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Original Research Paper

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A COMPARATIVE OBSERVATIONAL STUDY OF CORNEAL ENDOTHELIAL CHANGES IN TYPE 2 DIABETES MELLITUS WITH THAT OF NON DIABETIC PATIENTS USING NON CONTACT SPECULAR MICROSCOPY IN TERTIARY CARE CENTRE.

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ABSTRACT Endothelial layer of cornea is a fragile cell layer and its integrity and viability is important to maintain corneal transparency. This study aims to compare the corneal endothelial cell morphology and central corneal thickness in patients with and without type 2 diabetes. In this comparative observational study conducted for a period of 3 months on 100 subjects of which 50 were type 2 diabetics and 50 were non-diabetics. The central corneal thickness and corneal endothelial structure was examined for cell density, coefficient of variation of cell area, and percentage of hexagonal cells. The central corneal thickness was increased and endothelial cell density was decreased in type 2 diabetic patients (p value < 0.05). However, coefficient of variation of cell area, and percentage of hexagonality in diabetic patients was not significantly different from that of non-diabetic patients (p value > 0.05). Thus routine preoperative analysis of corneal endothelial morphology is importatnt.

KEYWORDS : Central corneal thickness, Endothelial cell density, Association

INTRODUCTION

The corneal endothelium is a single layer of cells that plays a major role in maintaining the optical transparency of the cornea through the Na+/K+ATPase pump activity. Corneal endothelial cells have the highest density at birth, which decreases by approximately 0.5% per year following aging.[1] Diabetes mellitus (DM) occurs when the pancreas is not able to produce enough insulin or the body becomes resistant to insulin, or both, resulting in increased blood glucose levels. This may lead to micro and macro vascular disorders.[2] Chronic hyperglycemia is characteristic of the disease and it does not spare any organ in the human body.[3] Reduced corneal ECD and swelling of the cornea are indicators of corneal dysfunction.[4]

Diabetic retinopathy remains the most commonly studied manifestation in eye. However, functional abnormalities have been documented in cornea too like decreased endothelial cell density (ECD), increased corneal thickness.[5]Corneal endothelial cell is responsible for maintaining the transparency of the cornea. There is limited ability of mitosis in corneal endothelium and once damaged, remaining cells enlarge to cover up the lost area.[6]

There will be an increase in variation of cell area called polymegathism or coefficient of variation (CV) and index of hexagonality or pleomorphism. Central corneal thickness (CCT) can be used as a marker of endothelial health and can be used to monitor corneal edema. There is a postulated association between corneal thickness and severity of diabetic retinopathy.[7]This study is done to compare the effect of type 2 diabetes on the corneal endothelium compared to non diabetics.

METHODOLOGY

A comparative observational study was conducted from May 2022 to July 2022 in the Department of Ophthalmology, Mandya Institute of Medical Sciences, Mandya , 100 subjects were recruited of which 50 were cases and 50 were controls. Cases and controls are defined as patients of type 2 diabetes mellitus and age matched non-diabetic individuals respectively. The study plan was approved by institutional ethic committee and informed consent was obtained from all subjects participating in the study. All patients with age above 40 years and diabetic disease duration more than 5 years and who are willing to consent for the study, presenting to Ophthalmology OPD were included in the study. The criteria for exclusion from the study were patients with conditions known to affect endothelial count like pseudoexfoliation, long term use of contact lenses, glaucoma or previous anterior segment surgery, uveitis, laser treatment and Presence of corneal abnormalities (e.g., corneal opacity, corneal degeneration and dystrophies, or corneal scarring).

Demographic data such as age, gender and relevant diabetic history were obtained including complete anterior and posterior segment evaluation was done. Non-contact specular microscope was then used to image the corneal endothelium. Using a fixed frame method of analysis and KSS software, 80 - 100 endothelial cells was photographed in centre of cornea. Further morphometric analysis and automated cell analysis was done to obtain mean corneal endothelial cell density (ECD), coefficient of variation of cell size (CV), percentage of hexagonality (6A), and central corneal thickness (CCT).

Statistical Analysis

All data collected were entered in Microsoft Excel sheet and were statistically analyzed based on average of data from both eyes. Data will be analysed using Statistical Package for the Social Sciences (SPSS) trial version. The corneal descriptors endothelial cell density, coefficient of variation, percentage of hexagonality and central corneal thickness will be obtained and will be expressed as mean with standard deviation (mean ± SD).

The data will be analysed for normality distribution. The Student's t-test will be employed to compare corneal descriptors between the cases and control groups. A value of $p \leq 0.05$ will be considered to be statistically significant.

RESULTS:

A total of 100 subjects were recruited for the study. Of the 100 subjects, 50 were cases and 50 were age matched controls. Mean age for cases of type 2 diabetes mellitus and controls were 55.15 ± 6.54 and 52.21 ± 8.34 years respectively (p value = 0.091).

