

# Corneal topography and higher-order aberrations in patients with type 2 diabetes mellitus

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# ABSTRACT

**Background:** Changes in blood sugar levels cause alterations in the anterior segment and retina of the eye. This study was aimed at evaluating corneal topography, aberrometry, and corneal asphericity in patients with treatment-naive type 2 diabetes mellitus (T2DM).

**Methods:** Participants with treatment-naive T2DM were enrolled in this cross-sectional study. The inclusion criteria were glycated hemoglobin A1c (Hb A1c)  $\geq$  7.5% and absence of other ocular or systemic diseases. Patients who refused to participate or had a history of topical or systemic steroid use, hyperlipidemia, hypertension, anemia, prior ocular disorder or surgery, diabetic retinopathy, glaucoma, cataract, active ocular inflammatory or infectious disease, or contact lens use were excluded. All participants underwent a comprehensive ophthalmic examination. The Pentacam HR Scheimpflug tomography system (Pentacam High Resolution; Oculus, Wetzlar, Germany) was used to measure the anterior-segment parameters.

**Results:** Sixty eyes of 30 patients with a male-to-female ratio of 1:1 were included; the mean (standard deviation [SD]) age and Hb A1c were 51.63 (6.73) years and 8.82% (1.31%), respectively. The mean (SD) values of central corneal thickness, root mean square (RMS) of total aberration, RMS of lower-order aberrations, RMS of higher-order aberrations, spherical aberration, 0° coma, 90° coma, flat anterior keratometry (K), steep anterior K, mean anterior K, anterior topographic astigmatism, flat posterior K, steep posterior K, mean posterior K, posterior topographic astigmatism, anterior corneal asphericity, and posterior corneal asphericity were 540.22 (24.47)  $\mu$ m, 1.72 (0.73)  $\mu$ m, 1.63 (0.73)  $\mu$ m, 0.51 (0.17)  $\mu$ m, + 0.31 (0.09)  $\mu$ m, - 0.06 (0.15) diopters (D), 0.003 (0.21) D, 43.87 (1.49) D, 44.69 (1.50) D, 44.28 (1.44) D, + 0.82 (0.83) D, - 6.25 (0.27) D, - 6.55 (0.31) D, - 6.40 (0.28) D, - 0.30 (0.15) D, - 0.32 (0.12) Q-value, and - 0.47 (0.17) Q-value, respectively.

**Conclusions:** We presented the mean values of Pentacam parameters for aberrometry, keratometry, and corneal asphericity in patients with treatment-naive T2DM. These values could serve as a baseline for prospective monitoring of the ocular health status of this cohort and for comparison with future cohorts of patients with well-controlled T2DM. Further studies are required to assess the presence and applicability of ocular changes following intensive blood glucose control in T2DM and further understand the related pathophysiology.

# **KEYWORDS**

corneal wavefront aberrations, diabetes mellitus, type 2 diabetes mellitus, type 1 diabetes mellitus, hyperglycemias, glycated hemoglobin A1c, Hb A1c, corneal topographies

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## **INTRODUCTION**

Diabetes mellitus (DM) is a metabolic disease characterized by elevated blood sugar levels [1]. The prevalence of type 2 DM (T2DM) is increasing worldwide, and the number of affected individuals is estimated to reach 510.8 million by 2030 [2]. Although the classic ocular complications are diabetic retinopathy and cataracts [3, 4], the ocular surface is involved in DM in different ways, such as recurrent corneal erosion and dry eye [5, 6]. Corneal complications of DM are present in 70% of the patients. Malfunctioned cellular and repair mechanisms and epithelial dysfunction cause clinical manifestations of abnormal tear film, corneal neuropathy, and reduced corneal sensitivity [7].

Keratometric parameters may be affected by DM; however, the correlation between changes in the corneal curvature and DM is controversial. DM increases the corneal curvature in patients with keratoconus [8]. Protective effects of DM include increasing the corneal radius, particularly against keratoconus development [9, 10]. However, DM decelerates age-related changes in the cornea, with steep and flat keratometry (K)-values showing less increase in patients with diabetes than in those without diabetes [11].

