

Assessment of Anterior Segment Changes and Correlation between Film Volume and Tear Film Stability in Diabetic Patients

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ABSTRACT

Background: Diabetes mellitus (DM) affects the anterior segment of the eye, comprising the lacrimal functional unit, leading to decreased tear production, altered tear composition, and an increased risk of dry eye disease. Early detection of tear film abnormalities in diabetic patients is crucial to prevent ocular discomfort and complications.

Objectives: This study aimed to assess anterior segment changes and evaluate the association between tear film stability and volume in diabetic cases compared to healthy controls.

Patients and Methods: Cross-sectional analytic study was performed on 108 eyes, divided into two groups: 54 diabetic patients and 54 age-matched controls. All participants underwent visual acuity testing, slit-lamp examination, intraocular pressure measurement, Schirmer 1 test, tear break-up time (TBUT), blinking rate per minute (BRM), and anterior segment optical coherence tomography (AS-OCT) for tear meniscus height (TMH). Data were statistically analyzed using SPSS.

Results: Diabetic patients showed significantly lower Schirmer 1 values (13.0 ± 5.4 mm) compared to controls (16.8 ± 5.2 mm, $p < 0.001$) and reduced TBUT (4.81 ± 1.95 s vs 7.02 ± 1.86 s, $p < 0.001$). BRM was significantly higher in diabetics (16.48 ± 2.95) than controls (11.12 ± 2.46 , $p < 0.001$). TMH was also lower in diabetics (253.67 ± 62.36 μ m) compared to controls (283.56 ± 75.08 μ m, $p = 0.029$). Significant positive associations have been observed between Schirmer 1 and TMH, and between TBUT and TMH, in both groups ($p < 0.001$).

Conclusion: Diabetes significantly impairs both tear film volume and stability, increasing the risk of dry eye disease. AS-OCT is a reliable, noninvasive method for early detection of tear film abnormalities in diabetic patients.

Keywords: Diabetes mellitus, tear film, Schirmer test, tear break-up time, AS-OCT.

INTRODUCTION

Diabetes mellitus is a chronic state of hyperglycemia that has many systemic and ocular complications. Other than the retina, DM also can affect structures of anterior segment of the eye such as iris, cornea, ciliary process, anterior chamber, lens, and post chamber ⁽¹⁾. Diabetes can impact the entire lacrimal functional unit (LFU), which involves the ocular surface (meibomian glands, conjunctiva, and cornea), the lacrimal gland, and the neuronal network that connects them. Damage to any component of the LFU may result in diminished production of tears, irregularities in blinking, and alterations in composition of tear film. Persons with chronic hyperglycemia are at heightened probability of developing lacrimal functional unit dysfunction, characterized by diminished corneal sensitivity, reduced quality and quantity of tear secretion, as well as abnormalities in tear composition observed in diabetics. Diabetes additionally could be related to meibomian gland dysfunction (MGD) resulting in defective lipid layer and a higher probability of evaporative dry eye ⁽²⁾ and fifty percent of cases with diabetes mellitus experience dry eye symptoms ⁽³⁾.

Corneal anomalies comprising superficial punctate keratitis, recurrent corneal erosion, constant epithelial defects, and injury to corneal endothelium, are frequently observed in cases with diabetes mellitus ⁽⁴⁾. Diabetic

cases exhibit elevated thickness of the cornea and persistent corneal swelling following cataract extraction and vitrectomy, which cannot be attributed to epithelial defects, indicating dysfunction of the corneal endothelium. Diabetic cases exhibit diminished corneal sensitivity as a component of widespread sensory neuropathy. Seventy percent of diabetic cases report diabetic keratopathy, characterized by a reduction in corneal endothelial cell density (CED) and hexagonality, as well as polymegathism, pleomorphism, increased central corneal thickness (CCT), elevated corneal autofluorescence, and diminished corneal sensitivity ⁽⁵⁾.

Dilated and tortuous conjunctival vessels are frequently observed in the inferior bulbar region, pterygia, and pinguecula. Tortuosity and dilation of veins constitute microvascular anomalies associated with diabetes ⁽⁶⁾. Diabetes can also influence the transparency of lenses and the pharmacological dilation of pupils. Cataracts in diabetic cases may result from the diabetes itself or from accelerated senile cataracts. Alterations in the eye's refractive condition may signify the emergence of diabetes. These conditions may be hypermetropia or myopia. Myopia may result from a rise in the curvature and thickness of the crystalline lens ⁽⁷⁾.

