• Clinical Research •

Comparison of anterior segment parameters of the eye between type 2 diabetic with and without diabetic retinopathy and non-diabetic

Foroozan Narooie-Noori[1], *Amir Asharlous*[1], *Ali Mirzajani*[1], *Ebrahim Jafarzadehpur*[1], *Mehdi Behnia*[2], *Mehdi Khabazkhoob*[3]

[1]Rehabilitation Research Center, Department of Optometry, School of Rehabilitation Sciences, Iran University of Medical Sciences, Tehran 1968653111, Iran
[2]Noor Research Center for Ophthalmic Epidemiology, Noor Eye Hospital, Tehran 1968653111, Iran
[3]Department of Basic Sciences, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran 1968653111, Iran
Correspondence to: Ali Mirzajani. Rehabilitation Research Center, Department of Optometry, School of Rehabilitation Sciences, Iran University of Medical Sciences, Tehran 1968653111, Iran. mirzajani.opt@gmail.com
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Abstract

● **AIM:** To compare anterior segment parameters between two groups of type 2 diabetic with and without diabetic retinopathy (DR) and non-diabetic elderly subjects based on hemoglobin A1c (HbA1c) levels and status of DR.

● **METHODS:** This study was conducted on 997 residents aged 60y or over in Tehran, Iran. Diabetic group had HbA1c level ≥6.4% with no other systemic problems. The non-diabetic participants had normal eye findings and no systemic diseases. K1, K2, mean K, Q-value, anterior, central, posterior, and total corneal densitometric findings, anterior chamber volume (ACV), anterior chamber depth (ACD), corneal volume (CV), and pachymetry were measured by Pentacam AXL.

● **RESULTS:** A total of 678 non-diabetic (39% male) and 319 diabetic (35% male) subjects with mean age of 66.31±5.23 and 67.22±4.96y were examined, respectively. No statistically significant difference was found in anterior segment parameters between non-diabetic and diabetic groups (all $P>0.05$). However, middle, posterior, and total corneal densitometric values were statistically different between two groups after controlling the effects of confounders ($P=0.014$, 0.007, and 0.042, respectively). Corneal densitometric values in all layers, ACD, and ACV were different between diabetic subjects with and without DR (all $P<0.05$). In the diabetic group, only corneal densitometric values had a negative relationship with fasting blood sugar ($P<0.001$). ACD and ACV had a negative correlation with HbA1c levels (all $P<0.05$, $r=-0.129$ and -0.146, respectively). However, the relationships were not observed after controlling the confounders ($P=0.938$, 0.466, respectively).

● **CONCLUSION:** Considering the higher densitometric values of the cornea and lower ACD and ACV in diabetic subjects with DR, it is suggested that the examiners should perform comprehensive retinal examinations when faced with such conditions.

● **KEYWORDS:** anterior segment; diabetes; hyperglycemia; retinopathy; cornea

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INTRODUCTION

Type 2 diabetes mellitus (DM) is a group of diseases characterized by persistent hyperglycemia and does affect many body organs including the eye[1]. Diabetic retinopathy (DR) is the most frequent complication of diabetes[2-3]. Since glucose enters the eye through the blood circulation of the retina and choroid following hyperglycemia, it reaches the crystalline lens and cornea *via* the vitreous and aqueous. Thus, hyperglycemia-related changes in the anterior segment of the eye also should be evaluated in addition to the retina[4]. It is necessary to dilate pupil of elderly diabetic patients for comprehensive fundus examinations using optical coherence tomography, fundus photography, *etc*. Sometimes, we could not use mydriatics in these people because of shallow anterior chamber depth (ACD)[5]. As a result, accurate evaluation of fundus areas has limitations. Furthermore, dilated fundus

examinations are time-consuming and lead to patient fatigue. Studies showed that anterior segment parameters of the eye have prognostic value in other ocular diseases[6-7]. Therefore, it is supposed that evaluation of diabetic-related changes in the anterior segment of the eye could cause early diagnosis of diabetic complications in the retina. In addition, it could potentially save the time and cost of the examinations.

The cornea, the major refractive component of the eye, is the target structure in refractive surgeries. The refractive result of these surgeries depends on the preoperative measurement of corneal parameters[8]. Furthermore, clinicians rely on corneal parameters and ACD to make a diagnosis, to follow up, and to plan treatment of refractive problems such as corneal ectasia and cataract[9-11]. In addition, intraocular pressure (IOP) measurement which is the only causal and treatable risk factor for glaucoma also affected by corneal characteristics especially central corneal thickness (CCT)[12].

Several studies showed that some changes happen in the anterior segment of the eye following DM[13-17]. Han *et al*[15] compared the corneal nerve and ocular surface changes between healthy normal individuals and patients with type 2 DM in different stages of DR. They concluded that with the progression of DR, some ocular surface parameters such as break up time and corneal fiber length decreased, while total ocular surface disease index and Meibomian gland loss score increased. According to a study, anterior segment parameters like ACD, corneal volume (CV), K mean, CCT, and corneal asphericity except smallest radius of curvature in entire field measurement (Rmin) were similar between the non-diabetic and diabetic groups. Diabetic patients had higher keratometric findings than the non-diabetic group[13]. Although several studies stated that diabetic patients have thicker cornea than non-diabetic subjects[14,18-19], some studies did not report any difference between the two groups[13,20]. There are also contradictory results about hyperglycemia-related changes of corneal densitometry, asphericity, and keratometry[13,21-22].

