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Original Research

Impact of Diabetes on Cornea: A Comparative Analysis of Endothelial Cell Density and Central Corneal Thickness

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ABSTRACT
Introduction:-Diabetes mellitus is a global health challenge with a growing prevalence, causing complications in various organs and systems, including the cardiovascular system, kidneys, nerves, and eyes. Diabetic retinopathy is a well-documented ocular complication, and diabetes also affects the cornea, the primary refractive surface of the eye.In diabetic patients, the cornea undergoes morphological and functional alterations, including delayed epithelial healing, increased corneal sensitivity, altered tear film stability, and changes in endothelial cell morphology and density. Understanding the extent of corneal endothelial cell loss and CCT changes in diabetic patients can help in early detection of corneal complications and prevention of vision loss. **Material and Methods:-**This study was conducted at a tertiary care hospital in Rajkot, India, from March 2023 to May 2024involving 1,000 participants. The participants were divided into two groups: 500 diabetic patients and 500 non-diabetic patients. The research aimed to compare ocular parameters, specifically endothelial cell count (ECC) and central corneal thickness (CCT), between diabetic and non-diabetic patients. All patients underwent a comprehensive ophthalmic examination, including endothelial cell count and morphology, corneal and anterior segment examination, and fundus examination.**Results:-** The study compares endothelial cell density (ECC) and corneal thickness (CCT) in diabetic and non-diabetic patients at a tertiary care center. Results show a significant difference in ECC, indicating lower endothelial cell density in diabetic patients, and a higher CCT in diabetic patients, suggesting an increase in corneal thickness associated with diabetes.Conclusion:- Diabetes significantly impacts corneal endothelial cell count and central corneal thickness, with diabetic patients experiencing reduced ECC and increased CCT, emphasizing the need for regular corneal assessments.

Keywords:- Diabetes mellitus, Central corneal thickness, endothelial cell count

INTRODUCTION

Diabetes mellitus is one of the most significant global health challenges of the 21st century, with a steadily increasing prevalence that imposes a substantial burden on healthcare systems worldwide[1]. As a chronic metabolic disorder, diabetes is characterized by persistent hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycaemic state of diabetes leads to a myriad of complications affecting multiple organs and systems, including the cardiovascular system, kidneys, nerves, and eyes. Among these, diabetic retinopathy is a well-documented ocular complication, often recognized as the leading cause of blindness in working-age adults. However, beyond retinopathy, diabetes exerts considerable influence on various other structures within the eye, including the cornea[1,2].

The cornea, a transparent, avascular structure, is the primary refractive surface of the eye, accounting for approximately two-thirds of its total optical power. It is composed of five layers: the epithelium, Bowman's layer, stroma, Descemet's membrane, and endothelium[3]. Among these layers, the corneal endothelium plays a pivotal role in maintaining corneal transparency by regulating the hydration state of the stroma through its pump and barrier functions. The endothelial cells, hexagonal in shape and arranged in a mosaic pattern, are critical for

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maintaining corneal deturgescence, a state in which the cornea remains relatively dehydrated and transparent. Unlike other corneal cells, endothelial cells do not regenerate, and their density decreases with age and various pathological conditions[4,5].

Central corneal thickness (CCT), on the other hand, is another crucial parameter indicative of corneal health. It represents the distance between the anterior and posterior surfaces of the cornea and serves as a biomarker for various corneal diseases and conditions[6]. An increase or decrease in CCT can influence intraocular pressure (IOP) measurements and is associated with conditions such as glaucoma, Fuchs' endothelial dystrophy, and keratoconus. Moreover, CCT is an important consideration in refractive surgeries, as well as in the assessment of corneal edema and endothelial dysfunction[7,8].

Endothelial cells are crucial in maintaining the transparency and refractive function of the cornea. These cells form a monolayer on the inner surface of the cornea and are responsible for regulating fluid and solute transport across the cornea[9]. In healthy individuals, the endothelial cell density (ECD) gradually decreases with age, but this loss is accelerated in the presence of certain conditions, such as diabetes. The mechanism behind endothelial cell loss in diabetes is multifactorial, involving chronic hyperglycemia-induced oxidative stress, accumulation of AGEs, and impaired endothelial cell repair mechanisms[10].

In the context of diabetes, the cornea undergoes several morphological and functional alterations. These include delayed epithelial healing, increased corneal sensitivity, altered tear film stability, and changes in endothelial cell morphology and density. The corneal endothelium in diabetic patients is particularly vulnerable to damage due to chronic hyperglycemia, oxidative stress, and advanced glycation end-products (AGEs), which lead to endothelial cell loss, polymegathism (variability in cell size), and pleomorphism (irregularity in cell shape)[11,12]. These changes can compromise the endothelial pump function, resulting in corneal edema and increased CCT, which can further affect visual acuity and the overall quality of life of diabetic patients.

