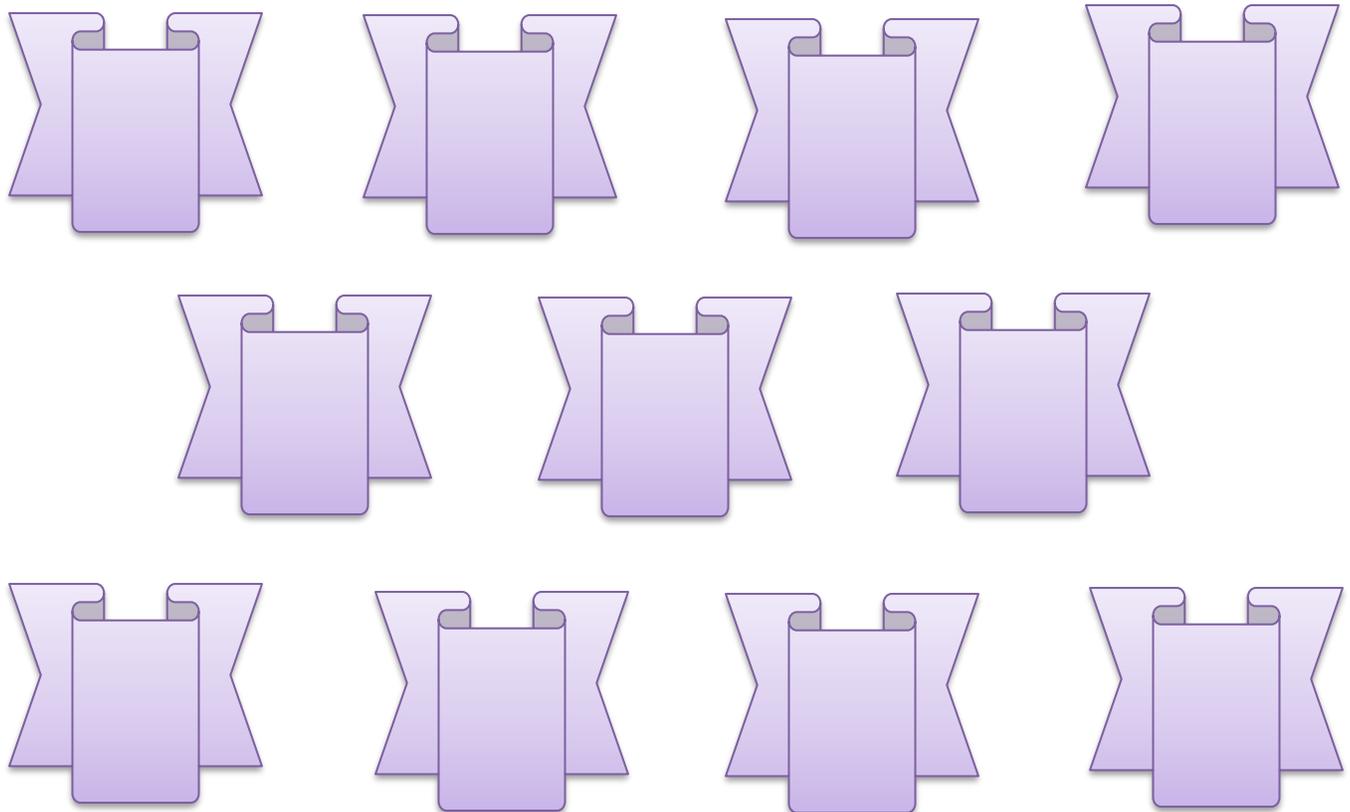


INTERNATIONAL JOURNAL OF MEDICAL ARTS



Volume 5, Issue 11, November 2023

<https://ijma.journals.ekb.eg/>



Print ISSN: 2636-4174

Online ISSN: 2682-3780



Available online at Journal Website
<https://ijma.journals.ekb.eg/>
 Main Subject [Ophthalmology]



Original Article

Effects of Type-II Diabetes Mellitus on Corneal Endothelial Cells

Samar Momtaz El-Kot *, Karim Abd El Latif Ahmed Gaballah,
 Ahmed Samir Montasser

Department of Ophthalmology, Faculty of Medicine, Helwan University, Helwan, Egypt

ABSTRACT

Article information

Received: 27-11-2023

Accepted: 22-12-2023

DOI: 10.21608/IJMA.2023.251601.1878.