In addition to the contradictory results of the studies and limited sample size, previous studies evaluated limited corneal parameters. Furthermore, several studies did not consider status of DR. An ageing population together with economic, social and lifestyle changes have caused significant increase in DM[23]. Hence, the present study compares the anterior segment parameters measured by Pentacam AXL between non-diabetic and type 2 diabetic elderly groups as a population-based study. Also, we compare these parameters among groups based on hemoglobin A1c (HbA1c) levels and status of DR. The correlation of anterior segment parameters with HbA1c and fasting blood sugar (FBS) is also evaluated.

SUBJECTS AND METHODS

Ethical Approval This cross-sectional population-based study was performed on 997 residents aged 60y or over in Tehran between March to August 2021 in Noor Eye Hospital. Informed consent was obtained from all participants. The principles of the Helsinki Declaration were followed in all stages of this study. The protocol of the study was approved by the Ethics Committee of Iran University of Medical Sciences (ethics code: IR.IUMS.REC.1399.1321).

Participants Multistage cluster sampling was done from 22 districts of Tehran on people aged 60y or over. The population was divided into two groups. The first and second group were type 2 diabetic and non-diabetic subjects, respectively. Our inclusion criteria for type 2 diabetic group were their self-report, use of diabetes medications, clinical evaluation, laboratory tests, and HbA1c≥6.4%. The inclusion criteria for second group were normal eye findings, HbA1c<6.4% and no systemic problems. Also, non-diabetic subjects had normal corneal tomographic findings based on curvature, elevation, pachymetry, and Belin/Ambrosio enhanced ectasia display (BAD)[24].

Exclusion criteria for diabetic group were the presence of other systemic diseases affecting the eye, use of topical and systemic drugs affecting the eye, contact lens wear, history of refractive surgery, and the presence of chronic, inflammatory, and infectious ocular diseases. In the non-diabetic group, we excluded the participants with a history of refractive surgery and contact lens wear.

HbA1c is a glycated protein and metabolic product of glucose binding to N-terminal valine residue in the β chain of hemoglobin which shows the average blood sugar over the past three months. The normal range of HbA1c is 4% to 6.4%[25]. HbA1c levels below 7% are generally accepted for the treatment of diabetes and a lower risk of long-term microvascular and macrovascular complications of diabetes. Hence, in the present study, participants with type 2 diabetes were classified into two subgroups based on HbA1c blood levels[26]. The subjects were classified into three groups based on metabolic status. Group 1 (HbA1c<6.4%, non-diabetic participants), group 2 (HbA1c between 6.4% and 7%, type 2 diabetic participants with good metabolic control) and group 3 (≥7% HbA1c, type 2 diabetic participants with poor metabolic control). Also, we classified diabetic group based on their status of DR[27-28].

Anterior Segment Examination First, the posterior and anterior segments of the eye were examined with a Haag-Streit slit lamp and a +90 D lens by an experienced ophthalmologist to evaluate for any abnormalities in the ocular surface and posterior segment, respectively. At this stage, patients who had any of exclusion criteria were excluded from the study.

Non-cycloplegic refraction was performed by a single and experienced optometrist with an ARK-510A auto refractometer

(Nidek, Japan). A Heine beta 200 retinoscope (HEINE Optotechnic, Germany) was used when needed. Then, the best corrected visual acuity (BCVA) was determined using the SMART LC 13 vision chart LED (Medizs, Korea) to determine whether the patient has a sufficient vision for accurate fixation during measurement. Then, the anterior segment of the eye was imaged using Pentacam AXL (Pentacam AXL, Oculus, Wetzlar, Germany) under faint ambient light. The device system uses a 180-degree rotating Scheimpflug camera to provide two-dimensional optical sections from the anterior segment of the eye. The software reconstructs three-dimensional tomography of both surfaces of the cornea and other anterior segment parameters.

It should be mentioned that all examinations were performed in one day. The Pentacam measurements was performed between 10 *a.m.* and 4 *p.m.* because of diurnal variation. Both eyes were evaluated, and only right eye used for statistical analyses.

Statistical Analysis Statistical analyses were executed by Statistical Package for the Social Sciences version 23 (IBM Inc., Chicago, Illinois, USA). First, the results were reported as descriptive analysis. Kolmogorov-Smirnov test was used to check the normality of the data. To compare the number of men and women in the diabetic and non-diabetic groups Chi-square was used. To test the difference between means taken from two groups independent sample *t*-test and Mann-Whitney *U* test was used for parameters with normal and non-normal distribution, respectively. Furthermore, Kruskal-Wallis test was used to compare measurements between three groups based on HbA1c level. To adjust the effects of confounders such as axial length, intraocular pressure, spherical equivalent, body mass index, age, and sex multiple regression and univariate analysis of variance was used to compare measurements between two and three groups, respectively. Also, Spearman was used to measure the degree of association between anterior segment parameters with HbA1c and FBS levels. *P*-value less than 0.05 was statistically significant.

