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Evaluation of Meibomian Glands Dysfunction in Type Two Diabetic Patients

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ABSTRACT

Background: Diabetes Mellitus is one of the most common leading causes of blindness. Cataract and retinopathy are well-known as ocular complications of diabetes, problems involving the ocular surface; dry eyes in particular, have been reported in diabetic patients**. Aim of the Work:** to evaluate Meibomian glands function in patients with type 2 diabetes Mellitus.

Materials and Methods: this prospective observational study compared changes in Meibomian glands and tear film function in type 2 diabetic patients with non-diabetic patients. It included 20 eyes of 11 patients with type two diabetes mellitus and 20 eyes of 11 healthy non-diabetic controls. Meibomian glands function was evaluated by grading of Meibomian gland loss by meibography. Tear film function was assessed by dry eye questionnaire, measuring tear breakup time (TBUT), the Schirmer I test & corneal and Conjunctival fluorescein staining.

Results: dry eye questionnaire results were significantly higher scoring in diabetic group comparing with non-diabetic. TBUT was significantly lower in diabetic, especially with longer diabetic duration, comparing with normal control. Schirmer 1 test, corneal and conjunctival fluorescein staining, was significantly higher in diabetic patients compared with normal control. Meibography showed significant high scoring in diabetic patients that represent significant decrease in Meibomian gland number compared with controls.

Conclusion: our data suggest that type 2 diabetes predisposes to various changes on the ocular surface Meibomian gland dysfunction (MGD) in type 2 diabetic patients is more severe compared with nondiabetic patients. It should be noted at an early stage and treated appropriately in order to prevent more severe eye complications. Therefore, close attention should be paid to the ocular surface, especially in long-term diabetes mellitus. Further studies are needed to increase the sample size and include fluctuations in blood sugar as a key factor in studying the ocular surface.

Keywords: Meibomian Glands Dysfunction, Type Two Diabetic Patients.

INTRODUCTION

Diabetes Mellitus is one of the most common leading causes of blindness. Cataract and retinopathy are well-known as ocular complications of diabetes, problems involving the ocular surface; dry eyes in particular, have been reported in diabetic patients **(1).**

The Meibomian gland synthesizes and produces lipids and proteins which form the outer layer of the tear film. These lipids decrease evaporation and promote stability of the tear film. The International Workshop on Meibomian Gland Dysfunction suggests that MGD is the most prevalent cause of evaporative dry eye and may play a role in aqueous-deficient dry eye [(2)].These patients suffer from a variety of corneal complications including superficial punctuate keratopathy, trophic ulceration, and persistent epithelial defect. Dry eye is an important contributor to these problems as dry eye can lead to vision deficit, scarring and perforation of the cornea and secondary bacterial infection **(1).** Insulin is essential for optimal sebaceous gland activity, and is known to induce glandular cell proliferation and lipid accumulation. Lack of Insulin, in turn, would promote dysfunction. Also, Insulin stimulates the proliferation of immortalized human Meibomian gland epithelial cells (HMGECs), whereas high glucose was found to be toxic for these epithelial cells [(3)]. Hyperglycemia contributes to lipolysis in adipocytes, and this response, if occurring in the Meibomian glands, could dramatically reduce the quality of tear film**(4).** Infrared Meibography is a non-contact imaging study exclusively for the purpose of observing the morphology of Meibomian glands *in vivo*. This system uses a background illumination device with an Infrared light transmittance filter that illuminates the MGs to assess their integrity[(5)]**.**

AIM OF THE STUDY

The aim of this study is to evaluate the changes of ocular surface and Meibomian Glands in type 2 diabetic patients comparing with normal population.

MATERIALS AND METHODS

It is a prospective observational study included 20 eyes of 11 patients with type two diabetes mellitus and 20 eyes of 11 healthy controls. It was carried out at outpatient clinic of Zahraa university hospital except Meibography which was done at Al-Durra specialized eye center from (October 2018 to March 2019).

Ethical approval:

The study protocol adhered to the tenets of the declaration of Helsinki and was approved by the ethical board of Al-Azhar University. All subjects enrolled gave informed consent prior to their inclusion in the study. Patients who had been previously diagnosed with type 2 diabetes mellitus by a physician were enrolled

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in the study group. For the control group, fasting blood glucose was measured to exclude diabetes even without a history of diabetes. There was no significant difference in age and gender between the diabetic and non-diabetic groups. The inclusion criteria were as follows: Type two diabetes mellitus and age of greater than 35 years old. Exclusion criteria: Subjects with secondary diabetes and those who on medication or have other diseases that can affect tear production such as: allergies, Sjogren syndrome, rheumatoid arthritis, Parkinson, Lupus, some medications such as antihistamines, tricyclic antidepressants, oral contraceptives and drugs used to treat high blood pressure and diuretics. Moreover, vitamin A deficiency and pregnancy were excluded, Ocular hypertension or high intraocular pressure and Contact lens wearer or LASIK surgery. All the patients completed an ocular surface disease index (OSDI) questionnaire for the assessment of ocular surface symptoms. Subjects were considered symptomatic if the value was 20 or greater.