*Corresponding author

Email: samarelkot@gmail.com

Citation: El-Kot SM, Gaballah KAA, Montasser AS. Effects of Type-II Diabetes Mellitus on Corneal Endothelial Cells. IJMA 2023 November; 5 [11]: 3817-3824. doi: 10.21608/IJMA.2023.251601.1878.

Background: Diabetes mellitus [DM] is a systemic metabolic disease. It is characterized by increase blood glucose level over a prolonged period of time. Diabetes is due to either the pancreas is not producing enough insulin, or the cells of the body are not responding properly to the insulin produced.

The Aim of the work: To measure the effect of diabetes type-II on corneal endothelial cells using specular microscopy versus normal individuals.

Patients and Methods: This is a case-control study including 96-eye of 48-diabetic patients' type-II from those attending the outpatient clinics of memorial institute of ophthalmology and Helwan University.

Results: The results of the current study revealed that the diabetes mellitus may have some adverse effects on corneal endothelial cell parameters. We have found that Specular microscopy is the only investigative tool that measures all corneal endothelial parameters together [CCT, CD, CV, HEX].

Conclusion: The current study revealed that diabetes mellitus may have an adverse effect on different corneal endothelial cell parameters especially on cell density.

Keywords: Type 2 Diabetes Mellitus; Corneal Topography; Corneal Endothelium; Corneal Pachymetry.



This is an open-access article registered under the Creative Commons, ShareAlike 4.0 International license [CC BY-SA 4.0] [<https://creativecommons.org/licenses/by-sa/4.0/legalcode>].

INTRODUCTION

Diabetes mellitus [DM] is a complex metabolic disorder characterized by chronic hyperglycemia and disturbances in carbohydrate, fat, and protein metabolism. It results from insufficient insulin production by the pancreas or ineffective utilization of produced insulin [1]. As a major global public health issue [2], DM is prevalent worldwide, with an increasing occurrence [3]. The two main types are Type I DM, characterized by autoimmune destruction of insulin-producing cells, and Type II DM, the most common form, involving genetic, environmental, and behavioral risk factors [4].

Type I DM involves autoimmune processes leading to beta cell destruction and absolute insulin deficiency, necessitating insulin therapy [5]. Auto-immune markers, alterations in T cell regulation, and the occurrence of other organ-specific autoimmune diseases characterize Type I DM [6]. The resulting deficiency in insulin secretion and abnormal pancreatic α -cell function lead to metabolic derangements and elevated glucagon levels [7].

Type II DM is marked by impaired insulin secretion and action, involving insulin resistance [8]. Insulin resistance results in compromised glucose uptake, incomplete suppression of hepatic glucose output, and impaired triglyceride uptake, driving hyperglycemia [9]. Clinical symptoms of DM include weight loss, polyuria, polydipsia, polyphagia, constipation, fatigue, cramps, blurred vision, and candidiasis [10].

Early identification of DM or pre-diabetes through screening is crucial, especially for individuals with risk factors like obesity, hypertension, and a family history of DM [11]. Diagnostic tests include random blood glucose, fasting blood glucose, and glycated hemoglobin A test [HbA1c] [12]. Acute complications of DM involve hypo-glycemia, hyperglycemic crises, diabetes keto-acidosis [DKA], and coma, while chronic complications include macrovascular [atherosclerosis] and microvascular [nephropathy, neuropathy, retinopathy] complications [11].

