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A Comparative Study on Corneal Endothelial Morphology between Diabetic and Healthy Subjects

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Abstract: ***Background**: Diabetes mellitus can cause structural and functional alterations in the corneal endothelium due to chronic hyperglycemia. Evaluation of corneal endothelial morphology by specular microscopy is important in diabetic patients, especially prior to intraocular surgeries. **Aim**: To compare corneal endothelial morphology between diabetic and healthy subjects using specular microscopy. **Methodology**: This cross-sectional comparative study included 200 eyes of 100 subjects, comprising 100 eyes of 50 diabetic patients and 100 eyes of 50 age-matched gender matched healthy controls. Corneal endothelial parameters including central corneal thickness (CCT), endothelial cell density (ECD), coefficient of variation (CV), and hexagonality (HEX) were assessed using specular microscopy. Statistical analysis was performed using Independent Student's t-test and Chi-square test. **Results**: Mean central corneal thickness was significantly higher in diabetic patients compared to controls (578 ± 33 µm vs 546 ± 28 µm; $P < 0.001$). Endothelial cell density was significantly lower in diabetics (2485 ± 214 cells/mm² vs 2678 ± 198 cells/mm²; $P < 0.001$). Coefficient of variation was significantly increased, while hexagonality was significantly reduced in diabetic patients compared to non-diabetic subjects ($P < 0.001$). **Conclusion**: Diabetes mellitus is associated with significant corneal endothelial morphological alterations. Specular microscopy may help in early detection of endothelial compromise and aid in better ophthalmic management of diabetic patients.*

Keywords: Diabetes mellitus, Corneal endothelium, Specular microscopy, Endothelial cell density, Central corneal thickness

1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterised by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both.[1] It is one of the most significant global health challenges, with rapidly increasing prevalence worldwide, particularly in developing countries such as India.[2] Long-standing diabetes is associated with widespread macrovascular and microvascular complications involving multiple organ systems, including the eye.[3] Ocular manifestations of diabetes are an important cause of visual morbidity and can affect both the anterior and posterior segments of the eye.[4]

Among the ocular complications, diabetic retinopathy has been extensively studied as a leading cause of preventable blindness. However, diabetes-related changes are not limited to the retina alone.[5] Increasing evidence suggests that chronic hyperglycemia can also affect the conjunctiva, tear film, cornea, lens, and optic nerve.[6] Corneal involvement in diabetes, commonly referred to as diabetic keratopathy, includes abnormalities such as delayed epithelial healing, recurrent erosions, reduced corneal sensitivity, increased corneal thickness, and endothelial dysfunction.[7]

A layer of hexagonal cells lining the posterior layer of cornea form corneal endothelial layer. They help in maintaining corneal transparency through their barrier and metabolic pump functions, which regulate stromal hydration.[8] Unlike corneal epithelial cells, endothelial cells possess minimal regenerative capacity. Therefore, any endothelial cell loss or morphological alteration may compromise corneal clarity, leading to corneal edema and visual impairment.[9]

There may be changes in the structure and function of the corneal endothelium due to persistent hyperglycemia. Factors such as oxidative stress, sorbitol accumulation, advanced glycation end products, mitochondrial dysfunction, and reduced Na^+/K^+-ATPase pump activity can all damage these cells.[10] These issues may reduce the number of endothelial cells, increase cell size differences (polymegathism), and alter cell shape of hexagonal cells (pleomorphism).[11]

Specular microscopy is a non-invasive way to closely examine the corneal endothelium.[12] It measures various parameters like endothelial cell density (ECD), coefficient of variation (CV), and the percentage of hexagonal cells, central corneal thickness(CCT) ,which help assess endothelial health.[13] Checking these parameters is especially important for diabetic patients who need eye surgery, as existing endothelial problems can increase the risk of corneal damage after intraocular surgery.[14]

Many studies have found changes in the corneal endothelium in people with diabetes, but the details vary between populations and study methods.[15] There is still little data from India, even though diabetes is common.[16] Finding these changes early can help us understand how diabetes affects the cornea and improve eye care before and after surgery.[17]

Hence, the present study was undertaken to compare corneal endothelial morphology between diabetic and healthy subjects using specular microscopy.