The correlation between 1st angle glaucoma and diabetes mellitus in the literature is equivocal. The diabetic patients are additionally more probable to get a

rare type of glaucoma, called neovascular glaucoma. This type of glaucoma is characterized by the development of novel blood vessels on the iris. These blood vessels obstruct the usual flow of fluid from the eye, resulting in elevated pressure inside the eye ⁽⁸⁾. In 2021 the international diabetes federation IDF estimated Egypt as the 10th country worldwide with about 10.9 million cases and a prevalence of 20.9% in adults, so early detection of anterior segment changes and tear film dysfunctions in diabetic cases is as important as other diabetic ocular complications and may help early treatment and decrease complications and patients' discomfort ⁽⁹⁾.

The goal of this research was to evaluate the tear film and correlating tear film volume and tear film stability in diabetic cases.

PATIENTS AND METHODS

This cross-sectional study included 108 eyes from patients who were recruited from the endocrinology clinic and referred to the ophthalmology clinic at Badr Hospitals, where they subjected to full eye examination and anterior segment OCT by RS-3000 advance. This study was conducted in a one-year duration (From 21 march 2022 to 21march 2023).

The 108 eyes were divided into two groups: **Group 1:** comprised 54 eyes from diabetic patients and **Group 2:** comprised 54 eyes from healthy controls.

Inclusion criteria: Diabetic patients aged ≥ 18 years (types 1 and 2).

Exclusion criteria: Patients who had undergone intraocular surgery or eyelid surgery, Patients with other eyelids abnormalities like ectropion, Patients with autoimmune diseases, Patients receiving steroid or immunosuppressive treatment, glaucoma patients and contact lens wearers.

All patients & control were subjected to the following in a single visit to the clinic: History taking, Measurement of visual acuity using Landolt's chart, A slit-lamp biomicroscopy of the anterior segment and a post- dilatation examination of the fundus and Measurement of intraocular pressure by applanation tonometer.

Schirmer test type1 without anesthesia.

The Schirmer test was conducted without a local anesthetic to assess total tear production, including both basal & reflex secretions. Each subject was instructed to sit erect in a poorly illuminated room. and to look upward as a typical Schirmer tear test strip was carefully positioned at the lateral one-third of the lower eyelid, avoiding contact with the cornea. After 5 minutes, the strip was removed, and the degree of wetting was measured in millimeters.

Tear break-up time.

One drop of distilled water was used to moisten the end of a fluorescein strip, and subsequently the strip was put to the temporal bulbar conjunctiva of the experimental individual. The participant was instructed to blink multiple times to distribute the dye across the conjunctival and corneal surfaces, followed by an instruction to keep an open look straight ahead. The slit lamp equipped with a cobalt blue filter has been utilized to examine the entire cornea for dry regions, which manifested as dark spots or streaks. The interval in seconds between the final blink & the initial emergence of a dry area was with a stopwatch as the tear break-up time. The mean of three successive tear break-up time measurements has been calculated.

Blinking rate per minute.

The blinking rate per minute was assessed in all cases by the same observer, who recorded the blinking frequency while each participant engaged in a regular conversation with the physician.

Tear meniscus height (TMH) determined utilizing anterior segment optical coherence tomography. A spectral domain SD-OCT 3000 advanced system equipped with a corneal adaptor module was utilized. Vertical pictures have been captured at the 6 o'clock position of the cornea three seconds post-blink, and a built-in caliper was utilized to quantify tear (TMH, described as the distance from the point of meniscus intersection with the superior cornea to the inferior eyelid.

Ethical Consideration:

This study was ethically approved by Helwan University's Research Ethics Committee. Written informed consent was obtained from all participants. The study protocol conformed to the Helsinki Declaration, the ethical norm of the World Medical Association for human subjects.

Statistical analysis: Applying the IBM Statistical Package for the Social Sciences (SPSS) software. Qualitative information has been presented as numbers and percentages, while quantitative information was expressed by standard deviation, mean, interquartile range, and median. Parametric and non-parametric significance tests have been carried out, including chi-square and Fisher's exact test for non-parametric information, as well as the student's t-test and Mann-Whitney U test for parametric and non-parametric numeric information, correspondingly. Correlation tests have been performed accordingly. The significance level has been established at p-value under 0.05.

RESULTS

This study included 108 patients, of whom 62 (57.4%) were women and 46 (42.6%) were men. The mean age was 43.1 ± 13.6 years, ranging from 19 to 71 years (Table 1).