Atherosclerosis can lead to myocardial infarction, unstable angina, strokes, and increased morbidity and mortality [13]. Microvascular complications, induced by chronic hyperglycemia, include diabetic nephropathy, neuropathy, and retinopathy [14].

Diabetic changes of the anterior segment include conjunctival microaneurysms, corneal epitheliopathy and adhesion disorders that occur

due to damaged epithelial barrier function and impaired epithelial healing, which also increases the risk of ocular surface diseases such as dry eye disease, superficial punctate keratitis, corneal infections, recurrent corneal erosion and persistent epithelial defects [15, 16].

The aim of this work is to measure the effect of diabetes type-II on corneal endothelial cells using specular microscopy versus normal individuals.

PATIENTS AND METHODS

This is a case-control study including 96-Eye from both genders divided into 48-diabetic eye [type II] and 48 normal eyes. The participating individuals were selected from the outpatient clinics of the memorial institute of ophthalmology and Helwan University.

Eligibility criteria for participation

Inclusion criteria: Volunteers aged 30-60 years old, best-corrected visual acuity is 6/6 [on the Snellen's chart] for each eye and both genders.

Exclusion criteria for this study encompass individuals with a history of intraocular surgery or ocular trauma within the past 6 months, corneal opacity, glaucoma, uveitis, use of contact lenses in the 3 months preceding the study, ongoing ocular infections, corneal guttata, corneal dystrophies including Fuch's endothelial dystrophy, corneal degeneration, smokers, pregnant and lactating females, and patients unable to provide informed consent. These criteria were established to ensure a focused examination of the impact of type II diabetes on corneal endothelial cells using specular microscopy, minimizing confounding factors that could influence the study outcomes.

All subjects taking part in this study were subjected to

History: Duration and treatment line of diabetes either insulin or oral treatment or both, ocular history as previous ocular surgeries, glaucoma and intra-vitreous injection, systemic history as cardiac, renal, hepatic and CNS problems and random blood glucose level was measured for all diabetic patients.

Ocular examination: Visual acuity is assessed using Snellen's chart. Pupillary reaction is assessed using a torch and slit-lamp.

The anterior segment is examined using a slit-lamp. Intraocular pressure is measured using a Goldmann applanation tonometer or air puff tonometer. The fundus is examined using fundus biomicroscopy and specular microscopy [Topcon SP-1P]. Specular microscopy analyzes the following parameters of endothelial cell morphology. The level of inconsistency among different observers in analyzing cell density is found to be approximately 0-6% for high-quality endothelial images [rated as excellent to good], and 6%-11% for images of fair quality.

The recorded parameters consisted of the mean density of endothelial cells [MCD] measured in cells per square millimeter [cell/mm²], with a minimum normal value of 2500 cells/mm². The coefficient of variation [CV] was calculated by dividing the standard deviation of cell area by the mean cell area, which served as an indicator of the level of variation in cell size [polymegathism] Its normal value is up to 30%. The CV can be expressed in decimal or percentage terms, provided that we used the percentage form in this study. Percentage of hexagonal cells [HEX] represents the degree of pleomorphism. HEX values above 60% are normal in adults. HEX is the indicative of the diminution of

endothelial cells functional reserve. Central corneal thickness [CCT] is normally 557.61 μm.

A sole examiner conducted this examination. The patient sat on a chair facing the Topcon SP-1P Specular Microscope. The patient's chin was positioned on the chin rest, and their forehead rested on a designated head area. The examiner instructed the patient to gaze at the red light emitted from inside the microscope for a brief period. By tapping on the center of the patient's pupil as shown on the monitor, the SP-1P microscope automatically aligned, adjusted focus, captured, and analyzed the image of the endothelial cells.

The panorama photography feature captures three separate images in distinct areas: central, nasal, and temporal. These images are then automatically merged to create a wider area for observing and analyzing endothelial cells. This expanded cell area enables faster and more comprehensive evaluation of the patient's endothelium condition compared to traditional analysis methods. The panorama function is particularly beneficial in cases where the patient has a reduced number of cells and limited availability. Additionally, the pleomorphic/ polymegathic histogram can be displayed in color. The entire operation takes a few seconds.