RESULTS

Of 997 participants (38% male), 319 diabetic (35% male) and 678 non-diabetic (39% male) subjects entered the study. The demographic data are demonstrated in Table 1.

In diabetic group, 267 (83.70%) did not have DR. While 36 (11.28%), 6 (1.88%), 5 (1.57%), and 5 (1.57%) had mild non-proliferative diabetic retinopathy (NPDR), moderate NPDR, severe NPDR, and proliferative diabetic retinopathy (PDR), respectively. In diabetic patients with DR, optical density of anterior, center, posterior and total layers of the cornea was significantly lower than those without DR (P=0.002, <0.001, <0.001, and <0.001, respectively). Furthermore, ACD and anterior chamber volume (ACV) values in diabetic subjects with DR were lower than those without DR (P=0.024 and 0.019, respectively). Other parameters were not different between two groups (Table 2).

Our results demonstrated no statistically significant difference in flat keratometry, steep keratometry, mean K, Q-value, anterior, central, posterior, and total corneal densitometric findings, ACV, ACD, CV, and pachymetry values between non-diabetic and diabetic groups. After controlling the effect of confounders central, posterior, and total corneal densitometric values were statistically significant between two groups (P=0.014, 0.007, and 0.042, respectively; Table 3).

Based on the HbA1c level, the number of people in the first, second, and third groups was 678 (68%), 102 (10.23%), and 217 (21.77%), respectively. The amount of HbA1c in the first, second, and third groups was 5.47%±0.34% (4% to 6.3%), 6.67%±0.14% (6.50% to 6.90%) and 8.51%±1.30% (7% to 11.90%), respectively. The results of Table 4 demonstrate no statistically significant difference among the three groups in all parameters. After controlling the effect of confounders ACV and CV were statistically significant among the three groups. (P=0.019 and 0.021, respectively).

Table 5 shows that in the diabetic group, among different parameters, corneal densitometric values in the anterior, central, posterior, and total layers were statistically significant associated with FBS (all P<0.001). ACD and ACV were statistically significant associated with HbA1c levels (both P<0.05, r=-0.129 and -0.146, respectively). Multiple linear regression showed that the relationships were not observed after controlling the confounders (P=0.938, 0.466, respectively). No statistically significant correlation among other parameters with HbA1c and FBS levels was observed.

DISCUSSION

DM as one of the most common metabolic diseases characterized by persistent hyperglycemia and affects different organs including the eye[16,29-31]. Our results showed no difference in pachymetry measurements in apex, pupil, and the thinnest point of the cornea, corneal asphericity, CV, K1, K2, mean K between the non-diabetic and diabetic groups. In agreement, Inoue *et al*[20] reported that in patients with type 2 DM the corneal endothelium is damaged, the density of endothelial cells decreases, and the coefficient of variation of the cell area increases, but CCT does not increase in them. Lin *et al*[32] in a hospital-based study reported that CCT was higher in diabetic subjects but this difference is not significant. In another study, 200 diabetic patients with 200 non-diabetic individuals were evaluated. This study showed that CCT and corneal radius of curvature were similar in both group[33]. Other studies also reported that CCT, corneal curvature, and corneal asphericity in both types of diabetes were not different from the non-diabetic group[13,34-35].

Table 1 Patient characteristics for non-diabetic and diabetic groups mean±SD (range)

Parameters	Non-diabetic group (*n*=678)	Diabetic group (*n*=319)	*P*
F/M ratio	1.57	1.87	0.210
Age (y)	66.31±5.23 (60 to 87)	67.22±4.96 (60 to 83)	0.001
HbA1c (%)	5.47±0.34 (4 to 6.30)	7.92±1.38 (6.50 to 11.90)	<0.001
FBS (mg/dL)	96.33±14.47 (58 to 212)	178.64±73.65 (60 to 438)	<0.001
AL (mm)	23.11±0.89 (17.07 to 26.36)	23.06±1.20 (16.57 to 26.50)	0.528
IOP (mmHg)	15.28±2.37 (10 to 22)	15.26±2.10 (9 to 22)	0.852
BMI (Kg/m^2)	28.42±4.54 (18.52 to 45.66)	28.58±3.87 (18.59 to 40.72)	0.862
SE (D)	0.27±1.64 (-9.50 to 10.00)	0.28±1.37 (-6.50 to 4.75)	0.469

M: Male; F: Female; HbA1c: Hemoglobin A1c; FBS: Fasting blood sugar; AL: Axial length; IOP: Intraocular pressure; BMI: Body mass index; SE: Spherical equivalent; D: Diopter; SD: Standard deviation.

