Journal of Al Azhar University-Gaza *(Natural Sciences)*, 2018, 20 (2) : 39-48

Tear function evaluation of diabetic patients in Gaza Strip, Palestine

Khalid Awad , Mohammed Aljarousha

Department of Optometry, Faculty of Health Sciences, Islamic University-Gaza, Palestine

Received 10/4/2018 *Accepted* 3/9/2018

Abstract:

Background: Dry eye (DE) has been associated with diabetes mellitus (DM). The world escalating prevalence of diabetics is worrying which may project the escalating DE complaint rate. The changes in ocular surface integrity for instance, corneal staining, may indicate DE presence. Tear break-up time (TBUT) is among the vital procedures to assess pre-ocular tear film function and stability.

Objective: The study aimed to compare the dry eye symptoms and signs between diabetic patients and control subjects.

Methods: In a retrospective study, tear break up time (TBUT), Shirmer test I and II (ST), corneal fluorescein staining and symptoms were assessed for 59 diabetic patients and 60 control subjects from the Eye Hospital in Gaza. At least one dry eye (DE) symptoms, TBUT, ST I and II or corneal fluorescein staining was used in assigning patients into either DE or non-DE group. A "yes" or "no" response was further used for the discriminant analysis and tear abnormality (TBUT<10 seconds; ST< 5 mm).

Results: The percentage of DE was 23.7% in diabetic patient males and 44.1% in diabetic patient females. Additionally, the dry eye symptoms were significantly different between the male and female diabetic patients (p=0.023). The frequency of DE symptoms was significantly higher in diabetic patients (16.9%) than control subjects (11.7%). Additionally, the presence of dry eye symptoms was significantly different with diabetic patients (p=0.031). Itching and blurred vision were the two most commonly reported symptoms of diabetic patients and represented 44.1% and 40.7%, respectively. TBUT of diabetic patients was 11.50 ± 7.62 seconds and for control subjects was 13.25 ± 9.24 seconds. Additionally, there was a

significant difference between diabetes mellitus (DM) and non-diabetes mellitus patients regarding the volume of aqueous tear film secretion as evaluated by TBUT (p=0.041).

Conclusion: In the current study, the number of patients of dry eye symptoms was higher in diabetic patients than control subjects. Itching and blurred vision were the main symptoms of dry eye among control and DM cases. In addition, TBUT was significantly different between DM patients and control subjects.

Keywords: Tear break up time test, Shirmer test, corneal fluorescein staining, dry eye, diabetes mellitus.

Introduction

According to the dry eye workshop (DEWS, 2007), dry eye (DE) is defined as ‘‘a multifactorial disease that can affect ocular comfort, vision, and tear film stability, and can damage the ocular surface. It is also commonly known as a keratoconjunctivitis sicca or dysfunctional tear syndrome[2]. Dry eye disease is characterised by a progressive dysfunction of the lacrimal and meibomian glands that typically leads to decreased aqueous tear production and increased tear evaporation, respectively. People with keratitis sicca either do not generate sufficient tears or experience a malfunction of the tear film. In addition, the dry eye may occur due to inadequate aqueous tear production and exacerbated tear evaporation[3]. Specifically, Bron et al reported that the patient with meibomian gland dysfunction is at a high risk of developing a severe dry eye. Dry eye has been associated with diabetes mellitus (DM) [5]. The world escalating prevalence of diabetics is worrying which may project the escalating DE complaint rate[6]. The changes in ocular surface integrity for instance, corneal staining, may indicate dry eye presence[7]. Tear break-up time (TBUT) is among the vital procedures to assess pre-ocular tear film function and stability[8]. Many studies have found significantly decreased tear break up time scores in diabetic subjects[5, 9]. In contrast, other studies have reported neither a significant decrease in the aqueous tear flow nor any tear break up time impairment[10-11]. Gupta et al[12] used Schirmer test for the tear secretion and reported significantly reduced amount of tear film in the diabetic patients compared with normal group. The study also reported a reduced TBUT in diabetics compared to the controls. In Palestine, there is no available data in the literature

about the association between dry eye and diabetes mellitus. The results of this investigation may enhance the understanding of the relationship between DM and tear functions. The current study aimed to compare tear functions between DM patients and normal subjects in Gaza strip, Palestine.