Figure [1]: Showing specular microscopy Topcon SP-1P



Figure [2]: Showing panorama of the eye in which Center/Nasal/Temporal positions were photographed by Tapping the center of the pupil on the screen monitor



Figure [3]: Showing many marks on the screen as Examine, Mark for print / output, Print, Manual editing, Chinrest up / down, Overlay, Next



Figure [4]: Showing Pleomorphism



Figure [5]: Showing Polymegethism

Ethical aspects: The research study received approval from the Research Ethics Committee of the Faculty of Medicine at Helwan University. All individuals who took part in the study were provided with information regarding the study and willingly consented to participate by signing a clear and understandable informed consent document.

Statistical Analysis: The analysis of the data involved different approaches depending on the type of data. Frequencies and percentages were used to present qualitative data. To compare qualitative data, the Chi-square test and Fisher's Exact test were utilized. As for numerical data, their normality was assessed by examining the data distribution using tests like Kolmogorov-Smirnov and Shapiro-Wilk. Most data exhibited a normal [parametric] distribution, except for the duration of diabetes, UCVA, and BCVA data, which displayed a non-normal [non-parametric] distribution. For parametric data, mean and standard deviation [SD] values were used for presentation. In the case of non-parametric data, median and range values were used. The significance level was set at $P \leq 0.05$. The statistical analysis was performed using IBM SPSS Statistics for Windows, Version 23.0, produced by IBM Corp. in Armonk, NY.

RESULTS

Table [1] compares key demographics between diabetes [$n = 31$] and normal [$n = 24$] groups. Diabetic individuals are older on average [54.4 years vs. 39.4 years, $p < 0.001^*$], with no significant gender difference [$p = 0.732$]. The findings shed light on age and gender distinctions in these populations.

Table [2] examines the medical history of patients with diabetes [$n = 31$] compared to normal individuals [$n = 24$]. Significant differences were found in hypertension [25.8% vs. 0%, $p = 0.007^*$] and the prevalence of a free medical history [67.7% vs. 100%, $p = 0.003^*$]. No significant differences were observed in cardiac disease and stroke between the two groups.

Table [3] compares the ocular history of patients with diabetes [$n = 31$] to normal individuals [$n = 24$]. While there were no significant differences in intravitreal injections [IVI] and laser treatments, a significant distinction was found in the prevalence of a free ocular history [77.4% vs. 100%, $p = 0.015^*$].

Table [4] presents a comprehensive comparison of ocular parameters between individuals with

diabetes and those without [normal]. Significant differences were observed in uncorrected visual acuity [UCVA], best-corrected visual acuity [BCVA], pupil reactions, lens status, intraocular pressure [IOP], and certain hexagonality parameters.

Notably, diabetes patients exhibited higher minimum hexagonal cells, lower average hexagonal cells, and increased corneal density [CD]. These findings contribute valuable insights into the ocular characteristics associated with diabetes.

Table [1]: Baseline demographic characteristics of all studied individuals

| | | Diabetes [n = 31] | Normal [n = 24] | P-value |
|----------------|-----------|-------------------|-----------------|---------|
| Age [Years] | Mean [SD] | 54.4 [7.5] | 39.4 [7.8] | <0.001* |
| Gender [n [%]] | Male | 9 [29] | 8 [33.3] | |
| | Female | 22 [71] | 16 [66.7] | |

Table [2]: Medical History Comparison: Diabetes vs. Normal

| Medical history | Diabetes [n = 31] | | Normal [n = 24] | | P-value |
|----------------------|-------------------|------|-----------------|-----|---------------|
| | No. | % | No. | % | |
| Hypertension | 8 | 25.8 | 0 | 0 | 0.007* |
| Cardiac disease | 2 | 6.5 | 0 | 0 | 0.499 |
| Stroke | 2 | 6.5 | 0 | 0 | 0.499 |
| Free medical history | 21 | 67.7 | 24 | 100 | 0.003* |

