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Effect of Control of Diabetes Mellitus on Corneal Morphology

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Short Title: Control of Diabetes Mellitus on Corneal Morphology

Abstract

Purpose: Assess the effect of diabetic control on corneal morphological parameters between diabetics and non-diabetic (control) eyes of the same age group.

Methods: Cross-sectional comparative study included 156 eyes of 100 patients, between 40 to 70 years old and of both genders, 104 eyes in control (non-DM) group and 52 eyes in DM group. All included eyes examined using specular microscope (Tomey EM-3000) and Oculus Pentacam HR. Outcomes included assessment of specular microscope parameters (CED, CCT, NUM, AVG, SD, CV, MAX and MIN) and pentacam parameters (KI, K2, K mean, K max, corneal astigmatism, ACD, ACV, Q value, frontal and back elevation, pachymetric maps and pupil center).

Results: All studied specular microscope parameters, K max, ACD, ACV, Q value, frontal and back elevation were significantly affected in the DM group. Regarding level of HbA1c only NUM, AVG, SD, MIN and corneal asitgmatism were significantly affected. While duration of DM didn't significantly affect any of studied specular or pentacam derived parameters. State of DR was significantly affecting all studied specular derived parameters, corneal astigmatism, ACV, back elevation, thinnest location y-coordination, pachymetric apex and pupil center.

Conclusion: There were significant changes detected in diabetic group as endothelial changes and topographic changes.

Key words: Corneal morphological parameters, specular microscope, pentacam, diabetic keratopathy, control of DM (HbA1c level).

Introduction:

Corneal endothelium is a monolayer of hexagonal cells of limited regenerative power. Loss of these cells is compensated only by the migration, enlargement and increased heterogeneity of these cells, that is affecting corneal transparency and function.[1]

Diabetes mellitus (DM) may lead to micro- and macro-vascular disorders, which may introduce many ocular manifestations.[2] Several structural changes in cornea have been associated with DM that include a decrease in corneal endothelial cell density (CED) and hexagonality, with polymegethism (increased coefficient of variation (CV) of cell area), pleomorphism[3,4,5] and increase in keratometry values.[6,7]

Diabetic eye disease has also been associated with longer disease duration and difficulty controlling glucose levels.[8] Glycosylated hemoglobin (HbA1c) can be used as a parameter to gauge the severity and duration of glycemic control.[9]

Corneal endothelium can be evaluated well by specular microscopy, which is a non-contact photographic technique that allows visualization and analysis of the corneal endothelium as pachymetry, cell density, variation in size and shape.[10]

The Pentacam is a camera that was designed based on Scheimpflug's theory. Pentacam is capable of obtaining a three-dimensional image to evaluate various corneal parameters.[11]

Several studies had shown variable results while comparing corneal morphological parameters in diabetics with non-diabetic

subjects. In fact, Shenoy et al. concluded that evaluation of corneal endothelium in diabetic patients should be part of the protocol for eye care of diabetic patients.[12]

However, there have not been many studies that explain the alterations in the diabetic cornea by evaluating the corneal structure and correlating the changes with the duration and severity of the diabetic disease process to understand and manage these corneal changes.[13,14]

In this study, we used a cross sectional comparative study to assess the effect of diabetic control on corneal morphological parameters between diabetics and age-matched non-diabetic (control) eyes.

Patients and methods:

Patient enrollment

This is a cross-sectional comparative study on patients diagnosed with DM and control (non-diabetic) patients attended outpatients clinic of Mansoura Ophthalmic Center, Mansoura University in the period from May 2020 to May 2021. The study protocol was approved by the committee of institution review board and medical research ethics committee, faculty of medicine, Mansoura University. Written informed consent was obtained from all participants before inclusion in the study, explaining the value of the study and the procedures. The inclusion criteria where aged 40 to 70 years old, of both genders. The exclusion criteria were previous intraocular surgery, previous ocular inflammation, trauma, high error of refraction (> ±6 D in sphere or > ±3 D in cylinder), glaucoma and use of contact lens.

Patients of DM group were divided into several subgroups according to their control of DM (level of HbA1c), duration of DM and state of diabetic retinopathy (DR).

Study Protocol

Every patient had a complete ophthalmic examination which included uncorrected visual acuity and best corrected visual acuity using LogMAR VA chart, slit-lamp biomicroscopic examination (Haag Streit BP 900, Koeniz, Switzerland) for both anterior and posterior segment using Volk 90D accessory lens with slit lamp, refractive error using Topcon RM-800 autorefractometer. Intraocular tension measurement using Pulsair Tonometer (Keeler Pulsair Handheld Tonometer).

