



Alteration of Corneal Structure in Patients with Diabetes Mellitus

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ABSTRACT

Objective: To determine the alteration in corneal characteristics such as endothelial cell density, mean cell area, coefficient of variation in cell size, hexagonality percentage and central corneal thickness in diabetic patients by comparing with a non diabetic group in a tertiary care hospital in South India

Methods: A cross sectional study was done including 190 diabetic patients and 190 non diabetic subjects in the age group of 40-70 years enrolled over a period of 1 year. Demographic data was collected and specular microscopy and pachymetry was done for all the subjects. The corneal parameters were compared in the 2 groups using independent samples t test.

Results: The mean age in the diabetic group was 57.91 and non diabetic group was 56.09. The mean values of mean cell area (437.17 ± 134.32 and 394.11 ± 143.68) coefficient of variation in cell size (28.02 ± 9.94 and 22.68 ± 6.09) were significantly higher in diabetic group compared to the non diabetic group. Hexagonality percentage was significantly lower in the diabetic group (55.46 ± 19.65) compared to non diabetic group (75.94 ± 6.48). Among the diabetic population, duration of diabetes had significant correlation with central corneal thickness ($r = +0.190$) and HbA1c levels had significant negative correlation with endothelial cell density and hexagonality ($r = -0.318$ and $r = -0.239$ respectively).

Conclusions: Endothelial cell morphology was found to be altered in patients with diabetes compared to non diabetic subjects which was associated with duration of disease and glycemic control in diabetic patients. This may have implications in the careful selection and intraoperative precautions in patients undergoing intraocular procedures.

Keywords- endothelial cell, corneal morphology, specular microscopy, diabetes.

Introduction

Type II diabetes mellitus is a major public health concern in this modern day. The International Diabetes Federation (IDF) estimated the global prevalence of diabetes to be 366 million in 2011 and possibly reaching up to 552 million by 2030 with

South East Asian countries bearing the highest burden of the disease^[1]. Diabetes can affect almost all the structures in the eye. Although diabetic retinopathy has been exhaustively studied the corneal changes in diabetes are frequently overlooked. This includes endothelial defects,

punctate epithelial keratopathy, recurrent corneal erosions and persistent epithelial defects^[2]. Corneal endothelial characteristics affect the prognosis of any intraocular surgery like cataract surgery. This has relevance in the diabetic population where cataractogenesis is accelerated compared to the normal population.^[3] There are not much studies which report the corneal changes in diabetic patients in Kerala where the prevalence of diabetes is high and the visual problems related to diabetes is on the rise. This study investigates the alteration of corneal structure in diabetic patients compared to non diabetics.

Materials and Methods

A hospital based cross sectional study was done over a period of 1 year. 190 diabetic patients in the age group of 40-70 years were enrolled who either satisfied the ADA criteria for diabetes^[4] or had a physician diagnosis of diabetes. 190 subjects belonging to the same age group who did not satisfy the criteria for diabetes were included in the nondiabetic group. Patients with systemic disease other than diabetes, corneal infection or inflammation active or past, contact lens wear, glaucoma, previous ocular trauma or surgery were excluded from the study. Demographic data was collected. Slit lamp examination, intraocular pressure, specular microscopy and pachymetry was done followed by dilated fundus examination for all subjects. Diabetic retinopathy was graded based on ETDRS criteria^[5]. Data regarding diabetes including diabetic age, treatment modes and HbA1c levels were collected from diabetic patients. Intraocular pressure was measured by non contact tonometry. Specular microscopy and pachymetry was done using Topcon specular microscope. Statistical analysis was done using independent samples t test.

Results

190 persons were included in the diabetic group and 190 in the non diabetic group. The mean age in the diabetic group was 57.91 and the non diabetic group was 56.09 which was indicative of the groups being effectively age matched. In the diabetic group 48.4%

were males and 51.1% were females. The non diabetic group had 45.26% males and 54.74% females.

Comparison of mean values of endothelial cell parameters and central corneal thickness between the 2 groups using independent samples t-test showed that hexagonality percentage was significantly lower in the diabetic group (55.46±19.64) as compared to non diabetic group (75.94±6.47) (p<0.05). The coefficient of variation in cell size and mean cell area were significantly higher in the diabetic group as compared to non diabetic group (p<0.05).