Materials & methods

A retrospective study was performed using a case-controlled study based on the assessment of subjects attending the Eye Hospital in Gaza. A total number of 59 DM patients (21 males, 38 females) as well as 60 control subjects (24 males, 36 females) were included in this study by applying a convenience sampling method. The appropriate sample size was determined by using the PS Software13-14. Each age was matched to the nearest age with a range of ± 2 years. The clinical signs of DE disease were examined at 2 to 3 months for data collection by clinical practitioners who were responsible for verifying the examination and the diagnosis plan. The exclusion criteria were included patients who had ocular surgeries or laser treatment, vitamin A deficiency, cigarette smoking, contact lens wear, oral contraceptives and rheumatoid arthritis. DE in the current study was diagnosed based on one or more symptom or positive clinical signs which include dry sensation, eye itching, red eye, blurred vision, foreign body sensation, excess tearing, sensitivity to bright light, eye pain, and eye discharge. The responses ‘‘yes’’ or ‘‘no’’ were used for the discriminant analysis5,14. Shirmer test (ST) is an invasive method of assessing change in the flow of the tears in the tear pool15. This test uses non-toxic filter strips to measure aqueous tear secretion. Schirmer I is performed without corneal anesthesia while measuring total tear production which include examining reflex, and basic tear flow within a 5-minute period. Jones16 modified the Schirmer tear test II by the instillation of topical anesthetic being careful to remove excess fluid due to the irritation from the blotting paper. As a result, only the amount of basal secretion within 5 minutes is being measured. This test is indicated when the lacrimal deficiency is suspected based on the patient’s symptoms or the slit lamp findings.Values of the ST were obtained prospectively in the present research.

For TBUT, dye that readily mixes with the tear fluid was used. The tear film takes on a uniform fluorescent green appearance. The chin

and forehead were rested on a chin and forehead rests of slit lamp biomicroscopy respectively. The period from the last blink to the appearance of random dark spots and streaks in the tears was recorded as TBUT. The dark spots are caused by the migration of superficial lipids towards the ocular surface, rendering the surface dry3. Average of three consecutive readings was recorded for each measurement. Slit lamp biomicroscopy magnification was fixed at ×10. Results of the invasive TBUT were examined prospectively and patient with less than 10 seconds was diagnosed as having a dry eye in this present research.

Clinicians evaluated staining of the cornea by gently touching the lower tarsal plate with a fluorescein strip, and the patients were then asked to blink and look up17. This technique was observed through the SL-102/203 objective lens with a cobalt blue illumination when the corneal epithelial barrier has defects or erosions. Efron grading of corneal fluorescein staining ranged from 0 to 3 points (Grade 0 no staining of the corneal epithelial surface, Grade 1 mild staining limited to < 1/3 of the cornea, Grade 2, moderate staining of < 1/2 of the cornea, Grade 3, severe staining of > 1/2 of the cornea).

Statistical analysis

Data analysis was conducted using IBM SPSS (Version 20.0, SPSS Inc, Chicago, Illinois, USA). In this study, McNemar's test was used to compare the percentage of dry eye symptoms between DM patients and control subjects. In addition, Mann Whitney U test was used to compare the scores of the clinical signs between DM patients and control subjects. A value of $p<0.05$ was considered significant.

Results

Fifty-nine DM patients (59 eyes) and 60 control subjects (60 eyes) were involved in this study. Mean age of diabetic patients and control subjects was 59.25 ± 8.39 and 52.50 ± 9.82 years respectively. Demographic data of subjects was shown in Table 1. Based on the definition of at least one or more symptoms of the dry eye disease, the percentage of dry eye was 23.7% in DM males and 44.1% in DM females. A history of dry eye symptoms was 1.86 times higher among females compared with males. Additionally, the dry eye symptoms were significantly different between the male and female DM patients (p=0.023; Table 2). Itching and blurred vision were the two most

commonly reported symptoms of DM patients and represented 44.1% and 40.7%, respectively (Table 3). Table 4 shows that the frequency of patients with dry eye symptoms was higher in DM patients 16.9% than control subjects 11.7%. Additionally, the presence of dry eye symptoms were significantly different with DM patients (p=0.031).
Tear break-up time test was used for measuring tear functions. TBUT of DM patient was 11.50 ± 7.62 seconds and for control subjects was 13.25 ± 9.24 seconds. Additionally, there was a significant difference between diabetes mellitus and non-diabetes mellitus patients regarding the volume of aqueous tear film secretion as evaluated by TBUT (p=0.041; Table 5). Mean fluorescein staining for DM patients and control subjects were found to be 0.50 ± 2.00 and 0.00 ± 1.00 respectively (p=0.412; Table 5). The mean of ST I and II values found for DM patients were 21.34 ±11.75 mm and 11.32 ± 9.35 mm respectively. For control subjects, the mean of ST I and II values were 22.25 ± 11.30 mm and 12.14 ± 8.13 mm accordingly. However, no correlation was observed in both test values between the two study groups (p>0.05; Table 5).