Measurement of endothelial cell density (CED), central corneal thickness (CCT), number of counted cells (NUM), average cell size (AVG), standard deviation of mean cell area (SD), coefficient of variation (CV), maximum and minimal cell area (Max. and Min receptively). Which was evaluated in each subject using a non-contact specular microscope (Tomey EM-3000, Nagoya, Japan). **(Figure 1)**

Figure (1): Non-contact specular microscope (Tomey EM-3000) used in the study.

Measurement of Keratometry values (KI, K2, K mean and K max), corneal astigmatism, anterior chamber depth (ACD), anterior chamber volume (ACV), Q value, frontal and back elevation, pachymetric maps and pupil center was conducted using Oculus Pentacam HR (automatically rotating Scheimpflug camera). **(Figure 2)**

Figure (2): Oculus Pentacam HR used in the study.

The study sample were classified into two main groups:

Control (non-diabetic) group: Where fasting blood sugar of less than 110 mg/dL, 2 hours post prandial blood sugar less than 140mg/dl and HbA1c less than 5.7%, all without any treatment.

Diabetic group: Where patients diagnosed to have diabetes mellitus (DM) and on current treatment.

Diabetic group subdivided regarding their state of control of DM (level of HbA1c) into:

- **Good Control DM Group:** Where last HbA1c level of ≤ 7.5% with treatment.
- **Poor Control DM Group:** Where last HbA1c level of> 7.6% with treatment.

And regarding the type of currently used treatment for control of DM into:

- **Non-insulin dependent DM (NIDDM):** Where patients using oral hypoglycemic tablets for control of DM.
- **Insulin dependent DM (IDDM):** Where patients using insulin for control of DM.

And regarding duration of DM into:

- **≤ 10 years**.
- **10 years – < 20 years.**
- **≥ 20 years**.

And regarding state of diabetic retinopathy (DR) into:

- **No diabetic retinopathy.**
- **Non proliferative diabetic retinopathy group (NPDR).**
- **Proliferative diabetic retinopathy group (PDR).**

Specular microscope imaging technique: After a clear image of the central endothelium was captured, the centers of at least 100 contiguous endothelial cells were marked. Then number of endothelial cells and other cell parameters were then displayed on the computer screen. The microscopy was repeated 3 times for each measurement and the mean value used for analysis.

Pentacam imaging technique: In dim light room, patient asked to fixate straight ahead on the fixation target (blue circular ring) while keep his or her eye open. The image was focused and centered, after which the software automatically began taking the measurements.

Statistical Analysis of the Data:

Data were fed to the computer and analyzed using IBM SPSS software package version 25 "SPSS, Inc., Chicago, IL" and Microsoft Excel 2019 "Microsoft Corporation, New York, NY, USA". Significance of the obtained results was judged at the 5% level, P-values less than 0.05 was considered statistically significant. Quantitative variables were expressed as mean and standard deviation, median, inter-quartile range, minimum and maximum as appropriate while categorical variables were expressed as frequency and percentage. The used tests were: Independent sample T, Mann Whitney tests, Fisher exact, Chi-square test and Pearson's or Spearman's correlation coefficient depending on the nature of the data.

Results:

patient's characteristics

The data were collected and recorded from May 2020 to May 2021. The study included 156 eyes of 100 patients, aged between 40 to 70 years old, eyes were assigned into two groups. There were 104 eyes in control non-diabetic group, 55 males (52.9%) and 49 females (47.1%), versus 52 eyes in diabetic group with 23 males (44.2%) and 29 females (55.8%). **(Table 1)**

Table (1): Demographic characteristics of the studied eyes:

		Control group (n= 104)	DM group (n= 52)	P
Gender	**Male**	52.9% (55)	44.2% (23)	0.308
	Female	47.1% (49)	55.8% (29)	

Data is expressed as percentage and frequency. P is significant when < 0.05.

Of total 52 eyes of DM group, 28 eyes had good control of DM versus 24 eyes had poor controlled DM **(Figure 3)** With 16 eyes in NIDDM and 36 eyes in IDDM group. Regarding duration of DM, 12 eyes (23.1%) had DM for ≤ 10 years, 30 eyes (57.7%) had DM for >10 to < 20 years and 10eyes (19.2%) had DM for ≥ 20 years. Finally, in relation with state of DR, there were 12 eyes (23.1%) in non-DR group, 24 eyes (46.2%) in NPDR and 16 eyes (30.8%) in PDR group. **(Figure 4)** Uncorrected visual acuity (UCVA) was with a mean of 0.65 ± 0.29 and 0.36 ± 0.18 in the diabetic and control groups respectively. While the best-corrected visual acuity (BCVA) was with a mean of 0.41 ± 0.41 and 0.08 ± 0.09 in the diabetic and control groups respectively. Both UCVA and BCVA assessed by LogMAR chart.