2. Aim & Objective

Aim

The aim of this study is to compare the corneal endothelial morphology between type 2 diabetics and age and gender matched healthy controls

Objectives:

- To analyse the morphology of corneal endothelial cells in Type 2 Diabetic patients by specular microscopy.
- To compare the corneal endothelial Morphology between diabetic and age and gender matched healthy subjects

3. Methodology

This cross-sectional study was conducted at ophthalmology department in a tertiary care hospital. A total of 200 eyes with 100 eyes in each diabetic group and healthy control group were included in the study. Ethical approval obtained from institutional ethics committee. The inclusion criteria for cases were adults of Age above 40 years with type 2 diabetes mellitus diagnosed based on American Diabetes Association (ADA) criteria and controls included were age and gender matched healthy adults. Patients consenting for study are included.

Patients were excluded from the study if they had history of glaucoma/pre-existing corneal dystrophies /retinal diseases, scarred corneas or opacities and history of ocular trauma or contact lens users. Patients with other systemic comorbidities such as hypertension, chronic kidney disease, coronary artery disease other than type-2 diabetes mellitus were excluded. All the patients included in study underwent thorough Ocular evaluation, best corrected visual acuity by LogMAR chart, near vision by roman test numeral type, colour vision assessed with Ishihara chart and slit lamp examination of anterior segment, IOP measured using goldmann applanation tonometry, Corneal endothelial imaging was performed using a non-contact specular microscopy, which captured images in automatic mode, focusing on the central corneal zone. From the images obtained, key endothelial parameters were analysed, including endothelial cell density (ECD), central corneal thickness (CCT), coefficient of variation (CV), and hexagonality (HEX). This was repeated three times for each eye and image with the median number of ECD, CCT, CV, and hexagonality were used for analysis. Detailed fundus evaluation after dilation with – tropicamide 0.8% eyedrops + phenylephrine5% by a single examiner

Statistical Analysis

The study data were entered into Microsoft Excel and analysed with SPSS software version 23.0. Continuous variables are shown as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Differences between diabetic and non-diabetic groups were checked using the Independent Student's t-test for continuous data and the Chi-square test for categorical data like gender. The main parameters analysed were central corneal thickness (CCT), endothelial cell density (ECD), coefficient of variation (CV), and percentage of hexagonality (HEX). A P value less than 0.05 was considered statistically significant.

4. Results

A total of 200 eyes of 100 subjects were included in the present study, comprising 100 eyes of diabetic patients (Group A) and 100 eyes of healthy controls (Group B). The study population belonged to the age group above 40 years, with the majority of subjects in the 50–60 years age group. [Table 1]

The mean age of subjects in Group A was 57 ± 6 years, whereas in Group B it was 55 ± 6 years. The difference in mean age between the two groups is not statistically significant (P = 0.18), indicating that both groups were age matched. [Table.1] [figure.1]

Table 1: Distribution of age among both groups

Age Group (Years)	Group A – Diabetics (n = 50)	Percentage	Group B – Controls (n = 50)	Percentage
45–50	6	12%	7	14%
51–60	29	58%	28	56%
61–70	12	24%	11	22%
>70	3	6%	4	8%
Total	50	100%	50	100%
Mean Age ± SD	57 ± 6 years	—	55 ± 6 years	—

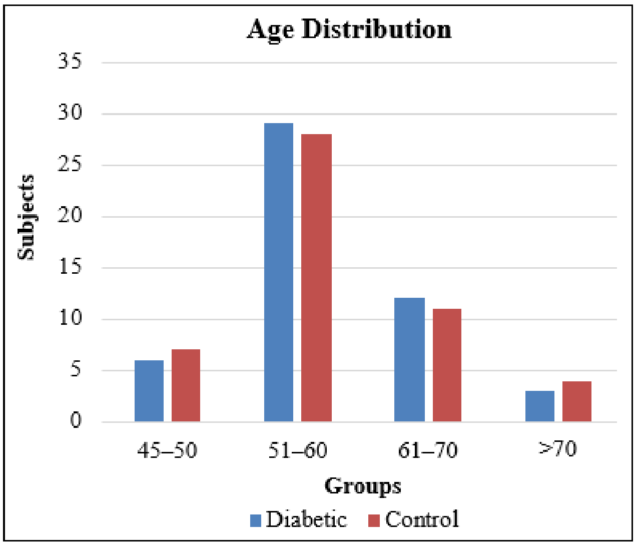

Figure 1: Age Distribution among groups

Among diabetic subjects, 27 (54%) were males and 23 (46%) were females[figure.2]. In the control group, 26 (52%) were males and 24 (48%) were females[figure.3]. The gender distribution between the two groups in statistically insignificant (P > 0.05). [Table.2].

