Corneal Analysis in Patients Presenting with Subjective Eye Complaints; Newly Diagnosed Prediabetic Patients

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Abstract

Aim: Subjective symptoms such as decreased visual quality The aim of this study was to detect possible corneal changes in prediabetic patients presenting with complaints.

Methods: The study included 56 newly diagnosed prediabetic patients with subjective visual complaints, no optic nerve and retina pathology, emmetropic, no history of trauma, and 70 healthy participants. After detailed anterior segment and Corneal with Sirius ® device Topography was evaluated and compared with HbA1c values.

Results: The mean age of patients in the prediabetic group was 57.23 ± 8.1 years, while it was 60.58 ± 6.74 years in the control group (p>0.05). The central corneal thickness (CCT) was 550.00 ± 45.00 µm in the prediabetic group and 553.00 ± 38.00 µm in the control group. The minimum corneal thickness (MCT) was 518.00 ± 41.00 µm in the prediabetic group and 533.00 ± 33.00 µm in the control group. Corneal densitometry values were significantly higher in the prediabetic group (23.47 ± 2.36 GSU) compared to the control group (21.76 ± 3.22 GSU) (p<0.001). The mean HbA1c values were 6.30 ± 1.10 in the prediabetic group and 5.20 ± 0.20 in the control group. The mean fasting blood glucose levels were 109 ± 26 mg/dL in the prediabetic group and 91 ± 8 mg/dL in the control group. Regarding corneal refractive parameters, the K1 value was 43.16 ± 1.36 D in the prediabetic group and 42.38 ± 1.38 D in the control group, while the K2 value was 44.15 ± 1.50 D in the prediabetic group and 43.66 ± 1.51 D in the control group. Statistical analysis demonstrated that as HbA1c values increased, corneal densitometry values also increased, with a significant positive correlation between the two parameters (r=0.279, p=0.002).

Conclusions: Prediabetic status was found to have an impact on corneal densitometry and should be considered as an adverse factor in relation to corneal thickness. In individuals with subjective visual complaints but no refractive changes, the possibility of prediabetic status and associated corneal alterations should be taken into account.

***Keywords**: Prediabetes; corneal densitometry; HbA1c*

1. Introduction

Prediabetes represents an intermediate stage between normal glucose metabolism and type 2 diabetes mellitus (T2DM). This condition is characterized by elevated blood glucose levels that do not meet the diagnostic threshold for diabetes. Emerging evidence suggests that prediabetes is not merely a benign state; rather, it constitutes a significant risk factor for the development of various microvascular and macrovascular complications, including retinopathy and cardiovascular disease.[1–3]

Epidemiological studies have demonstrated an alarming prevalence of prediabetes. In 2021, the global prevalence was estimated at 5.8% (298 million individuals) and is projected to rise to 6.5% (414 million) by 2045.[4] Considering the increased risk of diabetes-related complications, several studies have emphasized that ocular involvement in prediabetic populations may occur at rates concerning for healthcare professionals.[5–7] The underlying pathophysiology is believed to involve endothelial damage and microvascular dysfunction secondary to chronic hyperglycemic exposure.[7] Evidence from advanced imaging techniques, particularly optical coherence tomography (OCT), indicates that structural alterations can be detected at early stages, suggesting that ocular tissue damage—especially retinal involvement—may begin during the prediabetic phase.[8–9]

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Corneal topography has become an indispensable clinical tool for the diagnosis of various ocular disorders by enabling detailed morphological characterization of the cornea. This noninvasive method allows comprehensive assessment of corneal surfaces through numerous parameters facilitated by advanced imaging technologies.[10] Among the functions of these devices, corneal densitometry serves as a diagnostic technique that quantifies corneal density, thereby providing insights into its transparency and structural integrity. Based on the Scheimpflug imaging principle, corneal densitometry objectively evaluates corneal clarity by measuring the intensity of backscattered light from the corneal tissue.[11–12]

The present study aimed to investigate the presence of prediabetic status in patients presenting with new-onset, unexplained visual complaints and to evaluate its relationship with potential corneal alterations. Corneal thickness and transparency were primarily assessed by densitometry, along with other topographic parameters.