A relationship exists between higher-order aberrations (HOAs) and DM [12]. DM and accompanying hyperglycemia affect the corneal layers in many ways and increase HOAs compared to healthy eyes [12]. These changes are reversible, and HOAs decrease in response to glycemic control. The extent of corneal changes correlate with the disease duration [13]. Ocular wavefront aberrometry is used to monitor minor transient changes during the disease course and assess the optical quality of the eye during the treatment of DM [14]. Findings of aberration changes in patients with DM compared to controls are controversial. Some studies have found increased corneal aberrations in DM [12, 15]. However, Wiemer et al. found a slightly significant increase in HOAs only in some patients with DM [13].

Because of the worldwide increase in DM prevalence [5] and the possible effects of hyperglycemia on corneal dysfunction [12, 15, 16], measuring anterior-segment parameters in patients with poorly controlled or treatment-naive T2DM could help prospectively monitor the ocular health status of this cohort and compare future cohorts of patients with well-controlled T2DM. Thus, we aimed to evaluate the corneal topography, asphericity, and aberrometry parameters in patients with T2DM and hyperglycemia.

# **METHODS**

In this cross-sectional study, we recruited patients with treatment-naive T2DM in 2020. Assessments were performed at the Endocrinology Clinic of the Iran Melli Bank Hospital, Tehran, Iran, and Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran. The study protocol was approved by the Ethics Committee of the Iran University of Medical Sciences, Tehran, Iran. The study procedures followed the tenets of the Declaration of Helsinki. The study protocol was explained to all participants, and written informed consent was obtained.

Patients with uncontrolled T2DM and elevated blood glucose [17] were identified based on clinical symptoms and results of biochemical tests performed by endocrinologists at the Endocrinology Clinic of the Iran Melli Bank Hospital. Patients who met the inclusion criteria were referred to the Farabi Eye Hospital for a complete ocular assessment. The inclusion criteria were: age of 25 - 55 years, absence of prior complete or partial treatment of T2DM, and uncontrolled glucose with glycated hemoglobin A1c (Hb A1c)  $\geq$  7.5%, and a good-quality image. Patients who refused to participate or had a history of topical or systemic steroid use, hyperlipidemia, hypertension, anemia, prior ocular disorder or surgery, diabetic retinopathy, glaucoma, cataracts, active ocular inflammatory or infectious disease, or contact lens use were excluded.

All participants underwent a comprehensive ophthalmic examination, including objective refraction using Tonoref II (Auto Ref/Kerato/Tonometer, Nidek Co. Ltd., Japan) refined using a retinoscope (Heine, Beta 200, Heine Optotechnik, Herrsching, Germany); measurement of best-corrected distance visual acuity; a detailed slit-lamp (Haag Streit, Mason, OH, USA) examination to rule out ocular comorbidities, such as diabetic retinopathy, glaucoma, age-related macular degeneration, and cataract; and intraocular pressure measurement using the Goldmann applanation tonometer (AT-900; Haag-Streit AG, Koniz, Switzerland) mounted on the slit-lamp microscope. Patients who met the inclusion criteria were further assessed using ocular aberrometry and tomography [18]. Anterior-segment tomography assessment was performed using the Pentacam HR [18] Scheimpflug tomography system (Pentacam High Resolution; Oculus, Wetzlar, Germany), which enabled the physician to extract comprehensive data by quadratic refractive mapping, a dedicated corneal thickness profile, and Pentacam Zernike Analysis software to assess corneal aberrations (Figures 1 and 2). Data of patients with a good-quality image (displayed as OK in the Pentacam device report) were extracted.





Figure 1. Example of topographic maps from the Pentacam-HR device (Pentacam High Resolution; Oculus, Wetzlar, Germany) from the right (A) and left (B) eyes of a patients with treatment-naive type 2 diabetes mellitus.

All examinations were performed in one session and, in particular hours, by an expert optometrist to avoid bias. The findings were recorded in each patient's medical file. Topographic, aberrometric, and asphericity parameters were the central corneal thickness, root mean square (RMS) of total aberrations, RMS of lower-order aberrations (LOAs), RMS of HOAs, spherical aberration, 0° coma, 90° coma, anterior and posterior corneal K-values (mean, flat, and steep K), and anterior and posterior topographic astigmatism magnitude and asphericity (Q-value).