Table 1: Demographic data

		No.	%
Sex	Female	62	57.4
	Male	46	42.6
Age (years)	Mean \pm SD	43.1 \pm 13.6	
	Range	19-71	

The mean best corrected visual acuity (BCVA) in group 1 was 0.31 ranging from 0.1 to 1 while ranged from 0.5 to 1 in the control group Landolt chart was used. (Table 2)

Table 2: Best corrected visual acuity (BCVA)

	Min	Max	Mean	SD
BCVA				
Diabetics	0.1	1	0.31	0.23
Nondiabetics	0.5	1	0.7	0.31

Ten eyes (18.5%) had proliferative diabetic retinopathy (PDR) while 16 eyes (29.6%) had non-proliferative diabetic retinopathy, and 28 eyes (51.8%) had no clinically detectable diabetic retinopathy (Table 3).

Table 3: Diabetic Retinopathy grade

		No.	%
DR grade	No	28	51.8%
	NPDR	16	29.6%
	PDR	10	18.5%

* PDR. proliferative diabetic retinopathy * NPDR. non proliferative diabetic retinopathy.

Schirmer 1 test ranged from 5 mm to 25 mm I diabetic patients with mean value 13 \pm 5.40 mm as compared to mean value 16.78 \pm 5.22 mm in the control group which is statistically significant higher in group B of (non-diabetics) compared to group A (diabetics). P<0.001. (Table 4).

Table 4: Schirmer1 test

T test						
	Cases	N	Mean	Std. Deviation	Std. Error Mean	P value
schirmer1	Diabetics	54	13.000	5.4079	.7359	<0.001
	non diabetics	54	16.788	5.2256	.7247	

TBUT mean value was statistically significant higher in non-diabetics compared to diabetics. P<0.000. (Table 5)

Table 5: Tear break up time

T test						
	Cases	N	Mean	Std. Deviation	Std. Error Mean	P value
TBUT	Diabetics	54	4.815	1.9530	.2658	<0.000
	non diabetics	54	7.019	1.8629	.2583	

The rate of blinking per minute has been documented to differ from 13 to 20 per minute in group A with a mean value of 16.481 \pm 2.95 and a rate of 8 to 18 blink per minute with a mean of 11.115 \pm 2.46 in group B non-diabetics BRM mean value is statistically significant elevated in diabetics than non-diabetics. P-value < 0.000. (Table 6)

Table 6: Blinking rate per minute

T test						
	Cases	N	Mean	Std. Deviation	Std. Error Mean	P value
BRM	Diabetics	54	16.481	2.9508	.4016	<0.000
	non diabetics	54	11.115	2.4627	.3415	

The tear meniscus height ranged from 171 μ m to 407 μ m in group A diabetic patient with mean value 253.667 \pm 62.3584 μ m than a range of 149 μ m to 507 μ m with a mean value of 283.55 \pm 75.08 μ m which is statistically significant higher in group B non-diabetics compared to group A diabetic. P=0.029. (Table 7).

Table 7: Tear meniscus height

T test						P value
	Cases	N	Mean	Std. Deviation	Std. Error Mean	
TMH	Diabetics	54	253.667	62.3584	8.4859	
	non diabetics	54	283.558	75.0810	10.4119	=0.029

There was statistically significant positive correlation between schirmer and TMH in both dm and control. P-value equal 0.000, $r=0.564$ and P-value equal 0.000, $r= 0.693$ correspondingly. (Table 8)

Table 8: Correlation between schirmer 1 and tear meniscus height in diabetic and control

Cases			TMH	schirmer1
Diabetics	schirmer1	Pearson Correlation	.564**	1
		Sig. (2-tailed)	.000	
		N	54	54
Non diabetics	schirmer1	Pearson Correlation	.693**	1
		Sig. (2-tailed)	.000	
		N	54	54

A statistically significant positive association has been observed between and TMH representing tear film volume & TBUT representing tear film stability in both dm and control. P-value equal 0.000, $r=0.607$ and P-value equals 0.000, $r= 0.655$ correspondingly. (Table 9)

Table 9: Correlation between TBUT and tear meniscus height in diabetic and control

Correlations				
Cases			TMH	TBUT
Diabetics	TMH	Pearson Correlation	1	.607**
		Sig. (2-tailed)		.000
		N	54	54
Non diabetics	TMH	Pearson Correlation	1	.665**
		Sig. (2-tailed)		.000
		N	54	54
**, Association is significant at the 0.01 level (2-tailed).				

DISCUSSION

This study included 108 patients, 62 (57.4%) were women and 46 (42.6%) were men. Their mean age was 43.1 years with standard deviation ± 13.6 ranging from 19 to 71 years.

The mean BCVA in group 1 was 0.31 ranging from 0.1 to 1 while ranged from .5 to 1 in the control group Landolt chart was used.