Table [3]: Ocular History Comparison: Diabetes vs. Normal

| Ocular history | Diabetes [n = 31] | | Normal [n = 24] | | P-value |
|---------------------|-------------------|------|-----------------|-----|---------|
| | No. | % | No. | % | |
| IVI | 5 | 16.1 | 0 | 0 | 0.061 |
| Laser | 2 | 6.5 | 0 | 0 | 0.499 |
| Free ocular history | 24 | 77.4 | 24 | 100 | 0.015* |

Table [4]: Ocular Examination Parameters in Diabetes vs. Normal Group

| Variable | | Eye Examination [Diabetes] | Eye Examination [Normal] | P-value |
|--|----------------|----------------------------|--------------------------|---------|
| UCVA | Median [Range] | 0.2 [0.05 – 1] | 1 [0.1 – 1] | <0.001* |
| | Mean [SD] | 0.25 [0.24] | 0.8 [0.3] | |
| BCVA | Median [Range] | 0.3 [0.05 – 1] | 1 [0.05 – 1] | <0.001* |
| | Mean [SD] | 0.34 [0.26] | 0.86 [0.26] | |
| Pupil [n [%]] | Sluggish | 16 [33.3] | 0 [0] | <0.001* |
| | RRR | 32 [66.7] | 48 [100] | |
| Lens [n [%]] | Clear | 13 [27.1] | 44 [91.7] | <0.001* |
| | Pseudophakic | 2 [4.2] | 2 [4.2] | |
| | Cataractous | 33 [68.8] | 2 [4.2] | |
| IOP [mmHg] | Mean [SD] | 16.44 [1.98] | 12.44 [2.17] | <0.001* |
| CCT [µm] | Mean [SD] | 513.7 [27.1] | 525.1 [27] | 0.052 |
| CD [cells/mm] | Mean [SD] | 2651.5 [356.8] | 2825.6 [401.2] | 0.028* |
| CV [%] | Mean [SD] | 31.9 [5.09] | 32.6 [3.7] | 0.465 |
| Hexagonal cells [%] | Mean [SD] | 53.04 [8.85] | 50.3 [8.1] | 0.123 |
| Comparison of Hexagonality Parameters | | | | |
| Minimum Hexagonal cells | Mean [SD] | 170.3 [28.2] | 155.2 [25.5] | 0.007* |
| Maximum Hexagonal cells | Mean [SD] | 788.9 [135.1] | 747 [122.8] | 0.108 |
| Average Hexagonal cells | Mean [SD] | 384.7 [52.1] | 361.3 [53.3] | 0.032* |
| SD Hexagonal cells | Mean [SD] | 122.4 [25.3] | 117 [17.8] | 0.231 |

DISCUSSION

Diabetes mellitus is a systemic metabolic disorder that represents one of the most

common causes of retinopathy. The current study aimed to investigate the relationship between Diabetes mellitus type II and corneal endothelial cells. This relationship may be subsequently affected by the severity of

Diabetic retinopathy. The association between DR [diabetic retinopathy] and corneal endothelial cell loss might be explained by shared underlying mechanisms, such as the buildup of advanced glycation end products and heightened oxidative stress.

The current study was conducted by a non-contact specular microscopy [SP- 1P]. The specular microscope is a highly valuable noncontact technique used to capture detailed photographs of the corneal endothelium. By allowing for examination under significantly higher magnification, it can detect endothelial damage or diseases that may go unnoticed during a slit lamp examination. In fact, its magnification power is 100 times greater than that of slit lamp bio microscopy [17].