2. Materials and Methods

The study included 56 patients who presented to the Ophthalmology Clinic of Erzurum City Hospital between October 2024 and December 2024 with newly developed visual complaints and met the American Diabetes Association criteria for prediabetes (HbA1c: 5.7–6.4%), along with 70 healthy participants as the control group.[13] All patients underwent detailed anterior segment and fundus examinations.

Corneal parameters were evaluated using the Sirius topography device. Central corneal thickness was measured at the pupillary center, and corneal densitometry was assessed in the central 0–2 mm zone. Peripheral densitometry zones were excluded due to the reduced repeatability associated with the oval corneal structure.[14]

Best corrected visual acuity (BCVA) and intraocular pressure (IOP) were recorded. Patients with elevated IOP or reduced visual acuity were excluded. Those with topical or systemic medication use, corneal ulcers, keratoconus or other ectatic disorders, dry eye, congenital corneal diseases, or a history of keratitis were not included. Patients with ocular trauma, a history of ocular surgery, or contact lens use (rigid or soft) were also excluded, as were those with macular or optic nerve pathology identified on OCT imaging.

All measurements were performed with the Schwind© Sirius (Schwind Eye-Tech-Solutions GmbH & Co. KG) device. Parameters assessed included vertical and horizontal keratometry (K1, K2), central corneal thickness (CCT), minimum corneal thickness (MCT), anterior and posterior corneal elevations, and central corneal densitometry. Measurements were obtained in the same clinical setting, sequentially for each eye, by the same specialist physician, and at the same time of day to minimize diurnal variation. To reduce the influence of tear film, all patients received a single-dose, preservative-free 0.15% sodium hyaluronate drop prior to measurements.

The study was conducted with the approval of the ethics committee of the Erzurum Faculty of Medicine (BAEK 2025/06-160). Written informed consent was obtained from the patients in our study, which was conducted in accordance with the principles of the Declaration of Helsinki.

2.1. Statistical Analysis

Statistical analyses were performed using R software (R Core Team, version 4.3.0, Vienna, Austria) and IBM SPSS Statistics (version 27, IBM Corp., Armonk, NY, USA). Pearson correlation coefficients were calculated in R to examine linear relationships between variables. The Shapiro-Wilk test was applied to assess normality of distributions, and a significance level of $p<0.05$ was adopted. Correlation analysis was conducted in SPSS, while the correlation matrix was visualized as a heatmap using the ggplot2 and corrplot packages in R. In addition, multiple linear regression analysis was performed in SPSS to further evaluate the combined predictive capacity of the studied parameters. Paired t-tests were applied to compare right and left eye values within each group, with $p<0.05$ considered statistically significant. The study was conducted with the approval of the ethics committee of the Erzurum Faculty of Medicine (BAEK 2025/06-160). Written informed consent was obtained from the patients in our study, which was conducted in accordance with the principles of the Declaration of Helsinki.

3. Results

The mean age of patients in the prediabetic group was 57.23 ± 8.1 years, while in the control group it was 60.58 ± 6.74 years ($p>0.05$). Central corneal thickness (CCT) was 550.00 ± 45.00 µm in the prediabetic group and 553.00 ± 38.00 µm in the control group (Z=-0.488, $p=0.626$). Although CCT values were higher in the prediabetic group, the difference was not statistically significant. Similarly, HbA1c values showed a positive trend with CCT, but the relationship was not significant.

Minimum corneal thickness (MCT) was 518.00 ± 41.00 µm in the prediabetic group and 533.00 ± 33.00 µm in the control group (Z=-2.310, $p=0.023$). Corneal densitometry values were significantly higher in the prediabetic group (23.47 ± 2.36 GSU) compared to the control group (21.76 ± 3.22 GSU) (Z=-3.699, $p<0.001$). The mean HbA1c values were 6.30 ± 1.10 in the prediabetic group and 5.20 ± 0.20 in the control group.