Table: 1 Comparison of endothelial cell characteristics between diabetic and non diabetic groups

| | Group | N | Mean | Std. Deviation | P value |
|-----|--------------|-----|-----------|----------------|---------|
| CCT | Diabetic | 190 | 513.4684 | 37.47107 | 0.245 |
| | Non diabetic | 190 | 509.6316 | 25.68863 | |
| MCA | Diabetic | 190 | 437.1789 | 134.32240 | 0.003* |
| | Non diabetic | 190 | 394.1053 | 143.68001 | |
| CV | Diabetic | 190 | 28.0211 | 9.93575 | 0.000* |
| | Non diabetic | 190 | 22.6842 | 6.08887 | |
| ECD | Diabetic | 190 | 2492.1421 | 495.29613 | 0.751 |
| | Non diabetic | 190 | 2513.6526 | 793.76239 | |
| HX | Diabetic | 190 | 55.4684 | 19.64517 | 0.000* |
| | Non diabetic | 190 | 75.9474 | 6.47726 | |

CCT=Central corneal thickness, MCA=Mean cell area, CV=Coefficient of variation in cell size, ECD=Endothelial cell density, HX=%hexagonality, N=number of subjects
*Significant at p<0.05

The mean endothelial cell density was lower and mean central corneal thickness higher in the diabetic group compared to non diabetics. However this difference in means was not found to be statistically significant (Table 1).

Mean duration of diabetes was 8.48 years of which 99 had duration less than 10 years and 91 had duration of 10 years or more. Central corneal thickness was found to be significantly increased in patients with duration of diabetes of 10 or more years (521.64±35.84) as compared to those with duration less than 10 years (505.96±37.54). Duration of diabetes had significant correlation with central corneal thickness (r=+0.190). Endothelial cell density, mean cell area, coefficient of variation

in cell size and hexagonality% did not show any significant difference between the two groups (Table2).

The mean HbA1c level was 7.73. Among the patients with diabetes 112 had HbA1c more than or equal to 7 and 78 had HbA1c levels less than 7. The present study showed that endothelial cell density was significantly lower in patients with HbA1c levels more than 7 (2396.43 ± 528.02) as compared to those with HbA1c less than 7 (2629.58 ± 409.60) as also with hexagonality. HbA1c levels had significant negative correlation with endothelial cell density and hexagonality ($r = -0.318$ and $r = -0.239$ respectively). Central corneal thickness, mean cell area and coefficient of variation in cell size and did not show any significant difference between patients with HbA1c more than or equal to 7 and those with HbA1c less than 7.

Hexagonality% was found to be significantly lower in patients with diabetic retinopathy as compared to patients without diabetic retinopathy. Central corneal thickness, mean cell area, and coefficient of variation in cell size did not show any significant

variation between patients with and without diabetic retinopathy.

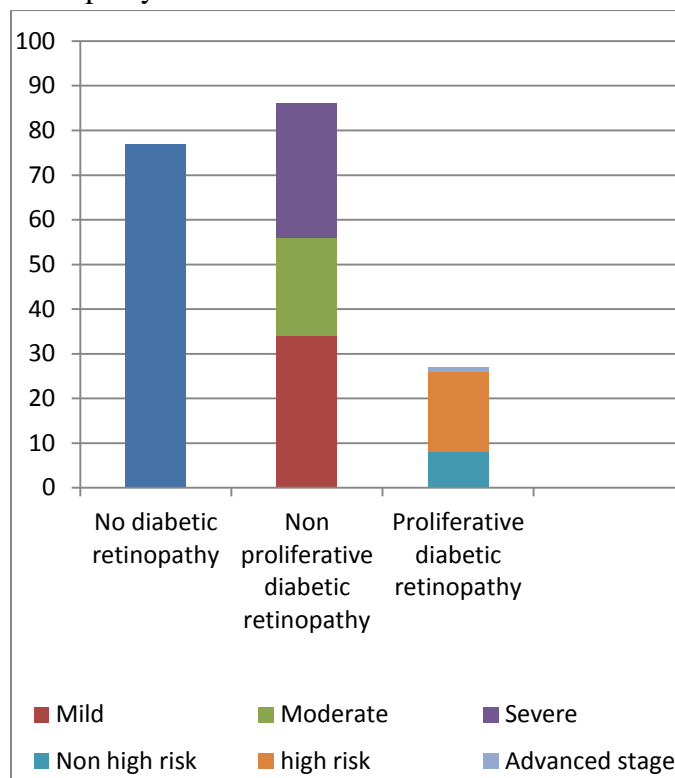


Fig 1 : Stages of diabetic retinopathy

Table 2 : Endothelial cell characteristics and CCT in relation to duration of diabetes, HbA1c levels and diabetic retinopathy in diabetic patients