All patients underwent a series of ocular surface examinations in the following order: tear film breakup time (TBUT), the Schirmer test 1, corneal and conjunctival fluorescein staining and meibography.

1- Tear Film Breakup Time (TBUT): TBUT was calculated after placing a fluorescein strip into the lower conjunctival fornix. The interval between the last complete blink and the first break spot was recorded. The average value of three measurements was recorded.

2- Schirmer 1 test:

Schirmer1 test was done by insertion a sterile strip in the mid lateral portion of the inferior fornix, and the patient was instructed to close his or her eyes gently for five minutes. The lengths of wet area of strips were measured in millimeters and recorded**.**

3- Corneal Fluorescein Staining:

It was done by placing a fluorescein strip into the lower conjunctival fornix after application of local anesthesia. Examination of the patient was done by slit lamp then comment on the intensity of corneal and conjunctival fluorescein staining was recorded. The Van Bijsterveld scheme was used for grading the four areas. The score for each eye was determined by summation of the four areas to reach a total of 0 to 12.

4- Evaluation of Meibomian Gland Function

The morphology of Meibomian glands was evaluated by using the infrared meibography model of corneal Topography (Sirius, Scandicci, Italy, 2012). The upper and lower eyelids were ectropionized and the images were captured. MGL was assigned by meiboscale grade 0 when there were approximately no (0%) glandular losses. Grades 1 (<25%) loss, grade 2 (26-50%) loss, grade 3 (51-75%) loss and grade 4 (>75%) loss.

Statistical Analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. So, p-value was considered significant as the following: P-value > 0.05: Non significant (NS), P-value < 0.05: Significant (S) , P-value < 0.01: Highly significant (HS).

RESULTS

The study included 22 participants were subjected to the observational study. The demographic characteristics of the participants were summarized in table (1).

Table (1): Demographic data of the study groups.

		Diabetic	**Control**
No.	Total= 22 patients	11 patients(20 eyes)	11 Subjects(20 eyes)
Gender	Male	8 (72.7%)	6 (54.5%)
	Female	3 (27.3%)	5 (45.5%)
Age	Mean ±SD	60.45 ± 12.76	43.73 ± 6.42
	Range	41 – 82	36 – 51
Diabetes Duration	Mean ±SD	14.09 ± 9.08	_____
	Range	2 - 25	_____

The Questionnaire results showed higher scoring in diabetic patients with mean 23.82 ± 5.02 than in control group with mean 12.18 ± 4.24. That indicates more MGD symptoms in DM group compared with non-diabetic group. 90% of the diabetic patients complaining of redness, the most common symptom, 80% had lacrimation and 65% had burning sensation. Sensitivity to wind, computer glare and air pollutant were the most conditions that affect the diabetic group with 70%, 55% and 45% respectively. On the other hand, only 18% of control group affected with burning and 18% with lacrimation. The Questionnaire scoring was highly significant (p<0.01).

Clinical assessment of Tear Film: As regard TBUT, the results of our study showed that 80% diabetics were ≤ 7 as compared with control group 10% were ≤ 7. It was significantly lower in diabetic group compared with non-diabetic group. Also, **Schirmer 1 test:** The measurements of Schirmer I test in DM patients were low compared with control group with average mean 7.73 ± 2.96 and 11.86 ±1.99 respectively (p<0.01), results in about 80% of diabetic patients were < 10 as compared with normal population only 18% were <10.

Meibomian Gland Morphology and Dysfunction in Diabetic Patients Compared with Nondiabetic Patients: The meibography score was significantly higher in the diabetic group compared with the nondiabetic group (p = 0.00). In the diabetic group, the mean value of the meibography score was 49.23 ± 17.86. By contrast, in the nondiabetic group, the mean value was 23.89 ± 4.27 (figure 1, 2, 3).

