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Original Article

# Endothelial Cell Count and Central Corneal Thickness in Type-2 Diabetes

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**Abstract**

**Objectives:** This study aimed at evaluating and comparing the values of Endothelial Cell Density (ECD) and Central Corneal Thickness (CCT) among Type 2 Diabetic cases and Non-Diabetics. It also aimed at finding the correlation between ECD and CCT with the diabetes duration, Random Blood Sugar (RBS) levels, and more severe stages of Diabetic Retinopathy (DR) in the diabetic subjects. **Design:** Comparative Cross-sectional. **Study Setting and Duration:** The data was collected from the General Outdoor Patient Department (OPD) of Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan within duration of 8 months from January to August 2021. **Methodology:** After taking the informed consent, a complete history of each subject was taken. ETDRS (Early Treatment Diabetic Retinopathy Study) visual acuity chart was used to evaluate Visual acuity and subjective refraction and then a complete slit-lamp anterior and posterior segment examination was performed followed by Specular Microscopy to measure the ECD and CCT. The diabetic subjects were checked for their RBS immediately after Specular Microscopy (TOMEY Specular Microscope EM-4000) using a digital glucometer and the readings were carefully recorded. **Results:** Results showed ECD to be significantly lower ($p = 0.000$) while CCT to be significantly higher ($p = 0.000$) in type-2 Diabetics than in Non-Diabetics. On correlation analysis, ECD was negatively correlated ($p<0.05$) while CCT was positively correlated ($p<0.05$) with diabetes duration, RBS, and severity of DR. **Conclusion:** This study concluded that the ECD and CCT were significantly different among diabetics and non-diabetics.

***Keywords:-*** Diabetic retinopathy, Endothelial cells, Specular Microscopy, Type-2 Diabetes

## Introduction

Diabetes is a major public health problem with a total of 134 million people affected by the disease (Tandon *et al.*, 2018). Several studies show evidence of the effect of diabetes on all the corneal layers. The cornea in diabetic individuals is more prone to serious abnormalities like increased fragility of epithelium, diminished corneal sensitivity, stromal edema, recurrent corneal erosions, and delayed wound healing particularly after intraocular surgical procedures. The corneal damage if severe can lead to serious complications that can ultimately result in vision loss (Bu *et al.*, 2022; Han *et al.*, 2019; Mete *et al.*, 2018). Morphological changes that occur in corneal endothelium due to diabetes as documented by several studies include reduced ECD, pleomorphism (reduced hexagonaliy of endothelial cells), polymegathism (increased variability in cell size), and increased CCT (Jha *et al.*, 2022; El-Agamy & Alsubaie, 2017; Jahangir *et al.*, 2017).

The literature presents varying reports on ECD and CCT in diabetics. ECD was reported to be affected by diabetes in several studies (Jha *et al.*, 2022; Çolak *et al.*, 2021; Chowdhury *et al.*, 2021; Kadri *et al.*,

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2021; Papadakou *et al.*, 2020; Durukan, 2020; Nagaraj *et al.*, 2018; Elsobky *et al.*, 2018; Mete *et al.*, 2018; El-Agamy and Alsubaie, 2017); whereas a few studies reported no significant difference between the diabetic and non-diabetic corneas (Sharma *et al.*, 2021; Meenakshisundaram *et al.*, 2020).

There is also rich literature on finding the relationship between Diabetes and CCT. Several studies suggest that Diabetes increases CCT (Fahmi *et al.*, 2022; Jha *et al.*, 2022; Chowdhury *et al.*, 2021; Kadri et al., 2021; Durukan, 2020; Sharma et al., 2021; Meenakshisundaram *et al.*, 2020; Nagaraj *et al., 2018*; Elsobky *et al.*, 2018; Mete *et al.*, 2018; El-Agamy and Alsubaie, 2017; Jahangir *et al.*, 2017; Islam, 2017; Khan *et al.*, 2017;) although a few studies report no differences between the diabetic and non-diabetic corneas (Çolak *et al.*, 2021; Papadakou *et al.*, 2020).