Data were extracted and analyzed using SPSS for Windows (version 22, Statistical Package for Social Sciences; SPSS Inc., IBM Corp., Armonk, NY, USA). The normality of data distribution was evaluated using the Kolmogorov – Smirnov and Shapiro – Wilk tests. Descriptive statistical indices of the mean and standard deviation (SD) were presented for each variable.





 $\label{eq:constraint} Figure \ 2. \ Example \ of \ wavefront \ analysis \ or \ Zernike \ Analysis \ software \ maps \ from \ the \ Pentacam-HR \ device \ (Pentacam \ High \ Resolution; Oculus, Wetzlar, Germany) \ from \ the \ right (A) \ and \ left (B) \ eyes \ of \ a \ patients \ with \ treatment-naive \ type \ 2 \ diabetes \ mellitus.$ 

# RESULTS

We included 60 eyes of 30 patients with treatment-naive T2DM without diabetic retinopathy, with a male-to-female ratio of 1:1 and a mean (SD) age and Hb A1c of 51.63 (6.73) years and 8.82% (1.31%), respectively. Table 1 summarizes the mean (SD) values of all aberrometric variables, K-values, and corneal asphericity obtained using the Pentacam.

The mean (SD) values of central corneal thickness, RMS of total aberration, RMS of LOAs, RMS of HOAs, spherical aberration, 0° coma, 90° coma, flat anterior K, steep anterior K, mean anterior K, anterior topographic astigmatism, flat posterior K, steep posterior K, mean posterior K, posterior topographic astigmatism, anterior

Variable	Values (n = 60 eyes)
CCT (µm), Mean± SD	540.22 ± 24.47
RMS-Total (µm), Mean± SD	$1.72 \pm 0.73$
RMS-LOA (µm), Mean± SD	$1.63 \pm 0.73$
RMS-HOA (µm), Mean± SD	$0.51 \pm 0.17$
Spherical aberration (µm), Mean± SD	+ 0.31 ± 0.09
0° coma (μm), Mean± SD	- 0.06 ± 0.15
90° coma (μm), Mean± SD	$0.003 \pm 0.21$
K flat: anterior (D), Mean± SD	43.87 ± 1.49
K steep: anterior (D), Mean± SD	44.69 ± 1.50
K mean: anterior (D), Mean± SD	$44.28 \pm 1.44$
Topographic astigmatism: anterior (D), Mean± SD	$+0.82 \pm 0.83$
K flat: posterior (D), Mean± SD	$-6.25 \pm 0.27$
K steep: posterior (D), Mean± SD	- 6.55 ± 0.31
K mean: posterior (D), Mean± SD	$-6.40 \pm 0.28$
Topographic astigmatism: posterior (D), Mean± SD	$-0.30 \pm 0.15$
Corneal anterior asphericity (Q value), Mean± SD	$-0.32 \pm 0.12$
Corneal posterior asphericity (Q value), Mean± SD	$-0.47 \pm 0.17$

Table 1. Mean Pentacam parameters for aberrometry, keratometry, and corneal asphericity of patients with treatment-naive type 2 diabetes mellitus

Abbreviations: CCT, central corneal thickness; µm, micrometers; SD, standard deviation; n, number of included eyes; RMS, root mean square; LOA, lower-order aberrations; HOA, higher-order aberrations; K, keratometry; D, diopters.

corneal asphericity, and posterior corneal asphericity were 540.22 (24.47)  $\mu$ m, 1.72 (0.73)  $\mu$ m, 1.63 (0.73)  $\mu$ m, 0.51 (0.17)  $\mu$ m, + 0.31 (0.09)  $\mu$ m, - 0.06 (0.15) diopters (D), 0.003 (0.21) D, 43.87 (1.49) D, 44.69 (1.50) D, 44.28 (1.44) D, + 0.82 (0.83) D, - 6.25 (0.27) D, - 6.55 (0.31) D, - 6.40 (0.28) D, - 0.30 (0.15) D, - 0.32 (0.12) Q-value, and - 0.47 (0.17) Q-value, respectively.