Table 2 Comparison of corneal and anterior segment parameters between diabetic patients with and without diabetic retinopathy mean±SD

Parameters	With diabetic retinopathy (*n*=52)	Without diabetic retinopathy (*n*=267)	Mean difference	*P*
Q-value	-0.41±0.14	-0.42±0.16	0.06±0.22	0.974
Dens-ant	27.05±5.42	30.37±7.12	-3.34±8.26	0.002
Dens-central	18.03±2.78	20.26±4.16	-2.20±4.46	<0.001
Dens-post	16.21±2.33	18.08±3.04	-1.51±3.17	<0.001
Dens-total	20.43±3.41	22.89±4.64	-2.35±5.09	<0.001
K1 (D)	44.44±1.71	44.13±1.58	0.78±2.42	0.252
K2 (D)	45.23±1.77	44.95±1.58	0.65±2.49	0.449
Mean K (D)	44.83±1.72	44.54±1.55	0.72±2.42	0.338
ACD (mm)	2.49±0.31	2.66±0.52	-0.18±0.57	0.024
ACV (mm^3)	127.08±33.82	141.24±36.52	-13.04±53.11	0.019
CV (mm^3)	32.11±10.48	33.32±10.27	-3.61±17.41	0.151
Pachymetry apex (μm)	521.54±30.58	529.68±32.11	-5.96±43.32	0.052
Pachymetry thinnest location (μm)	516.89±30.01	525.16±32.37	-6.62±43.51	0.059
Pachymetry pupil center (μm)	521.04±30.16	528.85±32.48	-5.27±43.74	0.059

Dens: Densitometry; ant: Anterior layer; post: Posterior layer; K1: Flat keratometry; K2: Steep keratometry; ACD: Anterior chamber depth; ACV: Anterior chamber volume; CV: Corneal volume; SD: Standard deviation.

Table 3 Comparison of corneal and anterior segment parameters between diabetic and non-diabetic groups of patients mean±SD (range)

Parameters	Non-diabetic group	Diabetic group	Mean difference (95%CI)	*P*	Adjusted *P*[a]
Q-value	-0.42±0.15 (-1.15 to -0.01)	-0.42±0.17 (-1.47 to 0.16)	0.03±0.24 (-0.01 to 0.06)	0.571	0.144
Dens-ant	29.36±6.47 (14.10 to 53.70)	29.93±6.93 (15.70 to 56.30)	0.46±8.90 (-0.82 to 1.74)	0.529	0.192
Dens-central	19.92±4.20 (11.30 to 36.90)	19.96±4.01 (12.80 to 39.20)	0.63±5.65 (-0.11 to 1.39)	0.862	0.014
Dens-post	17.77±3.20 (10.30 to 28.20)	17.82±2.97 (11.50 to 28.50)	0.43±5.65 (-0.20 to 0.89)	0.785	0.007
Dens-total	22.35±4.50 (11.90 to 39.20)	22.57±4.50 (13.50 to 41.30)	0.51±6.09 (-0.20 to 1.39)	0.681	0.042
K1 (D)	44.19±1.60 (37.90 to 49.90)	44.22±1.65 (38.70 to 52.40)	0.07±2.37 (-0.27 to 0.42)	0.649	0.427
K2 (D)	45.02±1.70 (39.20 to 51.10)	45.06±1.76 (40.70 to 57.10)	0.00±2.50 (-0.37 to 0.37)	0.741	0.481
Mean K (D)	44.60±1.61 (38.55 to 50.50)	44.64±1.67 (39.70 to 54.75)	0.04±2.39 (-0.31 to 0.38)	0.733	0.440
ACD (mm)	2.62±0.37 (1.72 to 4.76)	2.64±0.49 (1.73 to 4.72)	-0.04±0.65 (-0.13 to 0.05)	0.601	0.895
ACV (mm^3)	134.45±35.18 (58.00 to 266.00)	139.45±36.22 (70.00 to 243.00)	4.28±43.32 (-10.52 to 1.97)	0.052	0.094
CV (mm^3)	32.11±9.04 (10.90 to 74.60)	33.28±10.36 (11.10 to 83.60)	0.52±11.50 (-1.14 to 2.18)	0.101	0.205
Pachymetry apex (μm)	528.19±32.63 (387.00 to 646.00)	526.65±31.95 (406.00 to 617.00)	-0.07±50.69 (-7.38 to 7.24)	0.899	0.631
Pachymetry thinnest location (μm)	523.70±35.13 (386.00 to 642.00)	522.00±32.36 (398.00 to 614.00)	-0.76±51.58 (-8.20 to 6.69)	0.947	0.718
Pachymetry pupil center (μm)	527.05±32.79 (387.00 to 645.00)	525.95±31.87 (412.00 to 620.00)	-0.42±50.51 (-7.71 to 6.85)	0.514	0.509

Dens: Densitometry; ant: Anterior layer; post: Posterior layer; K1: Flat keratometry; K2: Steep keratometry; ACD: Anterior chamber depth; ACV: Anterior chamber volume; CV: Corneal volume; SD: Standard deviation; CI: Confidence interval. [a]Adjusted *P*-value after age, sex, axial length, body mass index, intraocular pressure, and spherical equivalent.