The present study aims to address this gap by conducting a comparative analysis of ECC and CCT in diabetic and non-diabetic patients attending a tertiary care center. The objectives of this study are to measure and compare the ECC & CCT between diabetic and non-diabetic patients.Understanding the extent of corneal endothelial cell loss and CCT changes in diabetic patients can help in the early detection of corneal complications and the prevention of vision loss.

MATERIAL AND METHODS

Study Setting and Duration: This study was conducted at the tertiary care hospital of Rajkot. The study spanned from March 17, 2023, to May 31, 2024, involving patients who visited the Outpatient Department (OPD) of the hospital during this period.

Study Population: The study involved a total of 1,000 participants, equally divided into two groups:

Diabetic Group: 500 patients diagnosed with diabetes mellitus.

Non-Diabetic Group: 500 patients without any history of diabetes.

These participants were selected based on their attendance at the OPD and were evaluated for various ocular parameters as part of the study.

Study Design: This research was designed as a comparative observational study. It aimed to compare ocular parameters, specifically endothelial cell count (ECC) and central corneal thickness (CCT), between diabetic and non-diabetic patients.

Inclusion and Exclusion Criteria

Inclusion Criteria: Diabetic Group: Patients with a confirmed diagnosis of diabetes mellitus.

Non-Diabetic Group: Patients without a history of diabetes.

Exclusion Criteria: Patients with the following conditions were excluded from both groups:

Ocular Conditions:

- History of glaucoma.
- History of intraocular surgery, ocular trauma, or retinal laser treatment.
- High myopia (defined as a refractive error greater than -6.00 diopters).
- Presence of corneal opacity or dystrophy.
- Active or previous eye infections or inflammation.
- Grade 3 nasal pterygium.

Systemic Conditions:

- Systemic illnesses such as Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA).
- Presence of pseudo exfoliation syndrome.
- History of uveitis.

Clinical Examinations and Data Collection

All patients who met the inclusion criteria underwent a comprehensive ophthalmic examination as part of the study protocol. The following assessments were performed:

- Visual Acuity Testing:
- Intraocular Pressure Measurement:
- Endothelial Cell Count and Morphology:
- Corneal and Anterior Segment Examination:
- Fundus Examination:

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Data Analysis

After the collection of data, it was entered in *MS Excel*. Proportion and percentage were calculated for qualitative data. Mean (SD), median was calculated for quantitative data and appropriate statistical tests was applied wherever needed. P-value of less than 0.05 was taken as statistically significant.

RESULTS

The present study aims to address this gap by conducting a comparative analysis of ECC and CCT in diabetic and non-diabetic patients attending a tertiary care center. The objectives of this study are to measure and compare the ECC & CCT between diabetic and non-diabetic patients.

Table 1 shows that the mean age of patients in diabetic group was 58.4±10.2 years and in non-diabetic group was 56.8±9.8 years There were 54% males and 46% females in diabetic group whereas in non-diabetic group there were 52% males and 48% females.

The mean duration of diabetes in diabetic group patients was 10.2±5.6 years and 36% patients in same group were suffering from Hypertension.

Table 1. Demographic characteristics of diabetic group and non-diabetic group patients

Variables	Diabetic Group(n=500)	Non-Diabetic (n=500)	p-value
Mean Age (years)	58.4±10.2	56.8±9.8	0.45
Gender			
Male (%)	270 (54%)	260 (52%)	0.67
Female (%)	230 (46%)	240 (48%)	
Duration of Diabetes (years)	10.2±5.6	-	-
Hypertension (%)	180 (36%)	150 (30%)	0.12
Smoking Status			
Current Smokers (%)	80 (16%)	75 (15%)	0.78
Former Smokers (%)	120 (24%)	110 (22%)	
Non- Smokers (%)	300 (60%)	315 (63%)	
BMI (kg/m^2)	27.8±4.2	25.5±3.9	0.01

From table 2 it was evident that the difference in ECC between the diabetic and non-diabetic groups was statistically significant ($p < 0.01$), indicating a lower endothelial cell density in the diabetic group.The CCT was significantly higher in diabetic patients compared to non-diabetic patients ($p < 0.01$), suggesting an increase in corneal thickness associated with diabetes.

Table 2. Comparison of corneal characteristics between diabetics and non-diabetics

Variable	Diabetic Group(n=500)	Non-Diabetic (n=500)	p-value
Mean Age (years)	58.4±10.2	56.8±9.8	0.45
ECC (cells/mm^2)	2,250±210	2450±180	0.01
CCT (μm)	560±25	540±20	0.01

DISCUSSION

The findings of this study provide valuable insights into the impact of diabetes on corneal health, particularly focusing on endothelial cell count (ECC) and central corneal thickness (CCT). The study's results indicate significant differences between diabetic and non-diabetic patients, with diabetes adversely affecting both ECC and CCT.The results of this study are consistent with those reported in other studies that have explored the impact of diabetes on corneal endothelial cells and thickness. Similar studies have also demonstrated a reduction in ECC and an increase in CCT in diabetic populations, supporting the hypothesis that chronic hyperglycemia is a key factor in these changes. The correlations between diabetes duration and corneal parameters found in this study further corroborate the chronic effects of diabetes on the cornea, as observed in previous research.