Discussion

In our study, DM patients had a significantly higher frequency of dry eye symptoms than non-DM subjects. This conforms to a several epidemiological studies showed a significant correlation between dry eye symptoms and DM [5, 18]. According to Hom and Deland (2006), 52.9% of patients with either DM had self-reported clinically relevant dry eye[19]. Manaviat et al[20] stated that there is a correlation between DM and dry eye disease. Seifart and Strempel (1994) revealed that diabetic patients had an increased rate of keratoconjunctivitis sicca, due to decreased corneal sensitivity, neuropathy involving innervations of lacrimal gland and loss of goblet cells. Diabetic patients usually have dry eye syndrome more often than non-diabetic patients because diabetes affects the tear film.[10] In addition, diabetic subjects have structured metabolic and functional abnormalities of the cornea and are at a high risk of developing corneal lesions, as reported in several experimental and clinical studies.[20,21]
Results from the current study showed a significant difference in TBUT values between DM and control subjects. The present findings are comparable to Aljarousha et al[5] who evaluated tear functions and ocular surface changes in diabetic patients in Malaysia. Their results

showed an average value of 5.00 ± 2.00 seconds in patients with DM versus 7.00 ± 3.00 seconds in control subjects, with a significant difference of TBUT between them. The authors also reported no significant difference was noted between the tear meniscus height values of both groups. On the other hand, Saito et al[11] found neither a significant decrease of aqueous tear flow nor an impaired tear break up time test among DM patients. In the present study, there was no significant association in corneal fluorescein staining between diabetic and non-diabetic subjects. In contrast, Ozdemir et al[7] reported that there is a significant association in corneal staining between diabetic and non-diabetic subjects. The ST I and II values in the present study showed an insignificant difference between diabetic and non-diabetic subjects consistency with a previous study[22]. Gupta et al[12], however, found that there is a significant association in ST I between diabetic and non-diabetic subjects.

It can be concluded that our findings support the suggestion that DM patients have an elevated frequency of dry eye symptoms. In addition, TBUT was significantly less in DM patients with dry eye disease in Gaza Strip, Palestine. We suggest a further prospective investigation to identify the relationship between DM and dry eye.

Table 1: Demographic data

	Sample size (n)	Age (Mean ± SD)	Female	Male
Diabetic patients	59	59.25 ± 8.39 yrs	38	21
Control subjects	60	52.50 ± 9.82 yrs	36	24

Abbreviations:
n: number; SD: standard deviation

Table 2: Comparison of dry eye symptoms prevalence between DM male patients and DM female patients

Variable	DM male patients N (%)	DM female patients N (%)	Total (n)	p-value
Based on ≥ one dry eye symptom	5 (23.8)	17 (44.7)	22	0.023

Abbreviations:
n: number; %: percentage; ≥: more than or equal; DM: diabetes mellitus
McNemar's test

Table 3: Frequency of dry eye symptoms in DM patients and control subjects

Symptoms	DM patients (n=59) N (%)	Control subjects (n=60) N (%)
F.B sensation	20 (33.9)	8 (13.3)
Red eye	18 (30.5)	15 (25)
Eye pain	12 (20.4)	7 (11.7)
Blurred vision	24 (40.7)	13 (21.7)
Eye itching	26 (44.1)	16 (26.7)
Eye watering	17 (28.8)	9 (15)
Burning sensation	13 (22)	11 (18.3)
Eye discharge	14 (23.7)	15 (25)
Others	5 (8.5)	2 (3.3)

Abbreviations:
N: number; %: percentage; DM: diabetes mellitus; F.B: foreign body; Others include: scratchiness, soreness, grittiness, heavy eyelids

Table 4: Comparison of dry eye symptoms prevalence between DM patients and Non-DM subjects

Variable	DM patients N (%)	Non-DM patients N (%)	Total (n)	p-value
Based on ≥ one dry eye symptom	22 (37.3)	16 (26.7)	38	0.031

Abbreviations:
n: number; %: percentage; ≥: more than or equal; DM: diabetes mellitus
McNemar's test

Table 5: Comparison of clinical signs scores between DM patients and non-DM subjects

Variable	DM patients (n=59) (Mean ± SD)	Non-DM subjects (n=60) (Mean ± SD)	p-value
TBUT (sec)	11.50 ± 7.62	13.25 ± 9.24	0.041
Shirmer test I (mm)	21.34 ±11.75	22.25 ± 11.30	0.623
Shirmer test II (mm)	11.32 ± 9.35	12.14 ± 8.13	0.521
F/S (grade) ^	0.50 ± 2.00	0.00 ± 1.00	0.412

Abbreviations:
n: number; DM: diabetes mellitus; sec: second; mm: millimeters; F/S: fluorescein stains score of the cornea; SD: standard deviation; TBUT: tear break up time test
^0, none; 1, mild; 2, moderate; 3, severe
Mann Whitney U test

Acknowledgment:
We would like to thank Optometry department from the Islamic University Gaza and the Eye Hospital in Gaza for their help in data collection.

