Original Article

Comparison of Dry Eye Parameters between Diabetics and Non-Diabetics in District of Kuantan, Pahang

Mohammed Aljarousha[1,2], Noor Ezailina Badarudin[1], Mohd Zulfaezal Che Azemin[1]

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[1] *Department of Optometry and Visual Science, Kulliyyah of Allied Health Sciences, International Islamic University Malaysia, Bandar Indera Mahkota, 25200 Kuantan, Pahang, Malaysia*

[2] *Department of Optometry, Faculty of Health Science, Islamic University of Gaza, Palestine*

Abstract

Introduction: **Diabetes may affect the human body's systems and organs, including the eye. Diabetic retinopathy is the 5th leading cause of blindness globally. Diabetic subjects demonstrated dry eye symptoms that were also supported by the low values of the clinical tests.**

Purpose: **This study aimed to compare the dry eye symptoms and signs between diabetics and non-diabetics and tear functions between diabetic subjects with and without dry eye.**

Methods: **This retrospective study was based on the observation of 643 medical files. Using a convenience sampling method, 88 subjects were found to report diabetes mellitus. The information extracted from the files included: date of first examination, age at first visit, gender, past ocular history, systemic disease, symptoms of dry eye disease and details of clinical diagnostic signs. Non-contact lens wearers were excluded. A group of 88, age and gender matched, control subjects were included for this comparison study.**

Results: **The percentage of dry eye symptoms was higher in diabetic subjects (15.9%) compared with non-diabetic subjects (13.6%; $p<0.001$). The percentage of dry eye symptoms was also higher in diabetics with dry eye (63%) than in diabetics without dry eye (36.9%; $p<0.001$). Tear break up time was significantly different between diabetics and non-diabetics ($p<0.001$) and between diabetics with and without dry eye ($p=0.046$). The corneal staining was significantly different between diabetic subjects with and without dry eye ($p=0.028$).**

Conclusion: **Dry eye symptoms were significantly associated with diabetics. Tear break up time was significantly shorter in diabetics with dry eye compared to diabetics without dry eye.**

Keywords: *Diabetes mellitus, dry eye syndromes, cornea, tears, signs and symptoms*

Introduction

Diabetes mellitus (DM) has become a major public health concern in recent times. The global prevalence of diabetes was estimated to be 246 million in 2007 and could possibly reach 380 million by 2025 (1). Approximately 80% of diabetes cases occur in the developing world, with Southeast Asian countries having the highest number of cases (2). Malaysia is reported to have a prevalence of 9.9% which is projected to rise to 12.3% by 2025, thus making it one of the worst affected countries in Asia (1,3). Diabetes mellitus is frequently accompanied by microvascular complications like nephropathy, neuropathy and retinopathy (4). Neuropathy affects multiple systems, such as cardiovascular, genitourinary and gastrointestinal (5). The development of retinopathy is correlated with poor glycemic control and duration of diabetes (6).

Diabetics often complain of dry eye symptoms, as confirmed with the Schirmer test (7). Some studies also suggested that the tear composition of diabetic patients is different from that of normal subjects (8,9). Damage to the microvasculature of the lacrimal gland in long-lasting diabetes might impair the lacrimation. Sensory neuropathy of the cornea in diabetics can also reduce tear secretion.

Dry eye (DE) is a multifactorial pathology characterized by a progressive dysfunction of the lacrimal and meibomian glands that typically leads to decreased aqueous tear production and increased tear evaporation, respectively (10–12). These disorders are associated with signs and symptoms of ocular discomfort such as stinging,

eye watering or redness and may cause serious irritation to the interpalpebral ocular surface, particularly the cornea.

Several studies have identified a relationship between diabetes and DE with an increase in the risk of DE in these patients (11,13). However, other studies found neither a significant decrease in the aqueous tear flow nor any tear break up time impairment (7).