Endothelial Cell Count (ECC)

The study found that diabetic patients had a significantly lower endothelial cell count compared to non-diabetic patients (2,250 ± 210 cells/mm² vs. 2,450 ± 180 cells/mm², $p < 0.01$). This reduction in ECC among diabetic individuals is consistent with existing literature, which suggests that chronic hyperglycemia can lead to endothelial cell dysfunction. The corneal endothelium plays a crucial role in maintaining corneal transparency by regulating fluid and solute transport. A lower ECC can compromise this function, potentially leading to corneal edema and other complications. **Kim et al.** reported for total ages, the subjects with type 2 diabetes showed significantly lower ECD, hexagonality, higher CV, and thicker CCT than the control group. This difference was more pronounced in patients with long-standing DM (≥ 10 years)[13].

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Central Corneal Thickness (CCT)

Central corneal thickness was observed to be significantly higher in diabetic patients compared to non-diabetic patients (560 ± 25 µm vs. 540 ± 20 µm, $p < 0.01$). Increased CCT in diabetic individuals is a well-documented phenomenon and is thought to result from osmotic changes within the corneal stroma due to hyperglycemia. The swelling of corneal tissues leads to increased thickness, which may also contribute to altered refractive properties and affect intraocular pressure measurements. **Wiemer et al.** found that central corneal thickness (CCT) increases in diabetic patients regardless of the severity of retinopathy. This indicates that corneal thickness changes might develop independently of other diabetic complications, underscoring the complexity of ocular pathology in diabetes[14].

Similarly, **Singh et al.** in their study reported that type 2 DM patient's corneas (540.51±32.578 µ) were thicker as compared to control group 517.51±22.155 µ (p-value <0.001). The mean ECD of control and diabetic group patients was 2723.75±287.253 cells/mm2 and 2716.11±296.081 cells/mm2, respectively, found insignificant (p-value=0.821).

On the other hand, **Storr-Paulsen et al.** observed a significant increase in CCT in diabetic patients, while no differences were found in endothelial cell density (ECD), coefficient of variation (CV), or hexagonality when compared to non-diabetic groups. This variation in findings highlights the diverse range of corneal parameters seen in diabetic populations, potentially influenced by factors such as the duration of diabetes, glycemic control, and individual patient characteristics[15]. Similarly, **Roszkowska et al.** found statistically significant reductions in ECD alongside increased CCT in diabetic patients compared to non-diabetic controls, emphasizing the complex and multifaceted nature of corneal changes in diabetes[16].

The results of this study have several important clinical implications. First, the significant reduction in ECC and the increase in CCT among diabetic patients suggest that these individuals are at a higher risk for corneal complications, particularly following ocular surgery, where endothelial cell loss is a concern. Surgeons should carefully evaluate corneal health in diabetic patients and consider these factors when planning procedures like cataract surgery or corneal transplants.

Additionally, **Lee et al.** reported increased CCT, reduced ECD, and higher CV in diabetic patients compared to non-diabetics. Their results indicate a gradual decline in corneal endothelial function linked to diabetes, which could affect long-term ocular health in these individuals[17]. Notably, diabetic patients with over ten years of disease duration showed endothelial cell changes marked by increased CCT, higher CV, lower ECD, and decreased hexagonality. This highlights the need to consider the duration of diabetes and its potential effects on corneal parameters in diabetic patients.

The study underscores the importance of regular corneal evaluations in diabetic patients, particularly those with a long history of the disease. Early detection of corneal endothelial changes can help in the timely management of potential complications, such as corneal edema, which may impact vision quality.

However, this study adds to the existing body of knowledge by providing a large sample size and a well-matched control group, strengthening the validity of the findings. The exclusion of confounding factors such as glaucoma, ocular trauma, and other systemic diseases enhances the specificity of the results, allowing for a clearer understanding of the direct effects of diabetes on corneal health.

Limitations

While the study provides robust evidence of the impact of diabetes on corneal health, there are some limitations to consider. First, the cross-sectional nature of the study limits the ability to establish causality between diabetes and corneal changes.

Additionally, while the study excluded several confounding conditions, other unmeasured factors such as glycemic control, duration of diabetes, and use of medications may have influenced the results. Future studies could explore these variables to provide a more comprehensive understanding of the mechanisms underlying corneal changes in diabetes

CONCLUSION

In conclusion, this study highlights the significant impact of diabetes on corneal endothelial cell count and central corneal thickness, with diabetic patients showing a marked reduction in ECC and an increase in CCT compared to non-diabetic controls. These findings underscore the importance of regular corneal assessments in diabetic patients and suggest that clinicians should consider these changes when managing ocular conditions in this population.

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