The present study highlights the alteration in ECD and CCT due to type 2 Diabetes. The reduced number of endothelial cells affects its normal function and results in loss of corneal clarity due to increased hydration of the cornea (Mete *et al.*, 2018). Therefore, the endothelial cell number must be evaluated in all diabetics before undergoing any intraocular surgical procedure.

**Research Methodology**

The study included 150 type-2 diabetic subjects (83 males, 67 females) and 150 non-diabetic subjects (78 males, 72 females). The mean age of individuals having diabetes was 56.15 ± 7.069 years (range=44-75) while non-diabetics had a mean age of 53.68 ± 8.285 years (range=40-72). All the subjects were taken from the General OPD of Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan using a Purposive non-probability sampling technique from January to August 2021. The mean diabetes duration of diabetics in years was 11.48 ± 6.272 (range=5-27).

Exclusion criteria included patients having a history of smoking, hypertension, corneal pathology, ocular trauma, laser treatment, intraocular surgery, ocular infection, pseudoexfoliation, glaucoma, contact lens use, and anisometropia of 2D.

After taking the informed consent, complete history was taken from all the subjects fulfilling the inclusion criteria. A complete ophthalmic examination of each subject was done that included vision measurement using an ETDRS distance visual acuity chart, objective refraction using an auto refractometer (Topcon), and then subjective refraction with ETDRS visual acuity chart using a trial box performed along with pin-hole visual acuity in patients having visual acuity less than 0 log MAR. Intraocular pressure was evaluated by an Ophthalmologist using a Goldmann applanation tonometer and then the fundus of each subject was examined with Slit-lamp Biomicroscope.

ECD and CCT were as measured using TOMEY Specular Microscope EM-4000 and the measurements were carefully recorded on the proforma. The diabetic subjects were checked for their RBS immediately after Specular Microscopy using a digital glucometer and the readings were recorded. Based on the stage of DR, diabetic subjects were divided into 7 categories using ETDRS classification for DR.

**Result**

Data from both groups (diabetic and non-diabetic) was not distributed normally; therefore Mann-Whitney U test was applied for comparing the means of Non-Diabetics and Type-2 Diabetics. Spearman's correlation was used to find the correlation between ECD and CCT with the diabetes duration, RBS levels, and more severe stages of DR.

This study included 150 Diabetics and 150 Non-Diabetics. The mean age of individuals having Diabetes was 56.15 + 7.069 years with a range of 44 to 75 years while the mean age of Non-Diabetics was 53.68 + 8.285 years having a range of 40 to 72 years. More than half of the Diabetic and Non-Diabetic individuals were male (55.3% and 52% respectively) and the remaining were female (44.7% and 48% respectively). The duration of diabetes in diabetics was categorized into four groups; the frequency of individuals in each group is shown in Figure 1. All the diabetics included in the study were checked for their RBS levels. The details are given in Table 1.

***Table 1: Random Blood Sugar Levels***

| Random Blood Sugar (RBS) | Mean | Standard deviation |
|---|---|---|
| | 425.83 mg/dL | 112.89 mg/dL |

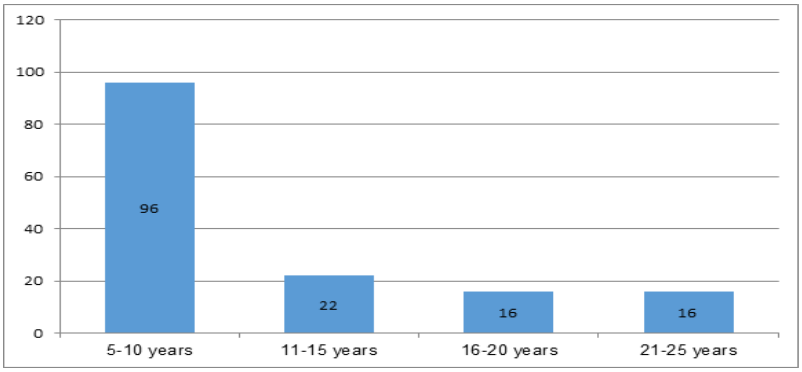


***Figure 1: Frequency Distribution of Duration of Diabetes***

Fundus examination was carried out in each patient either Diabetic or Non-Diabetic. The fundus of all the non-diabetic individuals was found to be healthy (n = 150, percentage = 100%) while the fundus of a majority of diabetic individuals showed some stage of DR. Among the diabetic group; 16.67% of individuals had normal fundi, 47.33% had Non-Proliferative Diabetic Retinopathy (NPDR), 34.67% had Proliferative Diabetic Retinopathy (PDR) and 1.33% had Advanced Diabetic Eye Disease (with normal intraocular pressure) as shown in Figure 2.