# DISCUSSION

We measured and presented the mean values of aberrometry, keratometry, and corneal asphericity parameters in patients with treatment-naive T2DM without diabetic retinopathy using the Pentacam HR device.

Diabetic complications in the cornea are numerous [19, 20]. However, the effects of DM on corneal parameters remain controversial. Kosker et al. revealed that the likelihood of developing DM increased significantly in patients with severe keratoconus compared to those with mild keratoconus, with an odds ratio of 2.691 (95% confidence interval, 1.330 - 5.445) [8]. Patients with keratoconus had a significantly higher prevalence of T2DM (6.75%) compared to matched controls (4.84%) [8]. While some studies have reported a protective effect of DM against keratoconus [9, 10], probably by inducing the cross-linking of corneal collagen fibers [10], another study [21] found that DM was not an independent predictor of keratoconus using a multivariate analysis.

Studies have assessed changes in various aspects of the anterior segment during bouts of hyperglycemia and after controlling for the disease, but the effects of DM on corneal topography and aberrometry have not been widely studied. Table 2 summarizes the mean Pentacam parameters for aberrometry, keratometry, and corneal asphericity of patients with DM in the literature [11, 15, 22-30], with the corresponding values in non-diabetic eyes [11, 23, 25-36]. However, to the best of our knowledge, no study has reported the RMS of the LOAs or HOAs, or magnitude of posterior topographic astigmatism in eyes with type 1 DM (T1DM) or T2DM. Knowing the mean values of these parameters is important because anterior-segment measurements can detect the early stages of T1DM [37]. Thus, a study on early topographic and aberrometric corneal readings in treatment-naive diabetic eyes with high hyperglycemic levels could pave the way for further understanding of the pathophysiology underlying corneal changes in patients with DM, may help in the early detection of diabetic eye disease, and prevent the occurrence of more serious complications.

We reported the values of corneal aberrometry parameters in T2DM with Hb A1c  $\geq$  7.5%. Corneal aberrometry can be affected by ocular diseases, and its values are essential for predicting refractive surgery outcomes [38]. Increased corneal aberrations deteriorates the quality of vision and distorts images [39].