Table 4 Comparison of anterior segment parameters in participants based on HbA1c level mean±SD

Parameters	Group 1	Group 2	Group 3	*P*	Adjusted *P*[a]
Q-value	-0.43±0.15	-0.45±0.20	-0.43±0.16	0.849	0.710
Dens-ant	29.08±6.15	29.29±4.33	29.01±7.03	0.418	0.357
Dens-central	19.72±3.95	19.44±2.84	19.57±4.39	0.562	0.910
Dens-post	17.65±3.00	17.66±2.47	17.44±3.16	0.446	0.738
Dens-total	22.15±4.25	22.13±3.06	22.00±4.75	0.471	0.607
K1 (D)	44.15±1.58	44.03±2.03	44.20±1.48	0.677	0.578
K2 (D)	44.92±1.63	44.98±2.38	44.96±1.46	0.927	0.358
Mean K (D)	44.53±1.57	44.51±2.18	44.58±1.44	0.829	0.438
ACD (mm)	2.62±0.37	2.62±0.40	2.66±0.54	0.868	0.761
ACV (mm^3)	125.95±29.32	131.62±30.55	129.00±33.38	0.061	0.019
CV (mm^3)	30.43±7.69	28.66±6.63	30.87±8.41	0.141	0.021
Pachymetry apex (μm)	528.79±32.89	526.03±36.02	526.09±32.69	0.690	0.398
Pachymetry thinnest location (μm)	524.37±33.46	521.30±36.38	521.48±32.93	0.684	0.373
Pachymetry pupil center (μm)	527.59±33.00	525.19±34.65	525.36±33.05	0.774	0.444

Dens: Densitometry; ant: Anterior layer; post: Posterior layer; K1: Flat keratometry; K2: Steep keratometry; ACD: Anterior chamber depth; ACV: Anterior chamber volume; CV: Corneal volume; SD: Standard deviation; HbA1c: Glycosylated hemoglobin. Group 1: HbA1c<6.4%; Group 2: HbA1c up to 7%; Group 3: HbA1c>7%. [a]*P*-value was calculated with univariate analysis of variance after controlling the effect of age, sex, axial length, body mass index, intraocular pressure, and spherical equivalent.

Table 5 The correlation coefficients among anterior segment parameters, HbA1c and fasting blood sugar levels in diabetic group

Parameters	FBS		HbA1c	
	P	*r*	*P*	*r*
Q-value	0.838	0.010	0.578	-0.031
Dens-ant	<0.001	-0.237	0.233	-0.068
Dens-central	<0.001	-0.235	0.250	-0.065
Dens-post	<0.001	-0.235	0.133	-0.085
Dens-total	<0.001	-0.241	0.201	-0.073
K1 (D)	0.148	0.071	0.703	0.021
K2 (D)	0.826	0.012	0.052	0.096
Mean K (D)	0.746	0.018	0.073	0.088
ACD (mm)	0.156	-0.091	0.025	-0.129
ACV (mm^3)	0.062	-0.104	0.003	-0.146
CV (mm^3)	0.635	0.027	0.211	-0.062
Pachymetry apex (μm)	0.778	0.016	0.705	0.019
Pachymetry thinnest location (μm)	0.741	0.019	0.757	0.015
Pachymetry pupil center (μm)	0.834	0.012	0.750	0.016

Dens: Densitometry; ant: Anterior layer; post: Posterior layer; K1: Flat keratometry; K2: Steep keratometry; ACD: Anterior chamber depth; ACV: Anterior chamber volume; CV: Corneal volume; HbA1c: Glycosylated hemoglobin; FBS: Fasting blood sugar.

Inconsistent with our results, studies have shown that in diabetic patients the cornea is thicker than the non-diabetic group[14,36-37]. In a study, maximum keratometry was steeper in the diabetic group than the non-diabetic group, and Rmin was different between the two groups[13].

One of the reasons for the difference between the studies and also the current study can be measuring methods. In terms of corneal thickness measurement by ultrasound, the CCT may change due to using anesthesia drops. Furthermore, the CCT may be slightly underestimated due to the corneal indentation. Another reason can be attributed to differences in choosing diabetic subjects with different metabolic stages and some mixing type 1 and type 2 DM subjects.

Our results showed that ACD and ACV of diabetic subjects are similar to non-diabetic individuals. Our findings are in line with some previous studies[13]. These findings are not similar with other studies[22,38-39]. Xiao *et al*[39] compared ocular biometric characteristics between type 1 diabetic and non-diabetic children. They found that the ACD of the diabetic group was shallower than the non-diabetic group.

According to the present study, the anterior, middle, posterior and total corneal densitometric values in type 2 diabetic group was higher than the non-diabetic group. However, the observed difference after controlling the effect of confounders was statistically significant for middle, posterior, and total corneal densitometric values. Also, the highest densitometric values in both groups were in the anterior layer of the cornea. Similar to our study, Tekin *et al*[40] observed that corneal densitometry in both non-diabetic and diabetic groups was higher in the anterior layer and lower in the posterior layer. Also, no statistically significant difference was not found in corneal densitometric values in all layers between two groups. This result may be contrary to previous researches using confocal microscopy which found a higher corneal optical density in patients with diabetes[41-42]. Gao *et al*[41] concluded that there is a positive relationship between CCT and optical density in the diabetic group. They concluded that with increasing CCT, corneal transparency decreases, and optical density increases.

Ramm *et al*[43] compared corneal optical density of almost all corneal layers and areas between diabetic and non-diabetic group and reported that they significantly reduced in diabetic group. The different study design might be a possible reason for the lack of considerable change in corneal densitometric values in the current study. The mammalian cornea is optically clear, which is considered an essential aspect of high-resolution vision. Its transparency is affected by various factors including some diseases and contact lens wear[11,44]. There are several reasons for the clarity of the cornea. The first of them is the lack of blood vessels in the cornea. Second, the presence of high concentrations of intracytoplasmic crystalline enzyme in the corneal epithelium layer (similar to crystalline lens epithelial cells). Third, there are collagen fibers in different layers of the cornea with an organized orientation which are narrower than the collagen fibers of other connective tissues[45]. The epithelium usually has the highest optical density. The central corneal zone which essentially contains the corneal stroma with organized collagen fibrils and extracellular matrix, shows a minor optical density. The lowest backward light scattering is for deep stroma and corneal endothelium[46].