Table 2: Gender Distribution among both groups

Gender	Group A (n = 50)	Group B (n = 50)
Males	27 (54%)	26 (52%)
Females	23 (46%)	24 (48%)

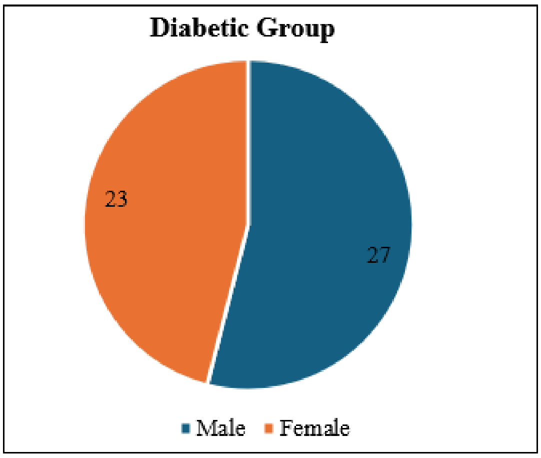

Figure 2: Gender distribution among diabetic group

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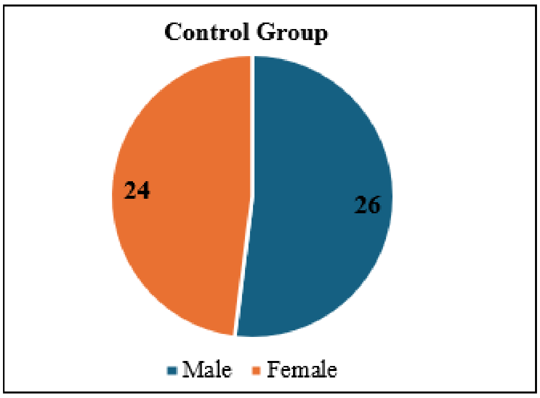

Figure 3: Gender distribution among control group

The mean central corneal thickness (CCT) in Group A was 578 ± 33 µm, while in Group B it was 546 ± 28 µm. The CCT was higher in diabetic patients and the difference was statistically significant ($P < 0.05$). [Table.3] [figure.4]

Table 3: Comparison of central corneal thickness (CCT) between diabetic and healthy groups

Group	CCT (µm)
Group B	546 ± 28
Group A	578 ± 33
P value	<0.001

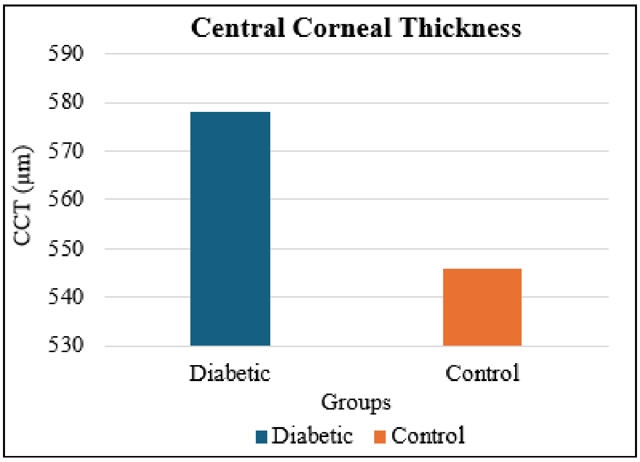

Figure 4: Central corneal thickness among both groups

Mean endothelial cell density (ECD) was significantly lower in Group A (2485 ± 214 cells/mm²) compared to Group B (2678 ± 198 cells/mm²) with P value < 0.05 statistically significant [table.4] [figure.5]

Table 4: Comparison of endothelial cell density (ECD) between diabetic and healthy groups