It is critical for clinicians to know about alterations in tear functions in diabetic subjects to initiate a proper management for DE which may affect their quality of life. To our knowledge, there is no available data in the literature about the tear functions of diabetic subjects in Malaysia. The study is also justified by the limited studies on Asian populations (14). The results of this investigation may enhance the understanding of the relationship between DM and tear functions. This study aimed to compare DE symptoms and signs between diabetics and non-diabetics and tear functions between diabetic subjects with and without DE.

Methods

A retrospective study was performed using a convenience sampling method based on the observations of data files of patients attending the Jalan Hospital Primary Care Clinic in Kuantan, Malaysia. Kuantan is the capital of Pahang which is one of the three states of the East Coast of Peninsular Malaysia. Kuantan covers an area of 2,960 km^2 (1,143 mi^2) with an estimated population of 488,709 people in 2014 (15)[15]. The study protocol was approved by local ethics committees. The study was carried out in accordance with the Declaration of Helsinki.

All of the information required for this study from October 1, 2007 to October 1, 2013 was supplied by the staff of the clinics. The clinical diagnostic was done by optometry students (3^{rd} and 4^{th} years) under the guidance of certified optometrists, who were responsible for verifying the examination and the diagnosis plan. Resident optometrists and students were committed to the patients and adhered to the guidelines. The information extracted from the files included: date of first examination, age at first visit, gender, past ocular history, systemic disease, symptoms of dry eye disease (one symptom or more) and details of clinical diagnostic signs including tear break up time (TBUT), corneal fluorescein staining and tear meniscus height). Non-contact lens wearers were excluded. DE was diagnosed by at least one reported symptom or positive clinical sign (TBUT<5 seconds). History of any previously confirmed systemic diagnosis of diabetes by a specialist was recorded (self-reported). Each age was matched to the nearest age with a range of +/- 2 years. Although the Schirmer test is one of the important methods of DE assessment, it was not included as a parameter in this study because the present study applied a retrospective design and no information about the Schirmer test was available in the medical files.

Statistical Analysis

Statistical analysis was conducted with IBM SPSS (Version 20.0, SPSS Inc., Chicago, Illinois, USA). McNemar's test and the non-parametric Wilcoxon signed-rank test were used for data analysis. A value of $p<0.05$ was considered significant.

Results

Eighty-eight subjects were found to report DM: 38 males and 50 females aged between 31 and 77 years with a mean (standard deviation) of 55 (10.1) years. For the purpose of comparison, 88 non-diabetic, age and gender matched subjects were chosen from the same patient pool: 38 males and 50 females with a mean (standard deviation) of 53 (7.3) years. There were no significant differences in matched or other unmatched characteristics between diabetic and non-diabetic subjects (Table 1).

Table 2 shows that the frequency of subjects with DE symptoms was higher in diabetic subjects (n=14) than in non-diabetic subjects (n=12). Additionally, the presence of DE symptoms was significantly different between diabetic and non-diabetic subjects ($p<0.001$). The frequency of DE symptoms was higher in diabetic subjects with DE (63%) than in diabetic subjects without DE (36.9%; $p<0.001$).

Tear functions were recorded based on the assessments of TBUT, corneal staining and tear meniscus height. The median (interquartile range) of TBUT in diabetic and non-diabetic subjects were 5 (2) and 7 (3) seconds, respectively ($p<0.001$; Table 3).

For diabetic patients, the median (interquartile range) of TBUT for the groups with and without DE were 3 (2) seconds and 6 (2), respectively ($p=0.046$; Table 4).

The corneal fluorescein staining grade median (interquartile range) was 0.50 (2) in

Table 1: Subjects' characteristics

	Diabetic subjects (N=88)	Non-diabetic subjects (N=88)	*p*-value
Mean age, years (SD)	55 (10.1)	53 (7.3)	0.166
Sex			
Male (%)	38 (43.0)	38 (43.0)	0.560
Female (%)	50 (57.0)	50 (57.0)	

SD: standard deviation

Table 2: Comparison of dry eye symptoms prevalence between DM patients and non-DM subjects