Variable	Values in patients with DM ( $n = 2426$ eves of	Values in healthy controls $(n = 10\ 199\ eves$
	1677 patients)	of 9251 controls)
	$T_{2}$	$N_{\rm eff} DM (1172 (40.0) / 1402 (50.1) [11]$
Sex (Men / Women), n (%)	12DM: 111(33.3) / 222(66.7) [11]	Non-DM: $11/2(40.9) / 1693(59.1) [11]$
	[11DM: 0(85.7) / 1(14.3) [15]	Non-DM: $18(37.7)/30(62.5)$ [25]
	12DM: 9(81.8) / 2(18.2) [15]	Non-DM: 43 (48.3) / 46 (51.7) [26]
	DM: 94 (52.2) / 86 (47.8) [22]	Non-DM: 14 (46.7) / 16 (53.3) [27]
	Not-mentioned 23	Non-DM: 333 (37.0) / 567 (63.0) [28]
	T1DM: 6 (85.7) / 1 (14.3) [24]	Non-DM: 18 (37.5) / 30 (62.5) [29]
	T2DM: 9 (81.8) / 2 (18.2) [24]	Non-DM: 29(42.0) / 40 (58.0) [30]
	T2DM: 22 (36.7) / 38 (63.3) [25]	Non-DM 22 (22) / 78 (78) [31]
	T2DM: 52 (48.6) / 55 (51.6) [26]	
	T1DM: 38 (63.3) / 22 (36.7) [27]	
	T2DM: 264 (51.7) / 247 (48.3) [28]	
	$T_{2}DM$ ; 21 (35) / 39 (65) [29]	
	T1DM: 58(569) / 44(431) [30]	
	T2DM: 54(53.5) / 47(46.5) [30]	
	120101.54 (55.5) / 47 (40.5) [50]	
Age (y), Mean ± SD	T2DM ( $n = 333$ ): 51.8 ± 6.1 [11]	Non-DM (n = $2865$ ): $50.1 \pm 6.0$ [11]
	$T1DM (n = 7): 42.29 \pm 9.19 [15]$	Non-DM ( $n = 137$ ): 44.2 ± 11.0 [23]
	$T2DM (n = 11): 57.09 \pm 6.44 [15]$	Non-DM ( $n = 48$ ): 70.21 ± 6.45 [25]
	DM (n = 180): 59.27 [22]	Non-DM $(n = 89)$ : 69.08 ± 9.13 [26]
	T2DM ( $n = 127$ ): 44.2 ± 11.0 [23]	Non-DM $(n = 30)$ : 9.6 ± 2.8 [27]
	$T1DM(n = 7): 42.29 \pm 9.57$ [24]	Non-DM ( $n = 900$ ): 67.9 ± 11.2 [28]
	$T2DM (n = 11): 57.09 \pm 6.59 [24]$	Non-DM $(n = 48)$ : 70.44 ± 5.68 [29]
	T2DM(n = 60); 72,38 + 5,66 [25]	Non-DM $(n = 69)$ : 36 6 + 14 2 [30]
	T2DM(n = 107), 71.85 + 8.04[26]	Non DM $(n = 100)$ , 28.45 + 3.23 [31]
	$T_{12DM}(n = 10^{7})$ , $T_{1.05} \pm 0.04 [20]$	$1001-D101 (11 - 100) \cdot 20.45 \pm 5.25 [51]$
	$11DM(n = 60): 11.2 \pm 3.1 [27]$	
	$12DM(n = 511): 65.6 \pm 11.1 [28]$	
	$12DM (n = 60): 72.58 \pm 5.64 [29]$	
	T1DM (n = 102): $39.9 \pm 10.8$ [30]	
	T2DM (n = 101): $56.4 \pm 7.0$ [30]	
Presence of DR, n (%)	DR in 72 (21.6) [11]	-
, , , ,	Not-mentioned [15]	
	Not-mentioned [22]	
	T1DM: 3 (42.9) moderate NPDR and 1 (14.3)	
	severe NDDR [24]	
	T2DM, 1 (0.1) mild NDDP [24]	
	T2DM: $I(9.1)$ Initial NFDR [24] T2DM: No NIDDR 42 (70.0); mild or moderate	
	NDDD 10 (16.7) $\rightarrow$	
	NPDR 10 (10.7); severe-NPDR of PDR 8 (13.3)	
	T2DM: NPDR not requiring laser [26]	
	T1DM: No-DR [27]	
	Not-mentioned 28	
	T2DM: No-NPDR in 39 (65); mild to moderate	
	NPDR in 12 (20); and severe-NPDR to PDR in 9	
	(15)[29]	
	T1DM with no-DR: 52 (51.0) [30]	
	T2DM with no-DR: 64 (63.4) 30	
Chaose control level $= (0)$ ==	Not mentioned [11]	Non DM $(n = 20)$ with Lth A1 a of 5.00 b
Marry L SD		1001-DW(11 = 50) with HD A1C of 5.90 ±
Mean ± SD	I I LIVI WITH A STADIE AND WEIL-CONTROLLED BLOOD	
	glucose level [15]	Non-DM (n = 48) with Hb A1c of $5.54 \pm$
	Not-mentioned [22]	0.38 [29]
	T2DM: 35 (27.6) with Hb A1c < 7.5% and 92	
	$(72.4)$ with Hb A1c $\geq$ 7.5% [23]	
	T2DM with a well-controlled blood glucose level	
	[24]	
	T2DM with Hb A1c of 7.02 ± 1.13 [25]	
	Not-mentioned [26]	
	T1DM with Hb A1c of $9.59 \pm 1.6 \%$ [27]	
	T2DM with Hb A1c of $7.54 \pm 1.78\%$ [28]	
	T2DM with Hb A1c of $7.03 \pm 1.16\%$ [20]	
	T1DM with Hb A1c of 21.0 + 11.7% [20]	
	T1DM WIII DD AIC 01 21.0 $\pm$ 11.7% [30]	