| | Duration of diabetes | | | HbA1c | | | Diabetic retinopathy | | |
|-----|-------------------------|-------------------------|---------|-------------------------|-------------------------|---------|-------------------------|-------------------------|---------|
| | ≥ 10 (n=91) | < 10 (n=99) | P value | ≥ 7 (n=112) | < 7 (n=78) | P value | Present (n=113) | Absent (n=77) | P value |
| CCT | Mean±SD 521.64±35.84 | Mean±SD 505.96±37.54 | 0.004* | Mean±SD 517.43±35.25 | Mean±SD 507.78±39.99 | 0.081 | Mean±SD 512.04±34.65 | Mean±SD 515.57±41.40 | 0.525 |
| MCA | 420.96±88.25 | 452.09±164.85 | 0.111 | 432.96±131.14 | 443.23±139.39 | 0.606 | 424.12±111.39 | 456.34±161.12 | 0.105 |
| CV | 28.51±9.93 | 27.58±9.97 | 0.521 | 28.29±10.79 | 27.62±8.62 | 0.650 | 29.13±10.30 | 26.39±9.20 | 0.062 |
| ECD | 2537.16±465.14 | 2450.76±520.39 | 0.231 | 2396.43±528.02 | 2629.58±409.60 | 0.001* | 2443.91±445.05 | 2562.92±556.46 | 0.104 |
| HX | 56.54±17.51 | 54.47±21.47 | 0.469 | 50.86±19.44 | 62.09±18.10 | 0.000* | 53.03±20.11 | 59.05±18.50 | 0.038* |

CCT=Central corneal thickness, MCA=Mean cell area, CV=Coefficient of variation in cell size, ECD=Endothelial cell density, HX=%hexagonality, SD=Standard deviation, n=number of subjects

*Significant at $p < 0.05$

Discussion

The present study analysed a group of 190 diabetic patients and 190 non diabetic patients. A comparative analysis of the two groups showed increased polymegathism and pleomorphism in diabetic corneas. The endothelial cell density was lower in the diabetic group compared to the non diabetic group but the difference was not found to be statistically significant similar to a study

conducted in Malaysian population by Choo et al^[6] which showed a decrease in hexagonality and endothelial cell density and an increase in mean cell area and coefficient of variation in cell size in diabetics compared to non diabetics. Studies by Sudhir et al^[7] and Inoue et al^[8] also showed similar results.

In the present study, the mean value of central corneal thickness was higher in the diabetic group compared to non diabetic group but this difference

was not found to be statistically significant. This finding is consistent with the findings of various investigators including Chooetal, Sudhiretal who found no significant difference in central corneal thickness between diabetic and non diabetic population.^{[6],[7]} However studies conducted by Ozdamaretal^[9] and Busted et al^[10] found that CCT was significantly higher in diabetic population. Lee etal observed that diabetic subjects had thicker corneas, less cell density and hexagonality, and more irregular cell size of the corneal endothelium than did the controls.^[11]

Central corneal thickness was found to be significantly increased in patients with duration of diabetes of 10 or more years as compared to those with duration less than 10 years. Endothelial cell density, mean cell area, coefficient of variation in cell size and hexagonality% did not show any significant difference between the two groups. This is supported by the findings of Lee etal^[11] which showed that the central corneal thickness was significantly correlated with diabetic duration after controlling for age. Various studies have shown that endothelial morphology and density did not show significant difference with duration of diabetes.^{[6],[7],[8],[9]}

HbA1c level is considered as an indicator of long term control of diabetes. Endothelial cell density and hexagonality was found to be significantly lower in patients with HbA1c levels more than 7 as compared to those with HbA1c less than 7. Central corneal thickness, mean cell area and coefficient of variation in cell size and hexagonality% did now show any significant difference between patients with HbA1c more than or equal to 7 and those with HbA1c less than 7. Storr Paulson A etal observed that in diabetic population, lower cell counts were associated with higher HbA1c values.^[12] HbA1c levels did not, however, have any impact on the CCT. Study by Ozdamar etal did not show significant correlation of central corneal thickness with respect to the level of glycosylated hemoglobin and disease duration among diabetic patients.^[9] As in the present study, various studies have shown that

endothelial cell morphology did not show significant difference with HbA1c levels.

In the present study, central corneal thickness, mean cell area, coefficient of variation in cell size did not show any significant variation between patients with and without diabetic retinopathy. Hexagonality% was found to be significantly lower in patients with diabetic retinopathy as compared to patients without diabetic retinopathy. Inoue etal showed that CCT was similar regardless of the stage of diabetic retinopathy.^[8] Endothelial cell density was not found to vary with retinopathy as observed in various studies.^{[6],[7],[8]} Gautametal observed that the endothelial cell density was significantly lower in patients with proliferative diabetic retinopathy when compared to diabetic patients who do not have diabetic retinopathy but difference was not statistically significant when compared with patients having background diabetic retinopathy.^[13]

Conclusions

Endothelial cell morphology was found to be altered in patients with diabetes compared to non diabetic subjects and these changes were associated with duration of disease and glycemic control. Morphological abnormalities in the endothelium and endothelial cell loss are associated with increased incidence of corneal edema. Hence examination of the corneal morphology may help in careful selection of patients and appropriate precautions in elective surgeries thus reducing postoperative complications.

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