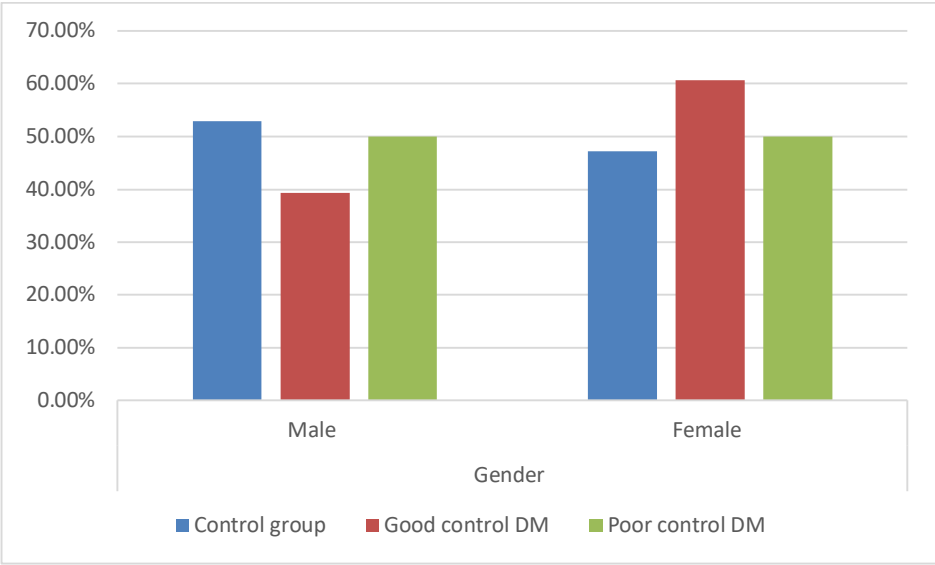

Figure (3): Demographic characteristics of the studied eyes regarding state of control of DM.

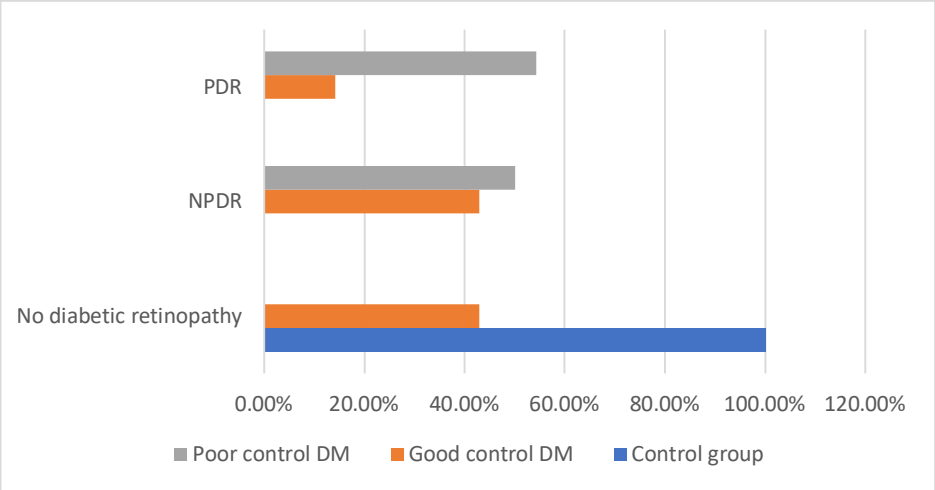

Figure (4): State of DR in studied eyes regarding state of control of DM.

Studied specular microscope derived parameters:

All studied specular microscope derived parameters (CED, CCT, number of counted cells, average cell area, standard deviation of mean cell area coefficient of variation, maximum cell and minimal cell area) were significantly affected in the diabetic group in comparison with control non-diabetic group. **(Table 2)** In relation with state of control of DM (HbA1c level) regarding studied specular derived parameters only number of counted cells, average cell area, standard deviation of mean cell area and minimal cell area were significantly affected in poor controlled DM than good controlled DM group. **(Table 3)** Duration of DM did not significantly affecting any of studied specular microscope derived parameters (CED, CCT, number of counted cells, average cell area, the standard deviation of mean cell area, coefficient of variant, maximum or minimal cell area). **(Table 4)** State of DR was significantly affecting all studied specular microscope derived parameters, except coefficient of variation which was non significantly increased. **(Table 5)**