Table (2): Meibomian gland dysfunction in diabetic group and control group**.**

Parameters	Mean		Range		p-value	Sig.
	control	DM group	control	DM group		
TBUT	8.68 ± 0.64	5.95 ± 2.14	7 –9	2 – 9	0.001	HS
Schirmer test	11.86 ±1.99	7.73 ± 2.96	8.5 –15	4 – 12	0.001	HS
fluorescein staining	3.36 ± 1.05	7.55 ± 2.67	2.5 –6	4 – 12	0.000	HS
Meibography	23.89 ± 4.27	49.23 ± 17.86	16.1 – 33.45	25.35 – 79.9	0.000	HS

Fig. (1) shows diabetic patient since 18 years, his Meiboscale = 66.1% grade 3 for his right eye.

Figure (1): Meibgraphy of the right eye with Meiboscale.

Fig. (2) shows diabetic patient since 2 years, her Meiboscale = 35.9% grade 2 for her right eye.

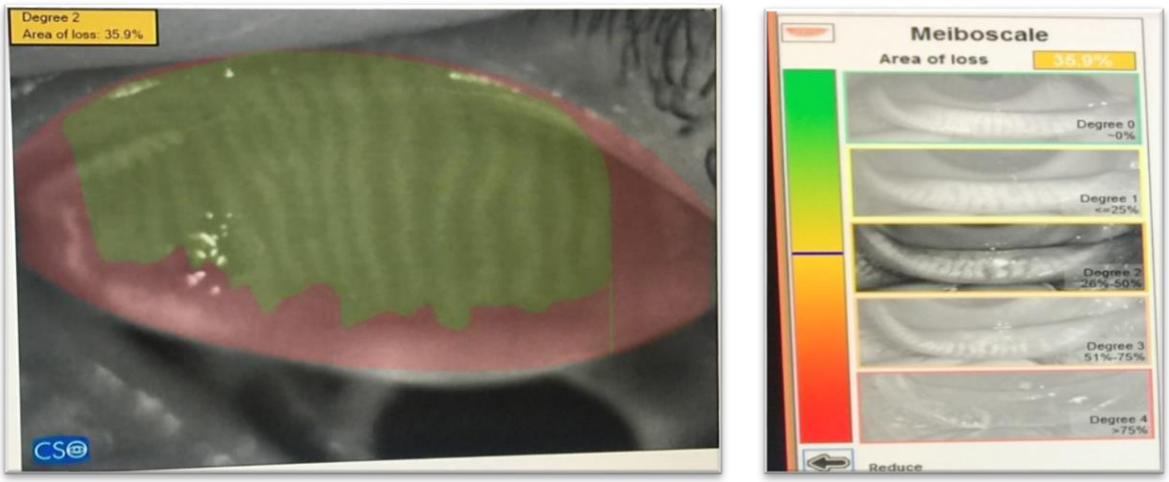

Figure (2): Meibgraphy of the right eye with Meiboscale= 35.9% grade 2.

Fig.(3) shows non-Diabetic participant, her Meiboscale = 16.1% grade 1 for her left eye.

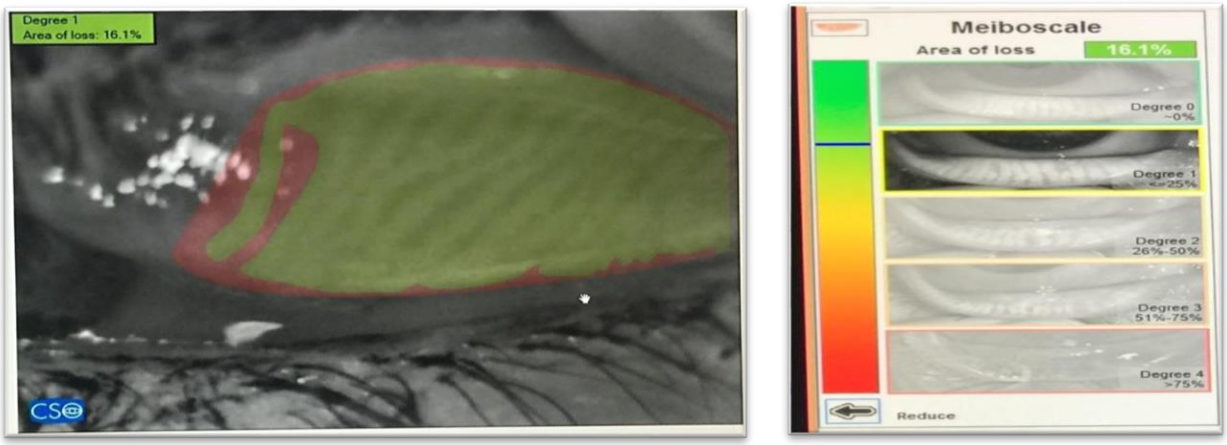

Figure (3): Meibgraphy of the left eye with Meiboscale 16.1%.