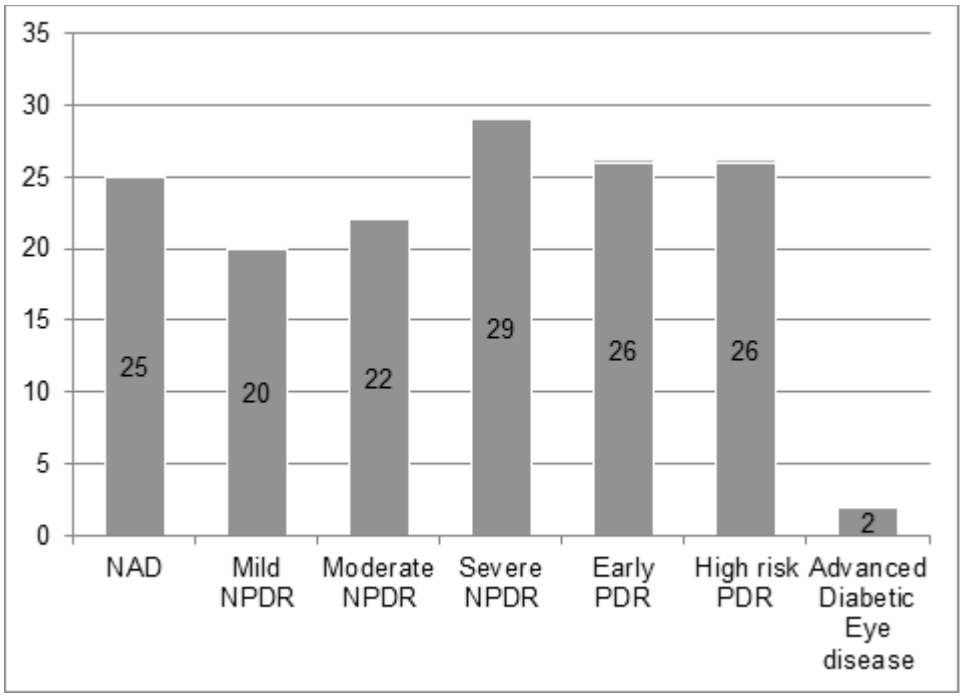


***Figure 2: Severity of Diabetic Retinopathy (OD)***

ECD and CCT was found to be significantly different between cases (n = 150) and controls (n = 150), p = 0.000 as shown in *Table 2*.

***Table 2: Comparison of Endothelial Cell Density and Central Corneal Thickness between Diabetics with Non-diabetics***

| Corneal Parameter | Study group | Median | U value | p-value |
|---|---|---|---|---|
| Endothelial Cell Density | Diabetics | 2450.000 | 2160.000 | 0.000 |
| | Non-diabetics | 2803.500 | | |
| Central Corneal Thickness | Diabetics | 528.00 | 1734.000 | 0.000 |
| | Non-diabetics | 482.00 | | |

ECD had a negative correlation ($p<0.05$) while CCT had a positive correlation ($p<0.05$) with diabetes duration, RBS levels, and severity of DR as shown in *Table 3*.