Studied pentacam derived parameters:

Regarding studied pentacam derived parameters, only K max, ACD, ACV, Q value, frontal and back elevation were significantly affected in diabetic group than control non-diabetic group. With K1, K2, K mean, corneal astigmatism, thinnest location y coordination, pachymetric apex and pupil center were non significantly different in diabetic group than control non-diabetic group. **(Table 2)** Only corneal astigmatism was significantly affected by state of control of DM (the level of HbA1c) regarding good controlled DM and poorly controlled DM. **(Table 3)** Duration of DM did not significantly affect any of studied pentacam derived parameters (K1, K2, K mean, K max, corneal astigmatism, ACD, ACV, Q value, front and back elevation, thinnest location y coordination, pachymetric apex and pupil center). **(Table 4)** State of DR was significantly affecting each of corneal astigmatism, ACV, back elevation, thinnest location y coordination, pachymetric apex and pupil center regarding pentacam derived parameters. **(Table 5)**

Table (2): Corneal parameters of the studied eyes:

	Control group (n= 104)	DM group (n= 52)	95% CI	P
Specular microscope derived parameters				
CED (cells/mm2)	2510.13 ± 287.363	2312.92 ± 199.894	-285.00, -109.4	**< 0.001**
CCT (µm)	500.94 ± 47.883	517.12 ± 43.025	31.17, 1.18	**0.035**
Number	243.85 ± 35.091	182.23 ± 57.915	-76.37, -46.86	**< 0.001**
AVG (μm^2)	396.64 ± 45.690	437.44 ± 105.587	16.86, 64.73	**0.001**
SD (μm^2)	154.61 ± 55.494	190.94 ± 71.465	15.79, 56.89	**0.001**
CV (%)	37.32 ± 5.027	58.50 ± 55.547	10.4, 31.9	**< 0.001**
Max (um2)	959.85 ± 206.306	1239.71 ± 428.623	179.60, 380.13	**< 0.001**
Min (um2)	98.95 ± 19.811	106.63 ± 23.685	0.58, 14.79	**0.034**
Pentacam derived parameters				
K1 (D)	44.12 ± 2.763	44.16 ± 1.714	-0.79, 0.87	0.923
K2 (D)	44.71 ± 3.705	44.82 ± 1.854	-0.96, 1.19	0.836
K mean (D)	43.72 ± 3.382	44.49 ± 1.498	-0.21, 1.74	0.121
K max (D)	43.90 ± 8.418	46.38 ± 2.289	0.13, 4.84	**0.039**
corneal astigmatism (D)	0.74 ± 0.366	0.75 ± 0.453	-0.13, 0.14	0.887
ACD (mm)	2.81 ± 0.266	2.56 ± 0.448	-0.36, -0.13	**0.001**
ACV (mm3)	178.40 ± 164.683	130.25 ± 28.596	-93.68, -2.63	**0.038**
Q value	-0.39 ± 0.157	-0.30 ± 0.232	0.03, 0.15	**0.006**
Frontal elevation	1.76 ± 1.227	3.31 ± 1.766	1.07, 2.03	**< 0.001**
Back elevation	3.06 ± 1.935	6.27 ± 3.805	2.31, 4.12	**< 0.001**
Thinnest location y co-ordination (µm)	533.66 ± 44.292	525.81 ± 47.114	-23.04, 7.33	0.308
Pachymetric apex (µm)	541.05 ± 42.626	538.31 ± 50.603	-17.98, 12.50	0.723
Pupil center (µm)	539.25 ± 50.552	532.12 ± 52.694	-24.34, 10.07	0.414

Data is expressed as mean and standard deviation. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05.

Table (3): Corneal measurements of the studied eyes regarding state of control of DM:

	Control group (n= 104)	Good control DM (n= 28)	Poor control DM (n= 24)	P	P1	P2	P3
Specular microscope derived parameters							
CED (cells/mm2)	2510.13 ± 287.363	2370.54 ± 221.940	2245.71 ± 148.402	**< 0.001**	**0.038**	**< 0.001**	0.259
CCT (µm)	482.33 ± 42.368	492.75 ± 52.438	517.12 ± 43.025	**0.001**	**0.034**	**0.002**	1
Number	243.85 ± 35.091	198.68 ± 60.662	163.04 ± 49.030	**< 0.001**	**< 0.001**	**< 0.001**	**0.010**
AVG (µm2)	396.64 ± 45.690	403.32 ± 31.677	477.25 ± 143.080	**< 0.001**	1	**< 0.001**	**< 0.001**
SD (µm2)	154.61 ± 55.494	169.07 ± 50.669	216.46 ± 83.960	**< 0.001**	0.775	**< 0.001**	**0.015**
CV (%)	37.32 ± 5.027	57.14 ± 76.221	60.08 ± 4.085	**0.001**	**0.014**	**0.007**	1
Max (um2)	959.85 ± 206.306	1225.64 ± 461.736	1256.13 ± 395.692	**< 0.001**	**< 0.001**	**< 0.001**	1
Min (um2)	98.95 ± 19.811	100.04 ± 17.612	114.33 ± 27.657	**0.005**	1	**0.004**	**0.044**
Pentacam derived parameters							
K1 (D)	44.12 ± 2.763	44.12 ± 2.089	44.21 ± 1.180	0.988	1	1	1
K2 (D)	44.71 ± 3.705	44.57 ± 2.111	45.12 ± 1.491	0.811	1	1	1
K mean (D)	43.72 ± 3.382	44.39 ± 1.634	44.61 ± 1.347	0.291	0.855	0.540	1
K max (D)	43.90 ± 8.418	46.44 ± 2.649	46.30 ± 1.836	0.118	0.272	0.397	1
Corneal astigmatism (D)	0.74 ± 0.366	0.62 ± 0.424	0.90 ± 0.444	**0.038**	0.416	0.226	**0.032**
ACD (mm)	2.81 ± 0.266	2.60 ± 0.279	2.53 ± 0.592	**< 0.001**	**0.010**	**0.001**	1
ACV (mm3)	178.40 ± 164.683	118.75 ± 22.528	143.67 ± 29.473	0.095	0.123	0.783	1
Q value	-0.39 ± 0.157	-0.30 ± 0.226	-0.31 ± 0.244	**0.024**	0.065	0.168	1
Frontal elevation	1.76 ± 1.227	3.21 ± 1.663	3.42 ± 1.909	**< 0.001**	**< 0.001**	**< 0.001**	1
Back elevation	3.06 ± 1.935	6.46 ± 3.892	6.04 ± 3.770	**< 0.001**	**< 0.001**	**< 0.001**	1
Thinnest location co-ordination (µm)	533.66 ± 44.292	538.64 ± 50.009	510.83 ± 39.391	0.051	1	0.076	0.080
Pachymetry apex (µm)	541.05 ± 42.626	547.04 ± 52.563	528.13 ± 47.263	0.306	1	0.627	0.405
Pupil center (µm)	539.25 ± 50.552	543.25 ± 56.581	519.13 ± 45.517	0.171	1	0.250	0.272

Data is expressed as mean and standard deviation. P is significant when < 0.05. P1: Control group and Good control DM group. P2: Control group and Poor control DM group. P3: Good control DM group and Poor control DM group.

Table (4): Corneal measurements of the studied eyes regarding duration of DM:

	≤ 10 years (n= 12)	**>10 to < 20 years (n= 30)**	**≥ 20** years (n= 10)	**P**	**P1**	**P2**	**P3**
Specular microscope derived parameters							
CED (cells/mm2)	2323.83 ± 173.412	2323.17 ± 207.276	2269.10 ± 220.437	0.750	1	1	1
CCT (µm)	496.00 ± 38.589	480.83 ± 42.786	499.60 ± 69.768	0.459	1	1	0.871
Number	187.17 ± 83.027	180.33 ± 49.511	182.00 ± 51.361	0.944	1	1	1
AVG (µm2)	460.75 ± 155.044	435.27 ± 98.515	416.00 ± 35.656	0.613	1	0.996	1
SD (µm2)	198.83 ± 90.929	197.40 ± 65.949	162.10 ± 60.622	0.372	1	0.707	0.547
CV (%)	47.17 ± 10.794	66.73 ± 71.911	47.40 ± 12.039	0.468	0.929	1	1
Max (um2)	1159.42 ± 410.956	1307.93 ± 459.144	1131.40 ± 343.828	0.411	0.949	1	0.797
Min (um2)	114.50 ± 27.927	105.80 ± 23.642	99.70 ± 16.925	0.336	0.859	0.450	1
Pentacam derived parameters							
K1 (D)	44.36 ± 1.186	43.95 ± 1.798	44.58 ± 2.031	0.551	1	1	0.961
K2 (D)	45.09 ± 0.937	44.64 ± 2.083	45.03 ± 2.042	0.727	1	1	1
K mean (D)	44.73 ± 1.054	44.37 ± 1.443	44.56 ± 2.126	0.770	1	1	1
K max (D)	47.11 ± 2.292	46.08 ± 2.322	46.40 ± 2.213	0.429	0.587	1	1
corneal astigmatism(D)	0.73 ± 0.319	0.71 ± 0.445	0.90 ± 0.606	0.520	1	1	0.796
ACD (mm)	2.72 ± 0.828	2.51 ± 0.243	2.55 ± 0.257	0.394	0.526	1	1
ACV (mm3)	122.33 ± 24.788	128.47 ± 23.050	145.10 ± 42.800	0.155	1	0.193	0.334
Q value	-0.25 ± 0.187	-0.33 ± 0.268	-0.28 ± 0.146	0.653	1	1	1
Frontal elevation	3.00 ± 2.174	3.80 ± 1.627	2.20 ± 1.033	0.033	0.509	0.815	0.036
Back elevation	6.00 ± 1.414	5.73 ± 3.750	8.20 ± 5.391	0.201	1	0.533	0.235
Thinnest location y coordination (µm)	533.58 ± 37.032	519.03 ± 42.455	536.80 ± 68.750	0.483	1	1	0.928
Pachymetry apex (µm)	541.58 ± 37.245	537.30 ± 48.357	537.40 ± 72.538	0.969	1	1	1
Pupil center (µm)	537.17 ± 35.667	530.70 ± 50.586	530.30 ± 76.745	0.933	1	1	1