Table 2. Demographic data and mean parameters for corneal thickness [11, 15, 22-28, 32, 33], aberrometry [11, 15, 25, 27, 29, 31, 33], keratometry [11, 15, 22-29, 32, 33], and corneal asphericity [15, 30, 33, 36] in patients with diabetes mellitus and healthy controls reported in the literature

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CCT (μm), Mean ± SD	$\begin{array}{l} T2DM \ (n=333): 535.3\pm 3.0 \ [11] \\ T1DM \ (n=14): 596.43\pm 19.39 \ [15] \\ T2DM \ (n=22): 587.05\pm 42.97 \ [15] \\ DM \ (n=360): 557.21\pm 3.51 \ [22] \\ T2DM \ (n=127): 532.67\pm 39.35 \ [23] \\ T1DM \ (n=7): 594.71\pm 19.58 \ [24] \\ T2DM \ (n=11): 588.18\pm 47.03 \ [24] \\ T2DM \ (n=60): 557.75\pm 34.72 \ [25] \\ T2DM \ (n=107): 552\pm 23 \ [26] \\ T1DM \ (n=60): 564.36\pm 26.5 \ [27] \\ T2DM \ (n=1022): 551.80\pm 34.10 \ [28] \end{array}$	Non-DM (n = 2865): $529.6 \pm 32.0$ [11] Non-DM (n = 137): $521.55 \pm 34.03$ [23] Non-DM (n = 48): $558.08 \pm 30.10$ [25] Non-DM (n = 89): $543 \pm 26$ [26] Non-DM (n = 30): $534.27 \pm 33.20$ [27] Non-DM (n = 1799): $542.63 \pm 33.79$ [28] Non-DM (n = 2509): $529.3 \pm 31.7$ [32] Non-DM (n = 666): $552.0 \pm 34.80$ [33]
RMS-Total (µm), Mean ± SD	NA	Non-DM (n = 56): $0.28 \pm 0.10$ [34]
RMS-LOA (µm), Mean ± SD	NA	No-DM (n = 100):1.011 ± 0.10 [31]
RMS-HOA (μm), Mean ± SD	$T1DM (n = 14): 0.634 \pm 0.228 [15] T2DM (n = 22): 0.527 \pm 0.245 [15]$	Non-DM (n = 35): 0.11 ± 0.03 [35]
Spherical aberration (μm), Mean ± SD	$T1DM (n = 14): 0.070 \pm 0.106 [15] T2DM (n = 22): 0.080 \pm 0.917 [15]$	Non-DM (n = 35): 0.21 ± 0.06 [35]
0° coma (µm), Mean ± SD	T1DM (n = 14): $-0.046 \pm 0.163$ [15] T2DM (n = 22): $0.024 \pm 0.130$ [15]	Non-DM (n = 35): 0.00 ± 0.11 [35]
90° coma (µm), Mean ± SD	T1DM (n = 14): $-0.354 \pm 0.306$ [15] T2DM (n = 22): $-0.300 \pm 0.292$ [15]	Non-DM (n = 35): - 0.04 ± 0.15 [35]
K flat: anterior (D), Mean ± SD	$\begin{array}{l} T2DM \ (n=333): 43.48 \pm 1.60 \ [11] \\ T1DM \ (n=14): 42.68 \pm 1.42 \ [15] \\ T2DM \ (n=22): 43.34 \pm 1.96 \ [15] \\ T2DM \ (n=60): 43.77 \pm 1.53 \ [29] \end{array}$	Non-DM (n = 2865): 43.30 ± 1.57 [11] Non-DM (n = 48): 43.88 ± 1.49 [29] Non-DM (n = 666): 42.58 ± 1.49 [33]