References

Lemp MA, Baudouin C, Baum J, Dogru M, Foulks GN, et al. 2007. Report of the Dry Eye WorkShop: The Definition and Classification of Dry Eye Disease. The Ocular Surface 5:65-204.

Behrens, A., Doyle, J. J., Stern, L., Chuck, R. S., McDonnell, P. J., Azar, D. T., Yiu, S. C. (2006). Dysfunctional tear syndrome: a Delphi approach to treatment recommendations. In *Cornea* (Vol. 25, pp. 900–907).

DEWS (2007c). Methodologies to diagnose and monitor dry eye disease: report of the

Diagnostic Methodology Subcommittee of the International Dry Eye Workshop (2007). Ocul Surf 5(2): 108–152.

Bron, A. J., Tomlinson, A., Foulks, G. N., Pepose, J. S., Baudouin, C., Geerling, G., Lemp, M. A. (2014). Rethinking Dry Eye Disease: A Perspective on Clinical Implications. The Ocular Surface, 12(2), S1–S31.

Aljarousha M, Badarudin NE, Che Azemin MZ. Comparison of dry eye parameters between diabetics and non-diabetics in district of Kuantan, Pahang. Malays J Med Sci. 2016;23:72–77.

Alves, M. D. C., Carvalheira, J. B., Módulo, C. M., & Rocha, E. M. (2008). Tear film and ocular surface changes in diabetes mellitus. Arquivos Brasileiros de Oftalmologia, 71(6), 96–103.

Ozdemir, M., Buyukbese, M. A., Cetinkaya, A., & Ozdemir, G. (2003). Risk factors for ocular surface disorders in patients with diabetes mellitus. Diabetes Research and Clinical Practice, 59(3), 195–199.

Sweeney, D. F., Millar, T. J., & Raju, S. R. (2013). Tear film stability: A review. Experimental Eye Research, 117, 28–38.

Yoon, K.-C., Im, S.-K., & Seo, M.-S. (2004). Changes of tear film and ocular surface in diabetes mellitus. Korean Journal of Ophthalmology, 18(2), 168–174.

Goebbels, M. (2000). Tear secretion and tear film function in insulin dependent diabetics. British Journal of Ophthalmology, 84(1), 19–21.

Saito, J., Enoki, M., Hara, M., Morishige, N., Chikama, T.-I., & Nishida, T. (2003). Correlation of corneal sensation, but not of basal or

reflex tear secretion, with the stage of diabetic retinopathy. Cornea, 22(1), 15–18.

Gupta, I., Mengi, R. K., & Bhardwaj, S. (2010). Tear secretion and tear film function in diabetics. JK Science, 12(4), 172–174.

Mohd-Ali, B., Liew, L. Y., Tai, H. J., & Wong, Y. Y. (2011). Tears evaluation of one sample of keratoconus patients in kuala lumpur. Medical Journal of Malaysia, 66(1), 53–55.

Awad, K. S., & Aljarousha, M. A. (2017). Comparison of Dry Eye Parameters between Keratoconus Patients and Control Subjects in Gaza Strip , Palestine, 325–328.

Cho, P., & Yap, M. (1993). Schirmer Test. I. A Review. Optometry and Vision Science, 70(2), 152–156.

Jones LT. The lacrimal secretory system and its treatment. Am J Ophthalmol 1966;62(July (1)):47–60.

Markoulli, M., Papas, E., Cole, N., & Holden, B. (2012). Corneal erosions in contact lens wear. Contact Lens & Anterior Eye : The Journal of the British Contact Lens Association, 35(1), 2–8.

Seifart, U., & Strempel, I. (1994). The dry eye and diabetes mellitus. Der Ophthalmologe : Zeitschrift Der Deutschen Ophthalmologischen Gesellschaft, 91(2), 235–239.

Hom, M., & De Land, P. (2006). Self-reported dry eyes and diabetic history. Optometry, 77(11), 554–558.

Manaviat, M. R., Rashidi, M., Afkhami-Ardekani, M., & Shoja, M. R. (2008). Prevalence of dry eye syndrome and diabetic retinopathy in type 2 diabetic patients. BMC Ophthalmology, 8, 10.

Li, D.-Q., Chen, Z., Song, X. J., Luo, L., & Pflugfelder, S. C. (2004). Stimulation of matrix metalloproteinases by hyperosmolarity via a JNK pathway in human corneal epithelial cells. Investigative Ophthalmology & Visual Science, 45(12), 4302–4311.

Najafi, L., Malek, M., Valojerdi, A. E., Aghili, R., Khamseh, M. E., Fallah, A. E., Behrouz, M. J. (2013). Dry eye and its correlation to diabetes microvascular complications in people with type 2 diabetes mellitus. Journal of Diabetes and ItsComplications, 27(5), 459–462.