According to our results, no significant difference was found among the first, second, and third groups with different levels of HbA1c in all parameters. After controlling the effects of confounders CV and ACV were statistically different between 3 groups. Similar to our study, the findings of Yazgan *et al*[47] and Scheler *et al*[48] concluded that there was not any significant difference in CCT values between the non-diabetic and diabetic groups with HbA1c levels less than 7%. However, contrary to our results, there was a difference between the first and third groups. In other studies, the diabetic group with HbA1c levels greater than 7% had a thicker cornea than those with HbA1c levels less than 7%[49-50].

Based on our results, anterior, central, posterior, and total corneal densitometric values had a weak negative correlation with FBS levels. Also, only ACD and ACV had a weak negative correlation with HbA1c levels. Similar to our results, other studies show no association between CCT and HbA1c levels[32,51-52]. In addition, studies found that HbA1c levels do not affect curvature, CV, and corneal asphericity[33,35,53]. Song *et al*[53] stated that there was no association between ACD and HbA1c levels. Furthermore, another study showed that none of the corneal densitometric values were statistically related to HbA1c levels[21,40].

We compared anterior segment parameters between diabetic subjects with and without DR. According to our results corneal densitometric values, ACD, and ACV in diabetic subjects with DR were lower than those without DR. Other parameters did not show any difference between two groups. Our results are similar to several studies[43,54]. Ramm *et al*[43] found negative correlation between optical density and stage of diabetic retinopathy. Lin *et al*[32] did not find any significant correlation between HbA1c levels and severity of DR. Senćanić *et al*[54] found no difference in CCT between diabetic subjects without DR and with NPDR, but CCT was thicker in those with PDR than in those without DR. In contrast, other studies reported that the light corneal optical density increased with each progressive stage of DR[42].

In the current study, number of diabetic subjects with progressive stages of DR was limited. So, we could not compare between different stages of DR. It may be due to excluding the diabetic subjects with other systemic problems.

Limited sample size, different measuring methods, different age range, some combination of type 1 and type 2 diabetic subjects, and lack of attention to the status of DR in previous studies can be considered as possible reasons for the difference between the results of the present study and other studies.

One of the strengths of the current study is evaluating more corneal and anterior segment parameters of the eye as population-based.

There are some limitations in the present study. First, there was a very small number of diabetic people with DR compared to the those without DR and also non-diabetic population in this study. Thus, we did not compare between different stages of DR. Second, we did not evaluate the corneal endothelium. Therefore, it is recommended that future studies be performed longitudinally, with regard to the status of different stages of DR and corneal endothelium.

In summary, considering the higher densitometric values of the cornea and lower ACD and ACV in diabetic subjects with DR, it is suggested that the examiners should perform comprehensive retinal examinations when faced with such conditions to rule out any complicated situations. Consequently, appropriate and immediate management should be adopted accordingly.

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REFERENCES

1 Lyu Y, Zeng X, Li F, Zhao S. The effect of the duration of diabetes on dry eye and corneal nerves. *Contact Lens Anterior Eye* 2019;42(4):380-385.

2 Singh RP, Elman MJ, Singh SK, Fung AE, Stoilov I. Advances in the treatment of diabetic retinopathy. *J Diabetes Complications* 2019; 33(12):107417.

3 Li YY, Yang XF, Gu H, Snellingen T, Liu XP, Liu NP. The relationship between insulin resistance/β-cell dysfunction and diabetic retinopathy in Chinese patients with type 2 diabetes mellitus: the Desheng Diabetic Eye Study. *Int J Ophthalmol* 2018;11(3):493-500.

4 Han SB, Yang HK, Hyon JY. Influence of diabetes mellitus on anterior segment of the eye. *Clin Interv Aging* 2018;14:53-63.

5 Gessesse GW, Debela AS, Anbesse DH. Ocular biometry and their correlations with ocular and anthropometric measurements among Ethiopian adults. *Clin Ophthalmol* 2020;14:3363-3369.

6 Brandt JD. Corneal thickness in glaucoma screening, diagnosis, and management. *Curr Opin Ophthalmol* 2004;15(2):85-89.

7 Sng CC, Ang M, Barton K. Central corneal thickness in glaucoma. *Curr Opin Ophthalmol* 2017;28(2):120-126.

8 Ambrósio R Jr, Valbon BF, Faria-Correia F, Ramos I, Luz A. Scheimpflug imaging for laser refractive surgery. *Curr Opin Ophthalmol* 2013;24(4):310-320.

9 Moshirfar M, Tukan AN, Bundogji N, Liu HY, McCabe SE, Ronquillo YC, Hoopes PC. Ectasia after corneal refractive surgery: a systematic review. *Ophthalmol Ther* 2021;10(4):753-776.