K steep: anterior (D), Mean ± SD	$\begin{array}{l} T2DM \ (n=333): 44.37 \pm 1.77 \ [11] \\ T1DM \ (n=14): 43.46 \pm 0.99 \ [15] \\ T2DM \ (n=22): 44.17 \pm 2.25 \ [15] \\ T1DM \ (n=60): 44.50 \pm 1.68 \ [27] \\ T2DM \ (n=60): 44.71 \pm 1.64 \ [29] \end{array}$	Non-DM (n = 2865): 44.13±1.64 [11] Non-DM (n = 30): 44.45 ± 1.73 [27] Non-DM (n = 48): 44.69 ± 1.63 [29] Non-DM (n = 666): 43.81 ± 1.55 [33]
K mean: anterior (D), Mean ± SD	T2DM (n = 60): 44.11 $\pm$ 1.54 [25] T1DM (n = 60): 43.27 $\pm$ 1.43 [27] T2DM (n = 60): 44.24 $\pm$ 1.55 [29]	Non-DM (n = 48): $44.34 \pm 1.57$ [25] Non-DM (n = 30): $43.32 \pm 1.46$ [27] Non-DM (n = 48): $44.28 \pm 1.54$ [29] Non-DM (n = 666): $43.20 \pm 1.45$ [33]
Topographic astigmatism: anterior (D), Mean ± SD	T2DM (n = 60): + 1.01 $\pm$ 0.75 [25] T2DM (n = 60): + 0.94 $\pm$ 0.69 [29]	Non-DM (n = 48): + 0.78 ± 0.49 [25] Non-DM (n = 48): + 0.81 ± 0.48 [29] Non-DM (n = 666): + 1.22 ± 0.87 [33]
K flat: posterior (D), Mean ± SD	T1DM (n = 14): - 6.10 $\pm$ 0.30 [15] T2DM (n = 22): - 6.10 $\pm$ 0.31 [15]	Non-DM (n = 666): - 6.04 $\pm$ 0.25 [33]
K steep: posterior (D), Mean ± SD	T1DM (n = 14): $-6.43 \pm 0.32$ [15] T2DM (n = 22): $-6.41 \pm 0.48$ [15]	Non-DM (n = 666): - 6.38 ± 0.28 [33]
K mean: posterior (D), Mean ± SD	T1DM (n = 60): 6.15 ± 0.26 [27]	Non-DM (n = 30): 6.23 ± 0.16 [27] Non-DM (n = 666): - 6.20 ± 0.24 [33]
Topographic astigmatism: posterior (D), Mean ± SD	NA	Non-DM (n = 666): + 0.35 ± 0.18 [33]
Corneal anterior asphericity (Q value), Mean ± SD	T1DM (n = 14): - 0.26 ± 0.12 [15] T2DM (n = 22): - 0.31 ± 0.12 [15] *T1DM (n = 102): 0.88 ± 0.01 (mean ± standard error) [30] *T2DM (n = 101): 0.88 ± 0.01 (mean ± standard error) [30]	*Non-DM (n = 69): 0.88 ± 0.01 (mean ± standard error) [30] Non-DM (n = 666): - 0.19 ± 0.16 [33] Non-DM (n = 1683): - 0.28 ± 0.18 [36]
Corneal posterior asphericity (Q value), Mean ± SD	T1DM (n = 14): - 0.28 ± 0.31 [15] T2DM (n = 22): - 0.30 ± 0.14 [15] *T1DM (n = 102): 0.69 ± 0.02 (mean ± standard error) [30] *T2DM (n = 101): 0.72 ± 0.02 (mean ± standard error) [30]	*Non-DM (n = 69): 0.69 ± 0.02 (mean ± standard error) [30] Non-DM (n = 666): - 0.20 ± 0.24 [33] Non-DM (n= 1683): - 0.26 ± 0.22 [36]