Table 1

Comparison of corneal parameter results of the prediabetic group and the control group

Parameter	Prediabetic Group (n=56)	Control Group (n=70)	P
Age (years)	57.00 ± 10.00 (29–77)	61.00 ± 8.00 (50–79)	0.098
CCT (µm)	550.00 ± 45.00 (454–685)	553.00 ± 38.00 (460–653)	0.626
MCT (µm)	518.00 ± 41.00 (430–651)	533.00 ± 33.00 (453–611)	0.023
Corneal Dens. (GSU)	23.47 ± 2.36 (18.82–30.59)	21.76 ± 3.22 (16.47–34.51)	<0.001
K1 (D)	43.16 ± 1.36 (40.96–46.20)	42.38 ± 1.38 (39.16–47.08)	0.002
K2 (D)	44.15 ± 1.50 (41.80–47.29)	43.66 ± 1.51 (39.92–49.95)	0.065
Ant. Elev. (µm)	1.0 ± 1.00 2.0 (–1–2)	1.00 ± 1.00 (–1–3)	0.580
Post. Elev. (µm)	2.00 ± 2.00 (–6–6)	3.00 ± 1.00 (–1–7)	0.095
Blood Glucose (mg/dL)	109 ± 26 (72–189)	91 ± 8 (75–105)	<0.001
HbA1c (%)	6.30 ± 1.10 (5.0–11.4)	5.20 ± 0.20 (4.9–5.7)	<0.001

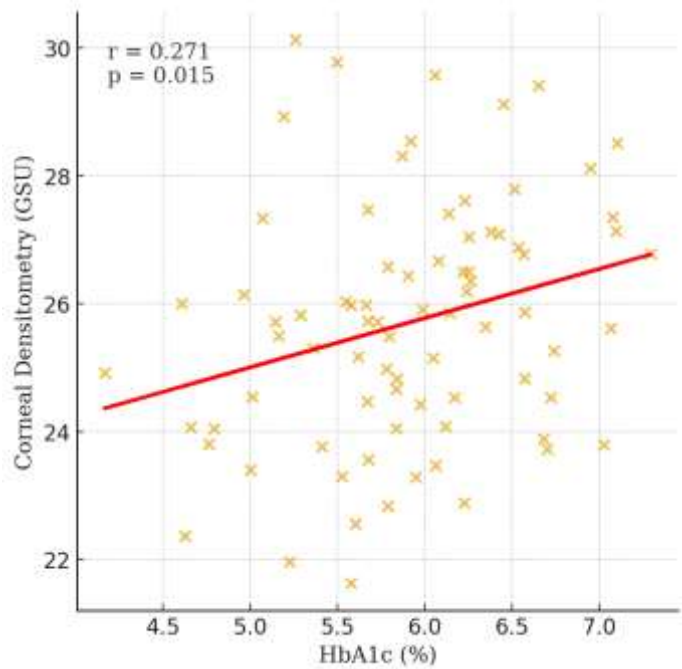
**Notes: Data are expressed as mean ± standard deviation (SD), with minimum and maximum values shown in parentheses. HbA1c values between 5.7–6.4% = prediabetes; HbA1c < 5.7% = control. CCT = Central Corneal Thickness; MCT = Minimum Corneal Thickness; GSU = Gray Scale Unit.*

Mean fasting blood glucose levels were 109 ± 26 mg/dL in the prediabetic group and 91 ± 8 mg/dL in the control group. Regarding refractive parameters, K1 was 43.16 ± 1.36 D in the prediabetic group and 42.38 ± 1.38 D in the control group (Z=3.166, *p*=0.002). K2 was 44.15 ± 1.50 D in the prediabetic group and 43.66 ± 1.51 D in the control group (Z=1.849, *p*=0.065) (Table 1).

Statistical evaluation demonstrated that corneal densitometry values increased in parallel with HbA1c levels, and a significant positive correlation was observed between these two parameters (r=0.279, *p*=0.002) (Figure 1). Fasting blood glucose values were also positively but not significantly correlated with corneal densitometry (r=0.038, *p*=0.672). The correlation between CCT and fasting blood glucose was similarly nonsignificant (r=0.145, *p*=0.104). Moreover, no significant correlations were found between corneal densitometry and either CCT or keratometry values in both groups (r=-0.111, *p*=0.215; r=0.005, *p*=0.959).