Data is expressed as mean and standard deviation. **P** is significant when < 0.05. **P1**: ≤ 10 years ***and*** >10 to < 20 years. **P2**: ≤ 10 years ***and*** ≥ 20 years. **P3:** >10 to < 20 years ***and*** ≥ 20 years.

Table (5): Corneal measurements of the studied eyes regarding state of diabetic retinopathy:

	No diabetic retinopathy	NPDR	PDR	P	P1	P2	P3
Specular microscope derived parameters							
CED (cells/mm2)	2474.00 ± 149.272	2217.89 ± 96.704	2298.75 ± 202.268	**0.008**	**0.015**	0.091	1
CCT (µm)	487.92 ± 38.500	445.11 ± 35.561	503.44 ± 33.116	**0.019**	0.206	1	**0.017**
Number	225.17 ± 66.015	161.33 ± 37.749	153.13 ± 59.889	**0.004**	**0.046**	**0.004**	1
AVG (μm^2)	389.08 ± 16.478	422.00 ± 26.972	497.69 ± 173.618	**0.035**	1	**0.038**	0.447
SD (μm^2)	158.33 ± 17.552	180.67 ± 7.483	245.00 ± 100.252	**0.002**	1	**0.004**	0.107
CV (%)	41.08 ± 4.033	58.33 ± 1.936	60.06 ± 7.929	0.598	1	1	1
Max (um2)	1046.33 ± 167.388	1059.56 ± 140.531	1529.69 ± 547.948	**0.006**	1	**0.012**	**0.033**
Min (um2)	102.08 ± 22.964	100.89 ± 12.015	121.75 ± 31.002	**0.017**	1	0.140	0.163
Pentacam derived parameters							
K1 (D)	43.59 ± 2.024	43.80 ± 1.474	44.13 ± 1.091	0.232	1	1	1
K2 (D)	44.12 ± 2.156	45.09 ± 1.881	44.89 ± 1.219	0.515	1	1	1
K mean (D)	44.43 ± 1.392	44.18 ± 1.835	44.49 ± 1.113	0.866	1	1	1
K max (D)	46.32 ± 2.903	46.86 ± 2.505	45.84 ± 1.295	0.666	1	1	1
Corneal astigmatism (D)	0.53 ± 0.345	1.21 ± 0.506	0.66 ± 0.276	**0.003**	**0.002**	1	**0.011**
ACD (mm)	2.75 ± 0.288	2.50 ± 0.264	2.58 ± 0.696	0.292	1	1	1
ACV (mm3)	131.92 ± 22.375	153.11 ± 39.432	129.88 ± 23.692	**0.016**	0.457	1	0.244
Q value	-0.36 ± 0.289	-0.38 ± 0.223	-0.27 ± 0.249	0.449	1	1	1
Frontal elevation	3.25 ± 2.094	3.44 ± 1.810	3.44 ± 1.896	0.963	1	1	1
Back elevation	5.17 ± 2.368	3.11 ± 2.315	7.44 ± 3.577	**0.008**	1	0.556	**0.026**
Thinnest location coordination (µm)	534.92 ± 36.448	477.22 ± 24.692	538.56 ± 34.821	**0.006**	**0.021**	1	**0.007**
Pachymetry apex (µm)	544.50 ± 38.448	489.33 ± 30.753	554.63 ± 43.758	**0.010**	0.058	1	**0.009**
Pupil center (µm)	536.58 ± 38.949	479.56 ± 26.660	547.19 ± 41.529	**0.008**	0.058	1	**0.009**