Continued Table 2. Demographic data and mean parameters for corneal thickness, aberrometry, keratometry , and corneal asphericity in patients with diabetes mellitus and healthy controls reported in the literature

Abbreviations: n, number, %, percentage; T2DM, type 2 diabetes mellitus; T1DM, type 1 diabetes mellitus; y, years; SD, standard deviation; DR, diabetic retinopathy; Hb A1c, glycated hemoglobin; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; CCT, central corneal thickness; µm, micrometers; RMS, root mean square; LOA, lower-order aberrations; HOA, higher-order aberrations; K, keratometry; D, diopters; NA, the mean (SD) value for this variable was not found in the literature search. Note: \*asphericity expressed in the conic constant or K-value.

Patients with poorly controlled DM report bouts of transient blurring of vision after treatment initiation, and refractive shifts are observed in this phase. Calvo-Maroto et al. reported increased total and internal coma, a type of HOAs, in patients with DM [15]. Another study revealed increased HOAs compared to the healthy population and decreased HOAs after treatment initiation in some patients with DM compared to baseline values [13]. This increase in HOAs in DM could be a useful factor for monitoring patients with DM [15]. A point to consider when interpreting these results is that elevated blood sugar levels lead to increased HOAs in the ocular system. The mean RMS of total and HOAs in the present study were higher than those in healthy controls (Table 2) [34, 35], indicating an increase in the corneal aberrations. This could be used as a basis for further studies and exploration of influential factors.

We reported the anterior and posterior corneal curvatures in the flat and steep meridians in patients with treatment-naive T2DM. These results can be applied for prospective monitoring of the ocular health status in this cohort and for comparison with future cohorts of patients with well-controlled T2DM. Sonmez et al. [40] assessed diabetic eyes before and after glycemic control by measuring refractive, keratometric, and topographic parameters. They observed a significant change in the flattest corneal meridian but no changes in other parameters, such as pachymetry, anterior-chamber depth, and other K-values [40]. Tai et al. found no significant changes in K-values 1 month after the treatment of patients with poorly controlled DM [41]. Hashemi et al. found no significant difference in the flat or steep K between patients with and without DM [11]. Calvo-Maroto et al. reported comparable anterior and posterior flat and steep K-values in patients with T1DM and T2DM [15].

We reported mean (SD) anterior and posterior corneal asphericity values of - 0.32 (0.12) and - 0.47 (0.17), respectively. Previous studies (Table 2) have reported similar mean corneal posterior asphericities in the eyes of patients with T1DM [15] and T2DM [15]. The Q-value is a parameter that provides information about the optical properties and corneal shape and quantifies the aspherical degree of the cornea [36]. With age, the corneal asphericity decreases in the anterior cornea and increases in the posterior cornea [33]. Changes in corneal asphericity are important in refractive surgery [42]. Interocular differences in corneal asphericity can deteriorate binocular vision performance [42]. Moreover, they modify the refractive features of the eyes [43]. Thus, knowledge of the mean values of corneal asphericity could be helpful in planning refractive surgery for patients with DM.

Few studies have investigated the effects of DM on corneal asphericity [15, 30]. Diabetic eyes tend to have changes mainly in the corneal periphery, while changes in the center maintain the prolate shape of the cornea [11]. In the eyes of patients with T1DM, a significant correlation was found between posterior corneal asphericity and total HOAs and between anterior corneal asphericity and total spherical aberration. Anterior corneal asphericity was inversely correlated with total and internal vertical coma [15]. The anterior and posterior corneal asphericities in patients with T1DM and T2DM are comparable to that in non-diabetic eyes [30]. The mean asphericity values in the present study were a bit higher than those in healthy controls (Table 2) [33, 36], indicating an increase in the corneal asphericity. This could be used as a basis for further studies and exploration of influential factors.

This study provides the mean Pentacam parameters for aberrometry, keratometry, and corneal asphericity in patients with treatment-naive T2DM and elevated blood glucose levels without diabetic retinopathy. These findings could be a basis for prospective monitoring of the ocular health status in this cohort and for comparison with future cohorts of patients with well-controlled T2DM. The limitations of this study include the small sample size, lack of a comparative normal group, and failure to present mean values for patients with DM with intensive control of blood glucose levels. Further studies are required to assess the presence and applicability of ocular changes following intensive control of blood glucose levels and further understand the related pathophysiology.

#### **CONCLUSIONS**

This study provides the mean Pentacam parameters for aberrometry, keratometry, and corneal asphericity in patients with treatment-naive T2DM. These values could serve as a baseline for prospective monitoring of the ocular health status of this cohort and for comparison with future cohorts of patients with well-controlled T2DM.

## **ETHICAL DECLARATIONS**

**Ethical approval:** The study protocol was approved by the Ethics Committee of the Iran University of Medical Sciences, Tehran, Iran. The study procedures followed the tenets of the Declaration of Helsinki. The study protocol was explained to all participants, and written informed consent was obtained. **Conflict of interest:** None.

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