DISCUSSION

Ocular surface abnormalities during the course of diabetes mellitus have been documented in recent years. Studies showed at least 50% of DM patients have either symptomatic or asymptomatic dry eye syndrome (DES)[6]. In our study, we evaluated Meibomian Gland changes in 20 eyes of diabetic patients compared with 20 eyes of healthy controls. We used questionnaire as indicate of OSD symptoms with scoring >20 in about 75% of diabetic patients which it was increased significantly compared with normal controls, The result is similar to **Zeng *et al.*[7]** who used (standard patient evaluation of eye dryness) the SPEED questionnaire **Sandrajohanna *et al.*** [8] reported that dry eye disease was higher in the type 2 diabetes group, with 76.31% with a significant difference between the diabetic and control groups; OSDI was significantly higher in the diabetic group ($p = 0.0002$) compared with control group and OSDI was also highly significant ($p<0.001$) in **Yu *et al.*[9].** The results were also coincident with **Li *et al.*[10]; Shamsheer and Arunachalam[11]; Kumar *et al.*[12]; Rathnakumar *et al.* [13] and Dhivya[14]. Pathan[15]** reported that the symptoms of MGD in type 2 Diabetes were highly significant especially burning (46.9%) and dryness (23.5%). On the other hand in another study by **DeMill *et al.*[16]** revealed that no significant difference of OSDI between diabetic peripheral neuropathy group and control group as one of the main inclusion criteria were age ≥ 18 years of age which is younger compared with our age group (≥35 years of age). As regard TBUT, the results of our study showed that 80% diabetics were ≤ 7 as compared with control group 10% were ≤ 7. It was significantly lower in diabetic group compared with non-diabetic group. Also, Schirmer test results in about 80% of diabetic patients were < 10 as compared with normal population only 18% were <10. It was noted that Schirmer test results were low in diabetic group compared with normal group. It is coincident with **Goebbels[17]; Dogru *et al.*[18]; Ozdmeir *et al.*[19]; Jin *et al.*[20]; Yu *et al.*[21]; Shaheen *et al.*[22]; Dhivya[14] and Kamel *et al.*[23].**

Also Shaheen *et al.*[22] suggested that TBUT and Schirmer test were highly significant ($p<0.002$) in diabetic compared with normal population, in **Dhivya[14]** recorded significant differences in TBUT and Schirmer test ($p<0.05$) among the study group with lower TBUT in patients with diabetic retinopathy (DR). Abnormal TBUT value (<10 secs) was seen in 40% of the diabetic group. Schirmer test was abnormal (<10mm/5min) in 54% of diabetic subjects. **Kesarwani *et al.*[24]** reported that significantly poorer Schirmer and TBUT were found in study groups (DR and DM groups) as compared to control group ($P < 0.001$). Also, **Zeng *et al.*[7] ; Gao *et al.*[25]** observed that Schirmer test showed highly significant difference between the diabetic and normal groups ($P < 0.001$) and also between the non-proliferative diabetic retinopathy (NPDR) or proliferative diabetic retinopathy (PDR) and the control group. Corneal & conjunctival staining in our study showed about 65% of diabetic patients scoring > 6 while in control group 10% were ≥6 which means that punctate staining in diabetic patients more than in control group. These results are similar to ***Ozdmeir et al.*[19]; *Jin et al.*[20]; *Li et al.* [10]; *Yu et al.*[21] and *Zeng et al.*[7].**

Finally in Meibography, Meiboscore was higher by 50% of diabetic patients were grade 3 and 4 that means more affection of Meibomian Glands while in control group ranging between grade 1 and 2. This was consistent with previous findings where diabetes was associated with MGD. Studies by **Shamsheer and Arunachalam[11],** compared with the control subjects, patients with type 2 DM had significantly higher Meiboscore. **Yu *et al.*[9]** showed that 57.63% of people in DM group had MG dropout, while it was 33% in control group, **Lin *et al.*[26]** revealed that the Meibography score was significantly higher in the diabetic group compared with the non-diabetic group ($p = 0.004$)

Our data showed that diabetes mellitus was closely related to the severity of Meibomian Gland abnormality (as reflected by the Meiboscore, which indicates Meibomian Gland loss).

CONCLUSION

Our data suggest that type 2 diabetes predisposes to various changes on the ocular surface Meibomian gland dysfunction (MGD) in type 2 diabetic patients is more severe as compared with non-diabetic subjects. It should be noted at an early stage and treated appropriately in order to prevent more severe eye complications. Therefore, close attention should be paid to the ocular surface, especially in long-term diabetes mellitus. Further studies are needed to increase the sample size and include fluctuations in blood sugar as a key factor in studying the ocular surface.

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