***Table 3: Correlation of Endothelial Cell Density and Central Corneal Thickness with Diabetes***

| Diabetes | Endothelial Cell Density | | Central Corneal Thickness | |
|---|---|---|---|---|
| | Correlation coefficient 'r' | p-value | Correlation coefficient 'r' | p-value |
| Duration of diabetes | -0.220 | 0.007 | 0.175 | 0.032 |
| Random blood sugar levels | -0.334 | 0.000 | 0.485 | 0.000 |
| Severity of diabetic retinopathy | -0.399 | 0.000 | 0.406 | 0.000 |

**DISCUSSION**

The diabetic cornea appears to be normal however, shows various structural changes. According to the findings of the current study, ECD was observed to be significantly less ($p=0.000$) in the diabetic group than in non-diabetics. The results of present study were consistent to those found in the previous studies. ECD was reported to be significantly less in type-2 diabetics as compared to non-diabetics (Jha *et al*., 2022; Kadri *et al*., 2021; Çolak *et al*., 2021; Papadakou *et al*., 2020; Durukan, 2020; Elsobky *et al*., 2018; Nagaraj *et al*., 2018; Mete *et al*., 2018; Islam *et al*., 2017; El-Agamy and Alsubaie, 2017).

The results of present study were incomparable to other studies who reported no significant difference in ECD of Diabetics and Non-Diabetics ($p>0.05$) (Sharma *et al*., 2021; Meenakshisundaram *et al*., 2020).

According to the findings of current study ECD had a negative correlation ($p<0.05$) with the diabetes duration, RBS and level of DR. The results of present study were found to be similar to those reported in previous studies. ECD was found to have a negative correlation with diabetes duration, glycemic control and severity of DR (Jha *et al*., 2021; Durukan, 2020; Papadakou *et al*., 2020; Elsobky *et al*., 2018). The reduced ECD was correlated ($p < 0.01$) to increased duration of diabetes and more severe stages of DR (Islam *et al*., 2017).

The results of present study were different from those reported in some studies. ECD was greater in diabetics with greater duration of diabetes. In some studies, no particular correlation ($p > 0.05$) of ECD was reported with diabetes duration, hemoglobin A1c levels and more severe stages of DR (Sharma *et al*., 2021; Meenakshisundaram *et al*., 2020; Islam *et al*., 2017; El-Agamy and Alsubaie, 2017).

The present study found the CCT to be significantly higher in the diabetics ($p=0.000$) than in non-diabetics. The results were consistent with those of other studies where significant difference ($p < 0.05$) in the values of CCT between Diabetics and Non-Diabetics was found (Fahmi *et al*., 2022; Kadri *et al*.,

2021; Meenakshisundaram *et al*., 2020; Durukan, 2020; Mete *et al*., 2018; Elsobky *et al*., 2018; Nagaraj *et al*., 2018; Jahangir *et al*., 2017; Islam, 2017; El-Agamy and Alsubaie, 2017; Khan *et al*., 2017).
The results of present study were different from the findings of various studies where no significant difference of CCT ($p > 0.05$) between non-diabetics and diabetics was reported (Çolak *et al*., 2021; Papadakou *et al*., 2020)
According to the current study findings, a positive correlation of CCT ($p < 0.05$) was found with the diabetes duration, RBS levels and severity of DR. The results of earlier studies were observed to be in accordance to these results (Jha *et al*., 2021; Kadri *et al*., 2021; Durukan, 2020; Elsobky *et al*., 2018).
The results of present study were found to be inconsistent to findings of prior studies. CCT was found to have no correlation ($p > 0.05$) with diabetes duration, glycemic control and more severe stages of DR (Sharma *et al*., 2021; Meenakshisundaram *et al*., 2020; El-Agamy and Alsubaie, 2017; Islam, 2017).
Studies reveal that the diabetes mellitus causes Advanced Glycation End products and excessive sorbitol accumulation in endothelial layer of cornea that result in loss of endothelial cells (Bu *et al*., 2022; Tandon *et al*., 2018). Diabetes also causes the activity of sodium-potassium ATPase pump to diminish that along with reduced endothelial cell number results in change in size and morphology of these cells. With the changes in the endothelial layer, its barrier function is compromised and hence increases the corneal thickness due to influx of aqueous fluid into the cornea (El-Agamy and Alsubaie, 2017).

## Conclusion

This study concluded that ECD was found to be less and CCT was found to be more in Diabetics than in Non-Diabetics. ECD showed negative correlation whereas CCT showed positive correlation to the diabetes duration, RBS, and level of DR.

## Conflicts of Interest

The authors declare that they have no conflict of interests.

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