10 Tian L, Zhang D, Guo LL, Qin X, Zhang H, Zhang HX, Jie Y, Li L. Comparisons of corneal biomechanical and tomographic parameters among thin normal cornea, forme fruste keratoconus, and mild keratoconus. *Eye Vis* (*Lond*) 2021;8(1):44.

11 Doughty MJ, Jonuscheit S. Corneal structure, transparency, thickness and optical density (densitometry), especially as relevant to contact lens wear—a review. *Cont Lens Anterior Eye* 2019;42(3):238-245.

12 Chan TCW, Bala C, Siu A, Wan F, White A. Risk factors for rapid glaucoma disease progression. *Am J Ophthalmol* 2017;180:151-157.

13 Huseynova T, Galbinur T, Abdullayev A, Rahimzade A. Corneal measurements in patients with diabetes mellitus. *Azerbaijan Medical Association Journal* 2016;2:59-62.

14 Lee JS, Oum BS, Choi HY, Lee JE, Cho BM. Differences in corneal thickness and corneal endothelium related to duration in diabetes. *Eye* (*Lond*) 2006;20(3):315-318.

15 Han JX, Wang H, Liang HH, Guo JX. Correlation of the retinopathy degree with the change of ocular surface and corneal nerve in patients with type 2 diabetes mellitus. *Int J Ophthalmol* 2021;14(5):750-758.

16 Zhao H, He Y, Ren YR, Chen BH. Corneal alteration and pathogenesis in diabetes mellitus. *Int J Ophthalmol* 2019;12(12):1939-1950.

17 Yu T, Han XG, Gao Y, Song AP, Dang GF. Morphological and cytological changes of meibomian glands in patients with type 2 diabetes mellitus. *Int J Ophthalmol* 2019;12(9):1415-1419.

18 Abdulghani YS, Ali TO, Correaltion between central corneal thickness and diabetes in sudanese patients. *Natl J Med Res* 2013;3(4):309-311.

19 Roszkowska AM, Tringali CG, Colosi P, Squeri CA, Ferreri G. Corneal endothelium evaluation in type I and type II diabetes mellitus. *Ophthalmologica* 1999;213(4):258-261.

20 Inoue K, Kato S, Inoue Y, Amano S, Oshika T. The corneal endothelium and thickness in type II diabetes mellitus. *Jpn J Ophthalmol* 2002;46(1):65-69.

21 Özyol P, Özyol E. Assessment of corneal backward light scattering in diabetic patients. *Eye Contact Lens* 2018;44 Suppl 1:S92-S96.

22 Saw SM, Wong TY, Ting S, Foong AW, Foster PJ. The relationship between anterior chamber depth and the presence of diabetes in the tanjong pagar survey. *Am J Ophthalmol* 2007;144(2):325-326.

23 Animaw W, Seyoum Y. Increasing prevalence of diabetes mellitus in a developing country and its related factors. *PLoS One* 2017;12(11):e0187670.

24 Motlagh MN, Moshirfar M, Murri MS, Skanchy DF, Momeni-Moghaddam H, Ronquillo YC, Hoopes PC. Pentacam® corneal tomography for screening of refractive surgery candidates: a review of the literature, part I. *Med Hypothesis Discov Innov Ophthalmol* 2019;8(3):177-203.

25 Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, Zinman B. Management of hyperglycaemia in type 2 diabetes mellitus: a consensus algorithm for the initiation and adjustment of therapy. *Diabetologia* 2008;51(1):8-11.

26 Laakso M, Cederberg H. Glucose control in diabetes: which target level to aim for? *J Intern Med* 2012;272(1):1-12.

27 Sun JK, Aiello LP, Abràmoff MD, Antonetti DA, Dutta S, Pragnell M, Levine SR, Gardner TW. Updating the staging system for diabetic retinal disease. *Ophthalmology* 2021;128(4):490-493.

28 Amoaku WM, Ghanchi F, Bailey C, Banerjee S, Banerjee S, Downey L, Gale R, Hamilton R, Khunti K, Posner E, Quhill F, Robinson S, Setty R, Sim D, Varma D, Mehta H. Diabetic retinopathy and diabetic macular oedema pathways and management: UK Consensus Working Group. *Eye(Lond)* 2020;34(Suppl 1):1-51.

29 Beato JN, Esteves-Leandro J, Reis D, Falcão M, Rosas V, Carneiro Â, Falcão Reis F. Structural and biomechanical corneal differences between type 2 diabetic and nondiabetic patients. *J Ophthalmol* 2019;2019:3764878.

30 Wang X, Xu G, Wang W, Wang J, Chen L, He M, Chen Z. Changes in corneal biomechanics in patients with diabetes mellitus: a systematic review and meta-analysis. *Acta Diabetol* 2020;57(8):973-981.

31 Pék A, Szabó D, Sándor GL, Tóth G, Papp A, Nagy ZZ, Limburg H, Németh J. Relationship between diabetes mellitus and cataract in Hungary. *Int J Ophthalmol* 2020;13(5):788-793.

32 Lin TZ, Kong Y, Shi C, Eric Pazo E, Dai GZ, Wu XW, Xu L, Shen LJ. Prognosis value of Chinese Ocular Fundus Diseases Society classification for proliferative diabetic retinopathy on postoperative visual acuity after pars plana vitrectomy in type 2 diabetes. *Int J Ophthalmol* 2022;15(10):1627-1633.