Some studies had focused on tear film changes in diabetics such as **Misra et al.** ⁽¹⁰⁾ who reported a reduction in tear film stability and lipid layer quality in patients with diabetes mellitus (DM).

Our investigation demonstrated that tear film variables, comprising the Schirmer 1 test, TBUT, and tear meniscus height, were significantly diminished, while BRM was comparatively elevated in the diabetes group in comparison with controls. These findings indicated that dry eye is a prominent characteristic of diabetic ocular

surface illness, accompanied by a reduction in both tear film volume and stability.

In our study Schirmer 1 test was significantly lower in diabetic group compared to control. This agreed with many studies as **Kesarwani et al.** ⁽¹¹⁾ who reported decreased tear film parameters such as TBUT and Schirmer test values in 80 eyes of 53 type II diabetic patients compared with 50 healthy eyes.

Yoon et al. ⁽¹²⁾ found that the severity of keratoepitheliopathy was severe, with both tear film characteristics and corneal sensitivity significantly diminished in noninsulin-dependent diabetic cases, comparing these findings with those of normal subjects.

Dogru et al. ⁽¹³⁾ reported that both BUT & basal tear secretion were diminished, particularly in cases of diabetes characterized by inadequate metabolic control and peripheral neuropathy; however, these factors weren't associated with the length of diabetes or the severity of retinopathy.

Ozdemir et al. ⁽¹⁴⁾ also reported similar findings, with decreased Schirmer 1 values and TBUT in type 2 diabetic patients compared to the control group.

In our research, mean Schirmer 1 test values showed a significant positive correlation with TBUT and TMH. This may have resulted from diminished corneal and conjunctival sensitivity in diabetics, as well as injury to the microvasculature of lacrimal gland, resulting to its compromised function ⁽¹⁵⁾.

In our study TBUT is statistically significant lower in diabetics than non-diabetics. This goes with the result of **Yoon et al.** ⁽¹²⁾ and **Ozdemir et al.** ⁽¹⁴⁾.

One research has observed insignificant variance in TBUT among diabetics and normal controls **Geobbels** ⁽¹⁵⁾.

Consistent blinking was crucial for the proper distribution of the tear film and the protection of the ocular surface. Anomalies in blinking could lead to inadequate tear distribution, hence causing harm to the ocular surface ⁽¹⁶⁾. Blinking was critical for preserving the integrity of the ocular surface. cases with dry eye have elevated blink rates compared to those with normal eyes. The frequency of blinking diminishes when the tear film is constant and rises when it is unstable because of ocular conditions and/or external factors ⁽¹⁷⁾.

In our study BRM the mean value was statistically significant higher in diabetics than non-diabetics. However, **Inoue et al.** ⁽⁴⁾ stated a reduction in the blinking rate in diabetics but with a rise in the interblinking period in a group of 167 of type 2 DM group compared to 76 controls in **Inoue et al.** ⁽⁴⁾. In our study both TBUT and BRM were significantly negative correlated in diabetics and in control.

Due to recent advancements in picture clarity and resolution, as well as dependable quantitative data and its non-invasive nature, the utilization of AS-OCT for assessing ocular surface tissues and tear film has progressively risen in both academic purposes and daily practice. Consequently, a tear meniscus examination with AS-OCT is beneficial for assessing diminished lacrimal function in cases with **Baek et al.** ⁽¹⁸⁾ observed that the tear meniscus OCT parameters have been diminished in cases with diabetes mellitus compared to the control group, and these values declined with increased severity of diabetic retinopathy. This corresponds to our findings, as we observed that TMH was reduced in cases with DM in comparison with the control group.

Also, **Baek et al.** ⁽¹⁸⁾ observed that the OCT parameters were significantly related to DM duration, while in our study TMH was negatively correlated with DM duration, BRM in our study and was positively correlated to Schirmer 1 test and TBUT.

In our study there is statistically significant positive association between schirmer and TMH in both DM and control as both are indicators of tear volume, and positive correlation between TBUT as a direct test of tear film stability and both TMH and schirmer 1. So, there is a positive association between the stability and volume of the tear film in diabetics.

CONCLUSION

It could be concluded that effects of diabetes on both the stability and volume of the tear film, can lead to to an increased risk of dry eye in diabetic patients. Since the rising prevalence of diabetes among the Egyptian population ,studying its influence on the tear film and other anterior segment structures is becoming increasingly important because of the major impact on the quality of life of diabetic patients and its potential to reduce sight-threatening complications.

DECLARATIONS

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