Data is expressed as mean and standard deviation. P is significant when < 0.05. P1: None & Early stages of DR. P2: None & Late stages of DR. P3: Early stages of DR and late stages of DR

Discussion:

Diabetes mellitus (DM) has a significant effect on the morphology, physiological aspects and clinical corneal condition. Changes can be detected at corneal epithelium, stroma and endothelium. These changes are expressed as diabetic keratopathy which has been reported differently in various studies.[15]

Global evaluation of diabetic corneas, using both specular microscopy and Pentacam Scheimpflug camera, can give us meticulous and integrative data regarding the impact of DM on human corneas.[16]

This present study was carried out to evaluate the effect of control and duration of diabetes millets on diabetic changes in corneal parameters. Using both Pentacam and specular microscope to determine diabetic corneal changes.

According to our study, concerning specular microscope derived parameters, there were highly significant decreases in endothelial cell density (CED) when comparing control non-diabetic group with DM group (P <0.001). Our results showed that, CED was of lower values in poorly controlled DM (where HbA1c >6.5%) than in good controlled DM (where HbA1c <6.5%) (P=0.259) and of lower values in DM for ≥ 20 years than DM for >10 to< 20 years, also than DM for ≤10 years(P=0.750). Although regarding both state of DM control and its duration the difference was not statistically significant. Also, CED had a significantly lower values in cases with non-diabetic retinopathy group than early and late stages of DR eyes according to our results (P=0.008).

Studies performed by Lee et al.[17] showed that the endothelium of the cornea is the tissue under metabolic stress in diabetics. That causes these morphological and functional changes in the cornea, with consequential damages as corneal decompensation against intraocular pressure.

El-Agamy and Alsubaie[18] found that CED values were lower in Type 1 DM patients than the healthy controls, with no correlation between CED with HbA1C level, which is correlated to our results. But unsimilar to our study, they found a positive correlation between duration of DM and CED. As the duration of DM was identified as a risk factor for changes the polymegathism and pleomorphism.

Taha et al.[19] endothelial cell density (CED) showed a highly significant difference between each of diabetic groups (good controlled and uncontrolled diabetic patients) and control group (p=0.001), with decreased values in diabetic patients. Furthermore, regression analyses conducted by Taha et al.[19] showed a positive correlation between HbA1c and CED. DM causes changes in corneal endothelial cell morphology similar to those induced by aging.[20]

Unlike Bayat et al.,[21] who found no difference in terms of endothelial parameters (CED and CV) between the DM and healthy groups.

In addition to less corneal endothelial cell density, our study demonstrated that the diabetic patients had thicker corneas, less hexagonality and more irregular cell size of the corneal endothelium than the controls.

Central corneal thickness (CCT) had a clinically significant difference between diabetic and non-diabetic groups (P=0.035). The CCT was non-significantly higher in poorly controlled diabetics (where HbA1c >6.5%) than in good controlled DM group (where HbA1c <6.5%) (P=1). Also, non-significantly higher CCT values with a duration of DM ≥ 20 years than DM for >10 to < 20 years, also than DM for ≤10 years (P=0.459). CCT was higher in patients with different stages of DR than non-DR patients by a significantly difference (P=0.019).

This finding is also consistent with previous reports on DM patients, such as those by Kumari and Saha,[22] Yazgan et al.,[23] Zhao et al.,[24] which reported that corneas in diabetic patients have a tendency to show higher CCT values. Other studies, for instance, demonstrated that there was no significant difference between diabetic and control groups.[18]

Lee et al.,[17] these authors had a pathogenic hypothesis for this CCT changes, which is corneal endothelial pump dysfunction in diabetic eyes causing corneal swelling.

On evaluating the coefficient of variant (CV) in this study, there was a highly significant increase in diabetic eyes compared with normal non-DM eyes (P<0.001). This increase indicated the presence of polymegathism, in which endothelial cells enlarge to fill the gaps between adjacent cells. Moreover, this increase was non-significant between state of control of DM (HbA1c level) and CV (P=1). This result was concordant with those obtained by El-Agamy and Alsubaie,[18] Taha et al.,[19] but not similar to those of Chen et al.[24] No studies showed a decrease in CV in diabetic patients.