Mean Central corneal thicknesses [CCT]:

In the present study, there was no significant difference found in the average thickness of the central cornea [CCT] between the group of individuals with diabetes and the group of individuals without diabetes. These findings align with a previous study conducted by **Beato et al.** [18], which examined the structure of the cornea and the morphological characteristics of the endothelium in type II diabetic patients and healthy individuals. The authors of that study reported that the duration of diabetes, levels of glycated hemoglobin [HbA1c], and the stage of diabetic retinopathy can impact the morphological properties of the cornea. Their study has used Scheimpflug tomography to measure Central corneal thickness [CCT], while the current study used the non-contact specular microscopy. This also consistent with results of **Zhang et al.** [19].

The insignificant difference between the two study groups may be because of good glycemic control of the diabetic patients in the time of the study as reported by study of **Storr-Paulsen et al.** [20], which concluded that, in individuals with well-managed blood sugar levels, type II diabetes mellitus does not affect the density or shape of corneal cells. However, elevated levels of blood glucose are linked to a decrease in endothelial cell density. Additionally, the thickness of the cornea [CCT] was found to be notably increased in those with diabetes.

Using non-contact specular microscopy three studies [21-23] reported conflicting results to the current study results. These studies showed increase in central corneal thickness in diabetic patients versus normal subjects. On the other

side, **Durukan et al.** [24] used ultrasound pachymeter to measure Central corneal thickness which was higher in the DM group than the normal group.

Cell density [CD]: The present study showed statistically significant lower median **Cell density [CD]** in diabetic patients than normal subjects. Many studies showed similar results [19, 22-24]. On the other hand, the study of **Beato et al.** [18] showed no statistically significant difference in the endothelial cell density between diabetic patients and normal individuals.

Coefficient of variation [CV]: The current study showed no statistically significant difference between mean CV between the diabetic patients and normal subjects. Many studies [18, 20, 24, 25, 26] showed similar results.

In contrast to this study, other studies [19, 21-23] showed increase in CV% between Diabetic group and normal group. This could be attributed to a few factors. Firstly, it's possible that the light ray used in specular microscopy does not align perfectly perpendicular to the surface of the cornea. Additionally, the cornea itself may not be entirely transparent, leading to potential damage in the reflected image of the endothelial cells. Another possibility is that the image captured during acquisition is unclear, making it challenging to accurately determine the centers of the cells. The edges of the cells may not be clearly visible, further complicating the precise marking of their centers.

Hexagonal cell %: Our study showed no statistical difference in the Hexagonal cell % between the two groups, which was in agreement with previous researches [18, 20, 25, 26]. In contrast to the current study, several reports [19, 21-24] showed hexagonal cell ratio decreased in the diabetic patient's group versus the normal individuals. The reason for this could be the incorrect identification of cell boundaries. Automatic detection of cell boundaries is a challenging process due to variations in lighting and optical artifacts. Moreover, even a few errors in the segmentation can greatly impact the accurate estimation of polymegethism and pleomorphism [27].

The segmentation process in a specular microscope is prone to errors. Therefore, it is necessary to create an algorithm that can accurately estimate these parameters from images that exhibit such characteristics.

Furthermore, the potential cause for variation in obtaining endothelial mosaic images is also an important factor. The specular microscope's ability to capture a wide range of endothelial images from various regions enhances its versatility. When there is a discrepancy between the boundaries marked by the CSM software and the actual cellular walls on the back surface of the corneal endothelium, the calculated areas may not accurately correspond to the true endothelial cell areas. These inaccuracies were found in all specular microscope software, to varying extents. This can also be attributed to the lack of precision in the software used. The accuracy of the software can easily be observed by examining the precision of the line traced along the cellular edges in the endothelial mosaic.

The evaluation of corneal endothelial morphological parameters has been carried out globally, but with conflicting results. Specular microscopy operates on a sampling process, where each sampling process inherently possesses some degree of error. The extent of sampling is determined by the number of cells counted. To obtain accurate outcomes, the endothelial sampling process captures a sufficient number of images to ensure the correct cell count.