Variable	DM subjects N (%)	Non-DM subjects N (%)	Total (n)	*p*-value
Based on ≥ one dry eye symptom	14 (15.9)	12 (13.6)	26	<0.001

DM: diabetes mellitus
McNemar's test

diabetic subjects versus 0 (1) in non-diabetic subjects (p=0.312; Table 3). The median (interquartile range) for diabetics with DE and diabetics without DE were 1 (2) and 0 (1), respectively (p=0.028; Table 4). Tear meniscus height was used for measuring tear film volume. The median (interquartile range) of tear meniscus height was 0.50 (0.60) mm in subjects with diabetes versus 0.75 (0.70) mm in non-diabetic subjects (p=0.064; Table 3). The tear meniscus height median (interquartile range) in diabetic subjects with DE was 0.50 (0.63) mm, compared to 0.68 (0.60) mm in diabetic subjects without DE (p=0.396; Table 4).

Discussion

The diabetic subjects in the current study had a higher frequency of DE symptoms compared to non-diabetic subjects. Additionally, there was a significant difference in the presence of DE symptoms between both groups. Although both groups were age and gender matched, the higher frequency of DE symptoms in diabetic subjects compared to non-diabetic subjects might be influenced by other confounding factors such as climate, lower level of education, economic status and closeness to rural areas. According to Seifart and Strempel (16), diabetic patients had an increased rate of dry eye due to decreased corneal sensitivity, neuropathy involving innervations of lacrimal gland and loss of goblet cells. Diabetics usually have DE more often than non-diabetic patients due to the affected tear film (7). In addition, several epidemiological studies showed higher risk factors for DE in diabetics compared to non-diabetic subjects (11,13,17). Most of the diabetic subjects in our study presented with complaints of itching and burning sensations. Dogru et al. (17) reported that diabetic subjects often complain of DE symptoms such as burning and foreign body sensations. In addition, Nepp et al. (18) revealed that the severity of DE symptoms correlated with the severity of diabetic retinopathy. 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 (19-23).

Results from the current study showed a significant difference in TBUT values between diabetic and non-diabetic subjects. The present findings are comparable to Yoon et al. (14) who evaluated tear functions and ocular surface changes in diabetic subjects in Korea. Their results showed an average value of 7.8 (2.1) seconds in subjects with diabetes versus 10.9 (1.6) seconds in non-diabetic subjects. A significant difference was noted between the TBUT values of diabetic and non-diabetic subjects. Based on their findings, the authors hypothesised that there was aqueous deficient dry eye among the subjects in their study. Our average TBUT values, 5.4 (2.1) seconds in diabetic subjects and 6.8 (2.4) seconds in

Table 3: Comparison of clinical signs scores between diabetes mellitus patients and non-diabetes mellitus

Variable	DM subjects (n=88) (median(IQR))	Non-DM subjects (n=88) (median (IQR))	*p*-value
TBUT (sec)	5.00 (2.00)	7.00 (3.00)	<0.001
F/S (grade) ^	0.50 (2.00)	0.00 (1.00)	0.312
TMH (mm)	0.50 (0.60)	0.75 (0.70)	0.064

Wilcoxon Signed Rank Test
^0, none; 1, mild; 2, moderate; 3, severe
TBUT: tear break up time test;
TMH: tear meniscus height;
F/S: fluorescein stains score of the cornea;
DM: diabetes mellitus;
Non-DM: non-diabetes mellitus;
Sec: second;
mm: millimeters
IQR: Interquartile Range

Table 4: Comparison of clinical signs scores among diabetes mellitus patients with and without dry eye

Variable	DM with DED (n=34) (Median(IQR))	DM without DED (n=34) (Median(IQR))	*p*-value
TBUT (sec)	3.00 (2.00)	6.00 (2.00)	0.046
F/S (grade)^	1.00 (2.00)	0.00 (1.00)	0.028
TMH (mm)	0.50 (0.63)	0.68 (0.60)	0.396