As stated by our study, CV non-significantly affected regarding the duration of DM (P=0.468) or state of DR (P=0.598).

Elsobky et al.,[25] found that the duration of diabetes and the severity of retinopathy were correlated significantly with pleomorphism, polymegathism and corneal thickness, but not with glycemic control. Corneal endothelial viability was correlated with grades of DR. Retinopathy grade could be a predictor for endothelial cell density. That is conflicting with our results, as we found that regarding levels of glycemic control there were a correlation between it and each of NUM, AVG, SD and MIN. While duration of DM was not correlated with corneal endothelial changes as pleomorphism, polymegathism or corneal thickness. And regarding state of DR all specular derived corneal parameters were affected, except CV values were p=0.598.

Concerning pentacam derived parameters, in this current study we did not find any significantly difference in K1, K2 and K mean (P=0.923, 0.836 and 0.121 receptively). Only, K max was showed a significantly difference between diabetic and controlled non-diabetic groups (P=0.039) and with no correlation between K max and glycemic control (HbA1c level) (P=1), DM duration (P=0.429) or the state of DR (P=0.666). Although corneal astigmatism was showed non significantly difference between diabetic and non-diabetic groups (P=0.887), there was a significantly difference between corneal astigmatism and glycemic control (HbA1c level) (P=0.032) and state of DR (P=0.003) and non-significant regarding DM duration (P=0.520).

Huseynova et al.,[8] regarding Pentacam derived corneal parameters, there was a significantly difference in K min and K max between diabetic and non-diabetic patients. While Uzel et al.,[26] Xiao et al.,[27] did not detect any difference in K1 or K2 when comparing the type1 DM and healthy non-diabetic groups.

Our DM eyes had significantly shallower ACD than our healthy non-diabetic group (P=0.001). Moreover, there was no correlation between ACD and state of control of DM (HbA1c level) (P=1), DM duration (P=0.394) or the state of DR (P=0.292). Multiple studies have investigated and found significantly shallower anterior chambers in DM patients compared to a healthy group.[26,27] They explain these results by the following theory, decreased anterior chamber may occur due to metabolic swelling of the lens which in turn occur due to impaired glucose. Consistent with results reported by Uzel et al.,[26] Wiemer et al..[28]

There was no statistically significant difference in ACD and ACV was found between DM and non-diabetic groups in results published by Huseynova et al..[8]

Also, as regards anterior corneal elevation (ACE) and posterior corneal elevation (PCE), there was highly significant difference between uncontrolled DM and healthy non-diabetic eyes according to our results (P<0.001). Both ACE and PCE were non significantly different in poorly controlled DM than good controlled group (P=1), with non-significant difference between the ACE or PCE and duration of DM (P=0.033, 0.201 receptively), only PCE was significantly increase in eyes with late stages of DR than non-DR eyes (P=0.008).

Storr-Paulsen et al.,[16] Taha et al.[19] reported that regarding Pentacam elevation indices (ACE, PCE), only PCE showed a significant increase in diabetic cases. Regression analyses conducted by Taha et al.[19] showed a positive correlation between HbA1c and PCE. This denotes a possible established effect of elevated blood sugar levels in uncontrolled DM type2 on PCE.

In comparison with results published by Huseynova et al.,[8] who could not demonstrate significant changes in both ACE and PCE in diabetic subjects of type 2 diabetes mellitus.

According to a hypothesis that DM causes premature aging of the eye which was determined by Storr-Paulsen et al.,[16] in diabetic cornea the asphericity would be affected more than in healthy subjects.

In the diabetic group, we found no significant difference regarding thinnest location y coordination (P=0.308), pachymetric apex (P=0.723) and pupillary center (P=0.414) in comparison with the controlled non-diabetic group. On the other hand, non-significant correlation was found between the state of control of DM or duration of DM and all of the thinnest locations y coordination, pachymetric apex and the pupillary center. Versus significant difference regarding state of DR with thinnest location y coordination (P=0.006), pachymetric apex (P=0.010) and pupillary center (P=0.008).

Conclusion:

There were significant changes detected in corneal parameters in diabetic eyes included in this study. These changes were affected by level glycemic control and the state of DR but not affected by the duration of DM. As poor diabetic control induces both retinopathy and keratopathy. Detailed corneal parameters examination should be included in diabetic cases routine eye testing in order to eliminate diabetic keratopathy specially all specular microscopic parameters and back elevation, especially in poorly controlled DM.

DATA AVAILABILITY

All data are included in this article.

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None

Conflict of Interest

Authors declare no conflicts of interest.

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Ethics declarations

Conflict of interest

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