Group	ECD (cells/mm²)
Group B	2678 ± 198
Group A	2485 ± 214
P value	<0.001

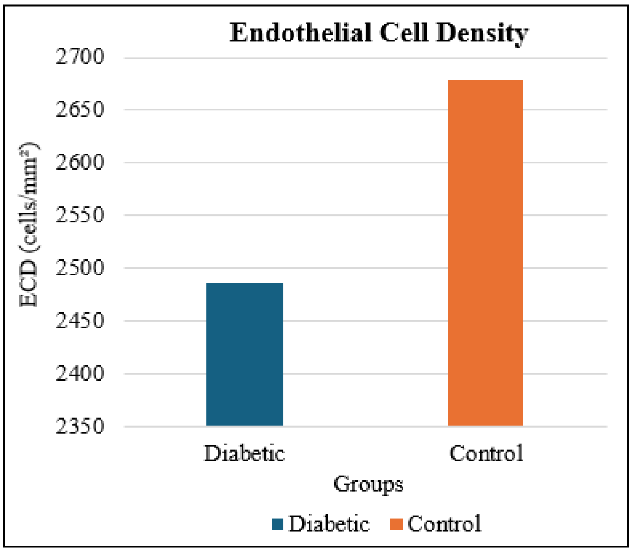

Figure 5: Endothelial cell density (ECD) among both groups

The mean coefficient of variation (CV) in diabetic patients was 39 ± 6%, whereas in non-diabetic subjects it was 34 ± 4%. This demonstrated statistically significant higher CV values in diabetic patients ($P < 0.05$), indicating increased polymegathism. [Table 5] [figure.6]

Table 5: Comparison of co efficient of variance (CV) between diabetic and healthy groups

Group	CV (%)
Group B	34 ± 4
Group A	39 ± 6
P value	<0.001

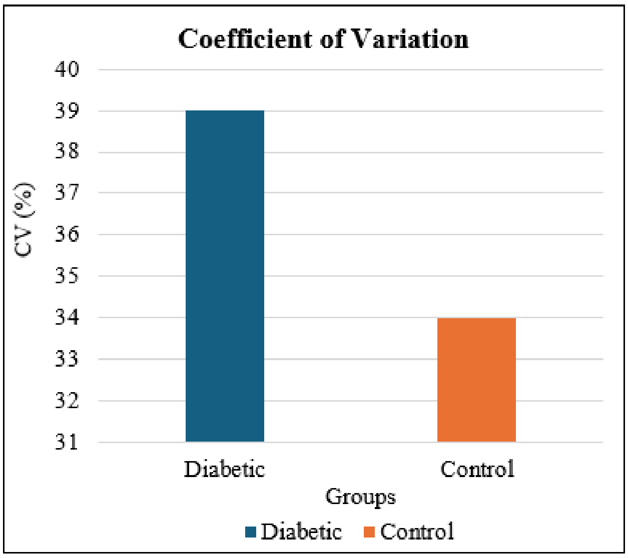

Figure 6: The mean coefficient of variation (CV) among both groups

Mean hexagonality in Group A patients was 46 ± 8%, while in Group B it was 55 ± 7%, with P value < 0.05 showing statistically significant lower hexagonality in diabetic patients, suggestive of endothelial pleomorphism [table.6] [figure.7]

Table 5: Comparison of hexagonality between diabetic and healthy groups

Group	Hexagonality (%)
Group B	55 ± 7
Group A	46 ± 8
P value	<0.001

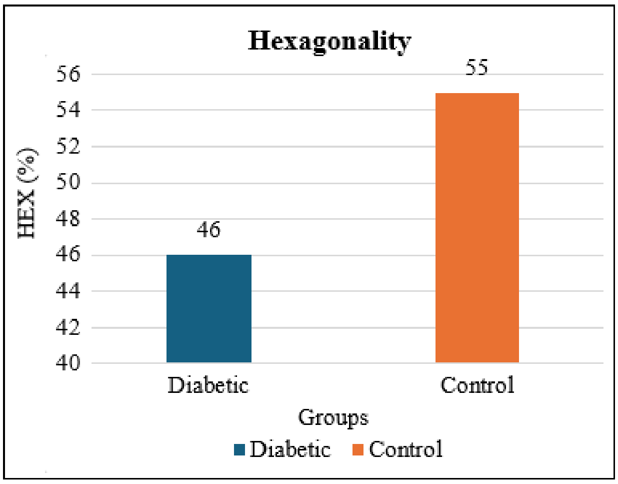

Figure 7: Hexagonality among both groups

5. Discussion

Diabetes mellitus is associated with several ocular complications. In recent years, increasing attention has been directed toward corneal endothelial alterations associated with chronic hyperglycemia.[18] The present study evaluated corneal endothelial morphology and central corneal thickness in diabetic patients and compared them with healthy controls using specular microscopy.