In non-contact specular microscopy, the captured endothelial image generally corresponds to the central area since the patient consistently focuses on the same spot. The sampling error decreases as the number of cells counted increases. In theory, if all cells were counted, the intrinsic error would be zero. However, in practicality, it is not feasible to scan the entire corneal endothelium, necessitating the acquisition of multiple images from different areas.

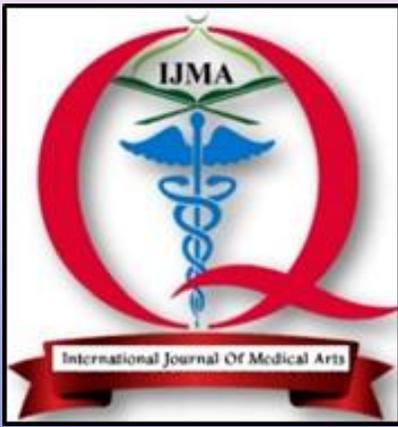
Conclusion: We have found that Specular microscopy is the only investigative tool that measures all corneal endothelial parameters together [CCT, CD, CV, HEX]. We reached the conclusion that assessing the corneal endothelium in individuals with diabetes should be included as a standard component of diabetic eye care protocols. The current study revealed that diabetes mellitus may have an adverse effect on different corneal endothelial cell parameters especially on cell density.

Financial and non-financial relations and activities of interest: None

REFERENCES

1. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med.* 1998 Jul;15[7]:539-53. doi: 10.1002/[SICI]1096-9136[199807]15:7<539::AID-DIA668>3.0.CO;2-S.
2. Shih KC, Lam KS, Tong L. A systematic review on the impact of diabetes mellitus on the ocular surface. *Nutr Diabetes.* 2017 Mar 20;7[3]:e251. doi: 10.1038/nutd.2017.4.
3. Markoulli M, Flanagan J, Tummanapalli SS, Wu J, Willcox M. The impact of diabetes on corneal nerve morphology and ocular surface integrity. *Ocul Surf.* 2018 Jan;16[1]:45-57. doi: 10.1016/j.jtos.2017.10.006.
4. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care.* 2004 May;27[5]:1047-53. doi: 10.2337/diacare.27.5.1047.
5. Kumar PJ, Clark M. Textbook of clinical medicine. Pub: Saunders [London]. 2002; 8[54]:1099-1121.
6. Hussain AN, Vincent MT. Type 1 Diabetes Mellitus. *Diabet Care.* 2007;15:787-89.
7. Holt RI. Diagnosis, epidemiology and pathogenesis of diabetes mellitus: an update for psychiatrists. *Br J Psychiatry Suppl.* 2004 Apr;47:S55-63. doi: 10.1192/bjp.184.47.s55.
8. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care.* 2011 Jan;34 Suppl 1[Suppl 1]:S62-9. doi: 10.2337/dc11-S062.
9. Baynes HW. Classification, pathophysiology, diagnosis and management of diabetes mellitus. *J diabetes metab.* 2015 May 1;6[5]: 1-9. doi: 10.4172/2155-6156.1000541.
10. Barse MA Jr, Han Y, Schneck ME, Barez S, Jacobsen C, Adams AJ. Local multifocal oscillatory potential abnormalities in diabetes and early diabetic retinopathy. *Invest Ophthalmol Vis Sci.* 2004 Sep;45[9]:3259-65. doi: 10.1167/iovs.04-0308.
11. Forbes JM, Cooper ME. Mechanisms of diabetic complications. *Physiol Rev.* 2013 Jan; 93[1]:137-88. doi: 10.1152/physrev.00045.2011.