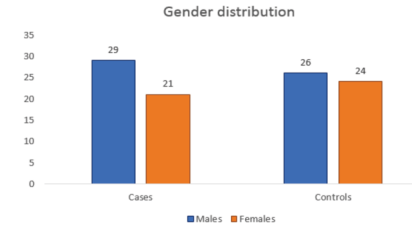

Figure 1. Gender Distribution Among Cases And Controls.

Out of 50 subjects in each group, the case group had 29 (58%) male and 21 (42%) female while the control group had 26 (52%) male and 24 (48%) female.

Table 1. Corneal Endothelial Cell Count (ecd), Cell Size Variation Coefficient (cv), Percentage Of Hexagonal Cells(6a), And Central Corneal Thickness (cct) In Diabetic And Non-diabetic Subjects In Mean ± Sd.

	Cases (n = 50)	Controls (n = 50)	P value*
CCT(μm)	568.43 ± 47.84	535.63 ± 64.04	0.043
ECD(cell/mm2)	2588.7 ± 220.5	2896.3 ± 296.8	0.039
CV(%)	31.93 ± 1.06	32.61 ± 0.92	0.324
6A(%)	46.94 ± 5.21	48.81 ± 6.64	0.092

CI (confidence interval) - 95%, SD - Standard Deviation, * - Student's t-test

The mean CCT in diabetic group was 568.43 ± 47.84 μm while in the non-diabetic controls was 535.63 ± 64.04 μm and results were statistically significant (p value = 0.043). The mean ECD in diabetic group was 2588.7 ± 220.5 cell/mm^2 while in the non-diabetic controls was 2896.3 ± 296.8 cell/mm^2 and the results were statistically significant (p value = 0.039). The mean CV in diabetic group was 31.93 ± 1.06 % while in non-diabetic controls was 32.61 ± 0.92 % , and the hexagonality in diabetic group was 46.94 ± 5.21 % while in non-diabetic controls was 48.81 ± 6.64 %. However, comparison of coefficient of variation (CV) and hexagonality (6A) in the two groups did not yield any statistically significant results (p value > 0.05).

DISCUSSION

The results of our study shows that there is significant association of diabetes with the corneal endothelial cell density and central corneal thickness while no significant association with the coefficient of variation and percentage of hexagonality. The key finding in our study is that the age difference between the cases and controls was not statistically significant. (p value = 0.091). Thus the groups were comparable.

The mean CCT in diabetic group was significantly increased compared to non-diabetic group (p value = 0.043). The studies conducted by Kim YJ et al, Storr Paulsen A et al, Durukan I, showed a significant increase in CCT.[1,5,11] The study conducted by Sumit SA et al showed minimal increase in CCT in diabetic groups.[3] Study conducted by Inoue K et al and Beato JN et al showed no significant association.[9,10]

The mean ECD was significantly reduced in cases when compared to control group (p value = 0.039). Studies conducted by Briggs S et al, El-Agamy A et al and Inoue K et al also showed significant association of diabetes on ECD similar to our study.[2,8,9] Study by Beato JN et al showed no significant association,[9] while study by Storr Paulsen A et al reduced ECD in cases with poor glycemic control.[5]

Our study did not show any significant association of diabetes with the cell size variation coefficient and percentage of hexagonality (p value > 0.05). Studies conducted by Storr Paulsen A et al and Beato JN et al also showed no significant association.[5,10] Other studies by Kim YJ et al, Shenoy R et al and El-Agamy A et al showed significant association.[1,4,8]

Endothelial layer of cornea is a fragile cell layer and its integrity and viability must be guarded during any intraocular procedure. Despite constant decline in cell population occurring throughout life, normal thickness and transparency of the tissue is maintained by change in size and shape of the existing endothelial cells. Additional stresses imposed on this layer markedly augment the normal aging process of accelerating cell loss. Decompensation of cornea with edema ensues at cell densities of 400–700 cells/mm2.[4] High glucose levels lead to increased activity of the aldose reductase, causing sorbitol buildup in the corneal epithelial and endothelial cells. This sorbitol acts as an osmotic agent and leads to swelling of endothelial cells. Also, DM diminishes Na+-K+ ATPase activity of the corneal endothelium, resulting in morphological and permeability changes in diabetic cornea, thereby leading to corneal destruction. Furthermore, endothelial pump function was proven to be affected by decreased ATP production as a result of slowing down of the Krebs cycle in diabetic cornea.[8]

CONCLUSION

Our study showed statistically significant reduction in corneal endothelial cell density and increase in central corneal thickness in diabetic patients compared to non-diabetic patients. With regard to hexagonality and coefficient of variation of cell size, our study, did not find any difference between cases and controls.Thus routine preoperative analysis of corneal endothelial morphology is important. There were no systemic or ocular factors at any point to induce corneal endothelial damage.

Conflict Of Interest

None declared

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