

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The mean endothelial cell density in HbA1C >7 % was 2306.38 ± 254.21 and in HbA1C ≤ 7% was 2432.56 ± 256.38. There was significant reduction in the mean ECD among study population with HbA1C > 7% (P< 0.05)

Table 4: Hexagonal Cells with HbA1C levels:

HbA1C	>7(N=29)	≤7(N=101)	Unpaired t test P value
Hexagonal Cells	41.62 ± 6.68	44.10 ± 5.14	0.037

Hexagonal Cells was correlated with HbA1C. There was significant reduction in the hexagonal cells among subjects with HbA1C>7%.Hexagonal cells in patients with HbA1C levels >7 % was 41.62 ± 6.68 compared to 44.10 ± 5.14 in other group, p value was 0.037.

Table 5: Comparison of mean ECD with duration of diabetes:

Duration of Diabetes Mellitus	>10 years(N=23)	≤10years (N=42)	Unpaired t test P value
ECD	2158.52 ± 203.13	2386.88 ± 295.55 0.002	0.002

The mean endothelial cell density was correlated with duration of diabetes. There was significant reduction in the mean ECD among diabetic patients with duration of diabetes >10 years (P<0.05) 64.6% of the diabetic patients had diabetes of >10 years duration and 35.4% had duration of diabetes of <10 years.

Discussion:

In developing countries, Type 2 diabetes mellitus (T2DM) and its complications have reached epidemic levels in the past three decades. Globally T2DM is approximately present 1 in every 11 adults and about 75% of patients of diabetes live in developing countries. [10]In diabetes, the complications are due to hyperglycemia which is toxic to cells of the body. Retina and cornea are profoundly affected by hyperglycemia leading to ocular complications. Corneal complications are called as diabetic keratopathy which is seen about 70% of diabetic patients. [11]

Demography:

In our study,the mean age of the study population was 61.59±5.38 years in the control group and mean age of cases was 61.79±5.08 with 71 (54.6%) males and 59 (45.4%) females. Parekh R et al in their study had 40% of the study subjects in the age group of 51-60years, with 60% males and 40% females. [2] The mean age of the study population in a study by Shukla EJ et al was 52.02 years in diabetic and 54.76 years in non diabetic subjects. [7]

Endothelial Cell Density (ECD) and Hexagonal Cells with HbA1C in diabetics:

Inoue K et al in their study investigated the corneal morphology in diabetic and non-diabetic patients and found a significant decrease in endothelial cell density in diabetic patients. [12] Sudhir et al concluded that, subjects with type 2 diabetes mellitus had lower endothelial cell counts in comparison with non-diabetic controls. [3] Our study was similar to above

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mentioned studies. The endothelial cell density was decreased in the diabetic group when compared with the non-diabetics.

Endothelial Cell Density (ECD) and HbA1C levels:

Manish Gupta et al found that mean ECD was lower in patients having HbA1c >7% than in patients with HbA1c < 7%.[13] El-Agamy A et al concluded that ECD was significantly lower in diabetic cornea group (2,491.98±261.08 cell/mm ^{2}) than in the control group (2,629.68±293.45 cell/mm ^{2}).They also concluded that diabetic patients with HbA1C ≤ 7.5 had higher but not statistically significant ECD (2537.62±311.86 cell/mm 2) than those with HbA1C % of >7.5 (2458.78±216.06 cell/mm 2) (p=0.293), and found higher hexagonality (35.58%±10.09%) than the other group (31.54%±10.17%) (p=0.144). [9] Shukla et al showed an increase in HbA1c was associated with decrease in ECD in their study population. [7] Our study results were also similar to the above mentioned study, but the differences in corneal parameters (ECD, hexagonal cells) were compared with patients having HbA1C >7% and ≤7%, and all the corneal parameters were found to be statistically significant with HbA1C.

Mean ECD with duration of diabetes:

Manish Gupta et al showed a significant impact on the ECD of cornea in patients with diabetic duration of more than 10 years compared to patients with diabetic duration of less than 10 years (p=0.007). [13] Shukla et al concluded that in the diabetic group, lower cell counts were associated with higher HbA1c values ($P < 0.05$). [7] Study by Choo et al found that diabetes of over 10 years' duration had a lower corneal endothelium density and lower hexagonality ratios, than those patients having diabetes of under 10 years' duration. [14] Our study was similar to this study, there was a significant difference in mean ECD which correlated with duration of diabetes (p=0.048).

Conclusion:

Research has indicated that diabetic corneas have poor surgical outcomes as compared to nondiabetics. So specular microscopy is simple tool to find out changes in corneal endothelium in patients with type 2 diabetes mellitus. Thus it is important to critically assess the corneal endothelium with specular microscopy in all patients with Type 2 DM. It should be a part of the routine preoperative assessment in all patients undergoing intraocular surgery, as predicting postoperative corneal complications would be possible based upon the parameters of specular microscopy.

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