Wilcoxon Signed Rank Test
^0, none; 1, mild; 2, moderate; 3, severe
TBUT: tear break up time test;
TMH: tear meniscus height;
F/S: fluorescein stains score of the cornea;
DM: diabetes mellitus;
Sec: second; mm: millimeters
DED: dry eye disease

non-diabetic subjects, are slightly lower than the earlier findings. A TBUT of less than 10 seconds is usually reported to be abnormal (24). The TBUT also varies depending on race. For example, Hong Kong Chinese had a reported TBUT of 7.8 seconds, Singaporean Chinese had a reported TBUT of 6.5 seconds (25), a Scotland population had a reported TBUT of around 15 seconds and Malaysians had a reported TBUT of 5 to 7 seconds (26). The different definitions for an abnormal TBUT are responsible for the differences in the values. The corneal staining results in the present study showed an insignificant difference between diabetic and non-diabetic subjects as opposed to a previous study conducted by Ozdemir et al. (27). This might be due to the difference in the severity of diabetes in the subjects.

Abnormal tear meniscus height was also common in the diabetic group. These findings may indicate that a decrease in tear secretion and abnormal tear composition give rise to superficial ocular lesions and subjective complaints in diabetic patients (12). However, the results found no significant correlation between diabetic and non-diabetic subjects.

In our study, diabetic subjects with DE had a significantly higher frequency of DE symptoms than diabetic subjects without DE. This conforms to a study by Najafi et al. (28) who found a significant correlation between DE and DM. According to Hom and Deland (29), 52.9% of patients with either diabetes or borderline diabetes had self-reported clinically relevant DE. Manaviat et al. (30) stated that there is a correlation between diabetes and DE. The

presence of DE in diabetic subjects was believed to be due to several factors. DE can result from either interruption of the tearing reflex pathways or from any process that affects the secretion of the tear film (30). In diabetes, it is possible that damage to the microvasculature of the lacrimal gland together with autonomic neuropathy contributes to the impairment of the gland.

Although the comparison of DE between diabetic and non-diabetic subjects has been reported previously, to our best knowledge, this is the first study comparing the DE parameters between diabetic subjects with and without DE. We found lower TBUT values in diabetic subjects with DE compared to diabetic subjects without DE. In addition, diabetic subjects with DE had higher scores of corneal staining compared to diabetic subjects without DE. However, we found no difference in tear meniscus height values between diabetic subjects with and without DE. To our knowledge, there is no reported data available in the literature about the tear functions of diabetic subjects in Malaysia. The results of this investigation may enhance the understanding of the relationship between DM and tear functions. Admittedly, the information about the types of DM [insulin-dependent diabetes mellitus (IDDM, type 1) and non-insulin-dependent diabetes mellitus (Non-IDDM, type 2)] and the three stages of diabetic retinopathy (DR) [background DR, pre-proliferative DR and proliferative DR] was not available in the current study. This is a limitation of the study. The patients were clinically examined for DE by the students. Resident optometrists further confirmed the clinical signs of DE. However, this is one of the limitations of the present study.

In Malaysia, the classification of the types of DM in relation to tear film should be incorporated in future studies. Furthermore, the three stages of DR in relation to symptoms and clinical signs of DE should be studied. It may also be recommended to the ministry of health to include DE clinical tests during DM screening.

Conclusion

Our findings support the suggestion that diabetic subjects have an elevated frequency of DE. In this study, the tear quality in diabetic subjects was affected, based on the TBUT value but not the measurements of corneal staining and tear meniscus height, compared to non-diabetic subjects. Similar observations can be reported in the comparison between the diabetics with and without DE. We suggest further prospective investigation to identify the relationship between diabetes and DE.

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Conflict of Interests

None.

Correspondence

Assistant Professor Dr. Mohd Zulfaezal Che Azemin
BEng (MMU), MEng Biomedical (Monash University, Melbourne), PhD Biomedical Engineering (RMIT, Melbourne)
Kulliyyah of Allied Health Sciences,
International Islamic University Malaysia,
Bandar Indera Mahkota, 25200 Kuantan,
Pahang, Malaysia.
E-mail: zulfaezal@iium.edu.my

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