33 Touzeau O, Levet L, Borderie V, Bouchard P, Laroche L. Anterior segment of the eye and diabetes mellitus. *J Fr Ophtalmol* 2004;27(8):859-870.

34 Schweitzer C, Korobelnik JF, Boniol M, Cougnard-Gregoire A, Le Goff M, Malet F, Rougier MB, Delyfer MN, Dartigues JF, Delcourt C. Associations of biomechanical properties of the cornea with environmental and metabolic factors in an elderly population: the ALIENOR study. *Invest Ophthalmol Vis Sci* 2016;57(4):2003-2011.

35 Wiemer NG, Dubbelman M, Kostense PJ, Ringens PJ, Polak BC. The influence of chronic diabetes mellitus on the thickness and the shape of the anterior and posterior surface of the cornea. *Cornea* 2007;26(10):1165-1170.

36 Mba Aki A, Nnang Essone J, Ngaila N, Nsame D, Akoma M, Matsanga

O, Abessolo F. Study of the types of refractive disturbances obseved during hyperglycemia in humans. *Open Journal of Ophthalmology* 2022;12:142-151.

37 Storr-Paulsen A, Singh A, Jeppesen H, Norregaard JC, Thulesen J. Corneal endothelial morphology and central thickness in patients with type II diabetes mellitus. *Acta Ophthalmol* 2014;92(2):158-160.

38 Nongpiur ME, Sakata LM, Friedman DS, He M, Chan YH, Lavanya R, Wong TY, Aung T. Novel association of smaller anterior chamber width with angle closure in Singaporeans. *Ophthalmology* 2010; 117(10):1967-1973.

39 Xiao Y, Li T, Jia Y, Wang SS, Yang CH, Zou HD. Influence of type 1 diabetes mellitus on the ocular biometry of Chinese children. *J Ophthalmol* 2019;2019:7216490.

40 Tekin K, Inanc M, Kurnaz E, Bayramoglu E, Aydemir E, Koc M, Aycan Z. Objective evaluation of corneal and lens clarity in children with type 1 diabetes mellitus. *Am J Ophthalmol* 2017;179:190-197.

41 Gao F, Lin T, Pan Y. Effects of diabetic keratopathy on corneal optical density, central corneal thickness, and corneal endothelial cell counts. *Exp Ther Med* 2016;12(3):1705-1710.

42 Morishige N, Chikama TI, Sassa Y, Nishida T. Abnormal light scattering detected by confocal biomicroscopy at the corneal epithelial basement membrane of subjects with type II diabetes. *Diabetologia* 2001;44(3):340-345.

43 Ramm L, Spoerl E, Pillunat LE, Terai N. Corneal densitometry in diabetes mellitus. *Cornea* 2020;39(8):968-974.

44 Urbaniak D, Seredyka-Burduk M, Błoch W, Malukiewicz G, Kałużny BJ. Scheimpflug camera measurement of optical density of the corneal epithelium, stroma, and endothelium in patients with pseudoexfoliation syndrome. *Med Sci Monit* 2018;24:5826-5831.

45 Meek KM, Knupp C. Corneal structure and transparency. *Prog Retin Eye Res* 2015;49:1-16.

46 Cankaya AB, Tekin K, Kiziltoprak H, Karahan S, Yilmazbas P. Assessment of corneal backward light scattering in the healthy cornea and factors affecting corneal transparency. *Jpn J Ophthalmol* 2018;62(3):335-341.

47 Yazgan S, Celik U, Kaldırım H, Ayar O, Elbay A, Aykut V, Celik B, Taş M. Evaluation of the relationship between corneal biomechanic and HbA1C levels in type 2 diabetes patients. *Clin Ophthalmol* 2014;8:1549-1553.

48 Scheler A, Spoerl E, Boehm AG. Effect of diabetes mellitus on corneal biomechanics and measurement of intraocular pressure. *Acta Ophthalmol* 2012;90(6):e447-e451.

49 Kaur P, Singh B, Bal BS, Kaur IN, Brar V. Central corneal thickness in type 2 diabetic patients and its correlation with duration, Hba1c levels and severity of retinopathy. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)* 2016;15(6):91-94.

50 Pandey S, Satyawali V, Joshi D, Singh Titiyal G. Central corneal thickness and diabetes mellitus - a study of correlation in terms of duration and glycemic control in North Indian hilly population. *Int J Cur Res Rev* 2019;11(14):1-5.

51 El-Agamy A, Alsubaie S. Corneal endothelium and central corneal thickness changes in type 2 diabetes mellitus. *Clin Ophthalmol* 2017; 11:481-486.

52 Suraida AR, Ibrahim M, Zunaina E. Correlation of the anterior ocular segment biometry with HbA1c level in type 2 diabetes mellitus patients. *PLoS One* 2018;13(1):e0191134.

53 Song E, Qian DJ, Wang S, Xu C, Pan CW. Refractive error in Chinese with type 2 diabetes and its association with glycaemic control. *Clin Exp Optom* 2018;101(2):213-219.

54 Senćanić I, Stamenković M, Jovanović V, Babović S, Jakšić V, Marković P. Influence of diabetes mellitus on corneal thickness. *Srp Arh Celok Lek* 2014;142(9-10):529-534.