12. Phillips PJ. Oral glucose tolerance testing. *Aust Fam Physician*. 2012 Jun;41[6]:391-3. PMID: 22675678.
13. Jia G, DeMarco VG, Sowers JR. Insulin resistance and hyperinsulinaemia in diabetic cardiomyopathy. *Nat Rev Endocrinol*. 2016; 12[3]:144-53. doi: 10.1038/nrendo.2015.216.
14. Chilelli NC, Burlina S, Lapolla A. AGEs, rather than hyperglycemia, are responsible for microvascular complications in diabetes: a "glycoxidation-centric" point of view. *Nutr Metab Cardiovasc Dis*. 2013 Oct;23[10]:913-9. doi: 10.1016/j.numecd.2013.04.004.
15. Leong YY, Tong L. Barrier function in the ocular surface: from conventional paradigms to new opportunities. *Ocul Surf*. 2015 Apr;13 [2]:103-9. doi: 10.1016/j.jtos.2014.10.003.
16. Vieira-Potter VJ, Karamichos D, Lee DJ. Ocular Complications of Diabetes and Therapeutic Approaches. *Biomed Res Int*. 2016;2016:3801570. doi: 10.1155/2016/3801570.
17. Kanski JJ, Bowling B, Nischal K. *Cornea: Clinical Ophthalmology: A systematic approach*. 8th ed. Edinburgh: Elsevier/Saunders; 2015. pp. 168–172.
18. Beato JN, Esteves-Leandro J, Reis D, Falcão M, Rosas V, Carneiro Â, Falcão Reis F. Evaluation of Corneal Structure and Endothelial Morphological Characteristics in Type 2 Diabetic and Non-Diabetic Patients. *Clin Ophthalmol*. 2020 Jul 14;14:1993-1999. doi: 10.2147/OPTH.S256244.
19. Zhang K, Zhao L, Zhu C, Nan W, Ding X, Dong Y, Zhao M. The effect of diabetes on corneal endothelium: a meta-analysis. *BMC Ophthalmol*. 2021 Feb 10;21[1]:78. doi: 10.1186/s12886-020-01785-3.
20. 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 Mar;92[2]:158-60. doi: 10.1111/aos.12064.
21. El-Agamy A, Alsubaie S. Corneal endothelium and central corneal thickness changes in type 2 diabetes mellitus. *Clin Ophthalmol*. 2017 Mar 2;11:481-486. doi: 10.2147/OPTH.S126217.
22. Taşlı NG, Icel E, Karakurt Y, Ucak T, Ugurlu A, Yilmaz H, Akbas EM. The findings of corneal specular microscopy in patients with type-2 diabetes mellitus. *BMC Ophthalmol*. 2020 Jun 3;20[1]:214. doi: 10.1186/s12886-020-01488-9.
23. Kim YJ, Kim TG. The effects of type 2 diabetes mellitus on the corneal endothelium and central corneal thickness. *Sci Rep*. 2021 Apr 15;11[1]:8324. doi: 10.1038/s41598-021-87896-3.
24. Durukan I. Corneal endothelial changes in type 2 diabetes mellitus relative to diabetic retinopathy. *Clin Exp Optom*. 2020 Jul;103 [4]:474-478. doi: 10.1111/cxo.12971.
25. Sudhir RR, Raman R, Sharma T. Changes in the corneal endothelial cell density and morphology in patients with type 2 diabetes mellitus: a population-based study, Sankara Nethralaya Diabetic Retinopathy and Molecular Genetics Study [SN-DREAMS, Report 23]. *Cornea*. 2012 Oct;31[10]:1119-22. doi: 10.1097/ICO.0b013e31823f8e00.
26. Islam QU, Mehboob MA, Amin ZA. Comparison of corneal morphological characteristics between diabetic and non diabetic population. *Pak J Med Sci*. 2017 Nov-Dec;33[6]:1307-1311. doi: 10.12669/pjms.336.13628.
27. Klais CM, Bühren J, Kohnen T. Comparison of endothelial cell count using confocal and contact specular microscopy. *Ophthalmologica*. 2003;217[2]:99-103. doi: 10.1159/000068562.



International Journal

<https://ijma.journals.ekb.eg/>

Print ISSN: 2636-4174

Online ISSN: 2682-3780

of Medical Arts