Figure 1

Hba1c and corneal densitometry values correlations



*Scatter plot showing the positive correlation between Hba1c and corneal densitometry values. (r=.279**, p=0,002). **Correlation is significant at the 0.01 level (2-tailed).*

4. Discussion

According to the results of our study, although retinal examination and optic nerve analysis were normal in patients with elevated blood glucose, several corneal parameters demonstrated significant alterations. Both central corneal thickness (CCT) and corneal densitometry values were higher in participants with impaired glucose metabolism compared to the control group, consistent with early corneal involvement in prediabetic individuals. While no significant associations were found between gender or age and corneal parameters, a statistically significant positive correlation was identified between HbA1c and corneal densitometry, suggesting that subclinical structural changes may develop even before the onset of overt diabetes.

The corneal endothelium plays a critical role in maintaining stromal deturgescence by regulating fluid transport through the sodium–potassium pump. Chronic hyperglycemia has been reported to cause endothelial dysfunction, irregular collagen organization, and increased corneal thickness.[15,16] Previous studies, including those by Modis et al., demonstrated that higher HbA1c levels are associated with endothelial morphological changes and increased corneal thickness.[18] In hyperglycemic conditions, excessive accumulation of polyols and advanced glycation end-products (AGEs) may impair endothelial metabolism, thereby reducing the functional capacity of the sodium–potassium pump.[19]

Corneal densitometry, based on the Scheimpflug imaging principle, provides an objective method to assess corneal transparency and detect early subclinical haze.[11,12] Recent studies have further emphasized that corneal densitometry is more sensitive than biomicroscopy in detecting microstructural changes in diabetic and prediabetic patients.[20,22] Our findings align with those reports, as densitometry changes were evident in topographic measurements even when slit-lamp biomicroscopy was unremarkable. Huseynova et al. also showed that densitometry values may vary considerably in diabetic individuals, reinforcing the role of this parameter in early disease monitoring.[23]

Importantly, our results suggest that the cornea may be affected in the prediabetic stage, even in the absence of retinal pathology, with increased corneal thickness potentially representing an early biomarker of ocular involvement. This finding is in agreement with recent evidence indicating that corneal changes may precede retinal microvascular damage.[24] In addition, the observed correlation between densitometry, CCT, blood glucose levels, and HbA1c underscores the clinical relevance of metabolic control for preserving corneal health.

Although statistically significant differences were observed, the increase in CCT may not necessarily be clinically relevant, as none of the patients presented with corneal edema. Other confounding factors such as hormonal fluctuations, corticosteroid exposure, or undetected subclinical edema could also influence CCT.[25-26] Moreover, the literature remains inconsistent regarding the relationship between IOP and corneal thickness, with some studies reporting a positive association and others showing no effect.[27]

Another consideration is the potential impact of pupil size on densitometry. While pharmacologic mydriasis was avoided in our cohort to prevent confounding lens changes, future studies may need to standardize pupil conditions more strictly.

In summary, our findings demonstrate that prediabetic status is associated with early corneal alterations, particularly increased densitometry and changes in corneal thickness. These results highlight the importance of including corneal imaging in the ophthalmic evaluation of prediabetic patients. Corneal densitometry may serve as a useful, noninvasive biomarker for early detection of ocular involvement in dysglycemia. Further longitudinal studies with larger cohorts are warranted to validate densitometry as a predictive tool for ocular complications in prediabetes.

5. Conclusion

In conclusion, our findings indicate that in individuals diagnosed with impaired fasting glucose who present with blurred vision but no refractive changes, corneal alterations may already be present. The ability to objectively measure corneal transparency and structural integrity makes corneal densitometry an indispensable tool for monitoring various conditions. Although the exact impact of prediabetic status on corneal endothelial morphology has not yet been

fully elucidated, our results suggest that early corneal changes may occur prior to overt diabetic complications. Further longitudinal studies are warranted to better clarify these mechanisms.

Statement of ethics

The study was conducted with the approval of the ethics committee of the Erzurum Faculty of Medicine (BAEK 2025/06-160). Written informed consent was obtained from the patients in our study, which was conducted in accordance with the principles of the Declaration of Helsinki.

genAI

No artificial intelligence-based tools or generative AI technologies were used in this study. The entire content of the manuscript was originally prepared, reviewed, and approved by both authors.

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Conflict of interest statement

The authors declare that they have no conflict of interest.

Availability of data and materials

This Data and materials are available to the researchers.

Author Contributions

Both authors contributed equally to the article. Both authors read and approved the final manuscript.

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