In the present study, diabetic patients demonstrated significantly increased central corneal thickness (CCT) compared to non-diabetic controls. The mean CCT in diabetic subjects was 578 ± 33 µm, whereas in controls it was 546 ± 28 µm ($P < 0.001$). Increase in central corneal thickness in diabetic patients may be attributed to endothelial pump dysfunction secondary to chronic metabolic stress. Hyperglycemia-induced impairment of Na^+/K^+ ATPase activity, sorbitol accumulation, oxidative stress, and altered endothelial permeability may contribute to stromal hydration and increased corneal thickness.[19]

Similar findings were reported by Storr-Paulsen et al., observed significantly increased CCT in diabetic individuals.[13] Comparable observations were also made by El-Agamy and Alsubaie[14] and Gao et al.,[20] suggesting that diabetes mellitus may alter endothelial barrier and pump functions leading to increased corneal thickness.

Our study demonstrated significantly reduced endothelial cell density (ECD) in diabetic patients compared to controls (2485 ± 214 cells/mm² vs 2678 ± 198 cells/mm²; $P < 0.001$). Reduction in endothelial cell density indicates chronic endothelial stress and loss of endothelial reserve associated with diabetes mellitus. Endothelial cells compensate for cell loss by polymegathism and redistribution, ultimately resulting in decreased cellular density.[21]

Similar to the findings in our study, Sudhir et al.,[17] also reported significantly lower endothelial cell density in diabetic subjects. Bikbova et al.[6] and Goldstein et al.,[10] also suggested that prolonged hyperglycemia contributes to endothelial cell apoptosis and metabolic dysfunction.

Coefficient of variation (CV) in diabetic patients in our study was significantly higher compared to controls (39 ± 6% vs 34 ± 4%; $P < 0.001$). Increased CV reflects polymegathism and increased variability in endothelial cell size. Polymegathism is considered an indicator of endothelial stress and compensatory remodeling following endothelial cell injury.[22]

Comparable results were reported by Choo et al.,[23] who found significantly increased CV values among diabetic patients. Similar findings were also demonstrated by Shenoy et al.[16] and Taşlı et al.,[15] supporting the concept that diabetes mellitus induces significant endothelial morphological instability.

Our study also demonstrated significantly reduced hexagonality in diabetic patients compared to controls (46 ± 8% vs 55 ± 7%; $P < 0.001$). Reduced percentage of hexagonal cells indicates pleomorphism and disruption of normal endothelial architecture. Morphological endothelial changes may reflect adaptive cellular remodeling in response to chronic metabolic injury.[24]

Similarly, Zhang et al.[11] in their meta-analysis concluded that diabetes mellitus is associated with decreased endothelial cell density and hexagonality along with increased CV. Raman et al.[25] and Ascaso et al.[26] also reported significant pleomorphic changes in diabetic corneas.

The endothelial alterations observed in diabetic patients may be explained by chronic hyperglycemia-induced metabolic dysfunction. Intracellular sorbitol accumulation acts as an osmotic agent causing endothelial cell swelling, while oxidative stress and mitochondrial dysfunction impair endothelial metabolism and pump function.[27] These changes can compromise corneal endothelial reserve and may increase susceptibility to postoperative corneal edema following intraocular surgeries.

6. Limitations of the Study

This study was conducted at a single tertiary care center, which may limit the generalisability of the findings to the broader population and duration of diabetes and glycemic control were not subgroup analysis with respect to endothelial parameters and larger sample size and longitudinal study are recommended to better evaluate the progression of corneal endothelial changes in diabetes mellitus.

7. Conclusion

The present study demonstrated significant corneal endothelial morphological alterations in diabetic patients compared to non-diabetic controls. Diabetic subjects showed increased central corneal thickness and coefficient of variation along with reduced endothelial cell density and hexagonality, indicating endothelial dysfunction, polymegathism, and pleomorphism associated with diabetes mellitus.

Chronic hyperglycemia and associated metabolic disturbances appear to adversely affect corneal endothelial structure and function. Since corneal endothelial cells possess limited regenerative capacity, these changes may compromise endothelial reserve and increase susceptibility to corneal stress during intraocular procedures.

The findings of our study emphasise the importance of routine corneal endothelial assessment in diabetic patients, especially prior to intraocular surgical procedures.

Routine assessment of corneal endothelial morphology using specular microscopy in diabetic patients may aid in early detection of endothelial compromise and assist ophthalmologists in better surgical planning.

Preoperative precautions such as using dispersive ocular viscodevices, reducing operating time and using minimal phaco power to avoid endothelial compromise by early detection with specular microscopy in diabetic individuals.

Conflicts of interest: nil

Financial interest's: nil

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