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Mohammed Aljarousha

Department of Optometry and Visual Science, Kulliyah of Allied Health Sciences, International Islamic University Malaysia, Selangor 53100, Malaysia

Aziimah A. Abd Rahman

Department of Optometry and Visual Science, Kulliyah of Allied Health Sciences, International Islamic University Malaysia, Selangor 53100, Malaysia, aziimahrahman@gmail.com

Noor E. Badarudin

Department of Optometry and Visual Science, Kulliyah of Allied Health Sciences, International Islamic University Malaysia, Selangor 53100, Malaysia

Mohd Z. Che Azemin

Department of Optometry and Visual Science, Kulliyah of Allied Health Sciences, International Islamic University Malaysia, Selangor 53100, Malaysia

Khalid Awad

Department of Optometry, Faculty of Health Science, Islamic University of Gaza, P.O. Box 108, Gaza, Palestina

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Prevalence and Risk Factors of Dry Eye Disease in Kuantan, Malaysia

Mohammed Aljarousha^{1,2}, Aziimah A Abd Rahman^{1*}, Noor E Badarudin¹, Mohd Z Che Azemin¹,
Khalid Awad²

1. Department of Optometry and Visual Science, Kulliyah of Allied Health Sciences,
International Islamic University Malaysia, Selangor 53100, Malaysia

2. Department of Optometry, Faculty of Health Science, Islamic University of Gaza, P.O. Box 108, Gaza City, Palestine

*E-mail: aziimahrahman@gmail.com

Abstract

Background: To determine the prevalence of dry eye disease (DED) at Jalan Hospital Eye Care, International Islamic University Malaysia (IIUM), Kuantan, Malaysia. **Methods:** The dry eye symptoms and tear breakup time test (TBUT) values retrieved from the medical records of 643 patients were retrospectively analysed. Dry eye cases with one or more symptom were included. 'Yes' or 'no' responses were used in discriminant analysis of tear abnormality (TBUT < 5 seconds). **Results:** The crude prevalence of DED was 48.5%, the age-adjusted prevalence was 43% in women <50 years of age, and 68.4% in those ≥50 years of age. Contact lens wear and low TBUT values were associated with DED risk in men. Age of ≥50 years and a low tear meniscus height (TMH) score were associated with risk of DED symptoms in women. **Conclusions:** The prevalence of DED in optometric outpatients at IIUM was relatively high, especially in the elderly population. Symptoms and signs were poorly associated with DED. TBUT performed well in diagnosing dry eye and may be useful to improve the assessment of patients with dry eye problems in this region.

Keywords: contact lens, dry eye, tear breakup time, tear meniscus height

Introduction

Dry eye disease (DED) is a multifactorial pathology that can cause ocular discomfort, affect vision and tear film stability, and damage the ocular surface.^{1,2} The prevalence of dry eye is estimated as 7% to 34% worldwide, 34.2% in Japan, 11% in Spain, 23.7% in China, 16.4% in India, 12.3% in Singapore, and 8.3% in Turkey.³⁻⁸ The incidence is higher in the elderly ≥50 years of age than in younger age groups,^{9,10} and the prevalence is about twice as high in women than in men.^{11,12} DED may impair functional visual acuity and contrast sensitivity. Because it reduces the ability to read, drive, and to use visual displays for a prolonged time,¹³ the quality of life is affected. Dry eye symptoms include stinging, grittiness, soreness, eye watering, light sensitivity, and deteriorating vision.¹⁴ The condition of the ocular surface may cause severe irritation, particularly in middle-aged and elderly patients.¹⁵

In Malaysia, data on the prevalence of DED and studies on the association of dry eye symptoms and signs are limited, with only two previous publications. The first is a prospective prevalence study of DED at the University Malaya Medical Centre (UMMC), and the other is a study of the incidence of DED in a general population sample

in Kuala Lumpur. The UMMC study was performed in 2002, when DED was considered a nonspecific condition.¹⁶ It was not until 2007 that DED became a specific diagnosis.¹⁷ Therefore, the incidence study in Kuala Lumpur was carried out after DED had become a specific disease. Prevalence is the number or proportion of all new and old patients with a disorder, or the occurrence of an event, during a defined period. Incidence is the rate at which a particular event occurs, as the number of new patients with a specific disorder occurring during a defined period in a population at risk.¹¹ Both studies were carried out in Kuala Lumpur on the west coast of Malaysia. The prevalence of DED varies by location and depends on the type of clinical examination, the method of diagnosis, and the population studied.¹⁰ To our knowledge, this is the first study of the prevalence of dry eye conducted on the East Coast of Malay Peninsula, a region with sandy beaches, windy conditions, and prolonged rainfall.¹⁸ The East Coast of Malaysia was chosen because of its low relative humidity, rural areas, and relatively low education level.¹⁹ Sullivan et al.²⁰ did not find a correlation of the symptoms and signs of dry eye. The clinical signs of dry eye are of limited value without a report of symptoms.²¹ This study investigated the association of dry eye symptoms with signs and identified predictors of DED in a panel of

variables that included age, contact lens wear, the tear breakup time test (TBUT), corneal fluorescein staining, and tear meniscus height (TMH). A study of this type has not been performed in Malaysia.

Methods

The medical records of 643 patients, 244 men and 399 women were selected using a convenience sampling method. Kuantan is the capital of Pahang, one of the three states on the east coast of the Peninsular Malaysia. It covers an area of 2,960 km² and had an estimated population of 592,128 people in 2014.²² The study protocol was approved by the local ethics committees and conducted following the ethical guidelines of the Declaration of Helsinki. The patient records were retrieved from the IIUM optometry clinic at the Jalan Hospital Department of Optometry and Visual Science, Kulliyah of Allied Health Sciences, International Islamic University Malaysia (IIUM) patient data, entered from October 1, 2007 to October 1, 2013. The patients were clinically evaluated for DED by third and fourth year students under the guidance of certified optometrists who were responsible for verifying the examination and the diagnosis plan. Resident optometrists and students provided patient care with strict adherence to the treatment guidelines. The collected patient data included the date of the first examination, age at first visit, sex, past ocular history, systemic diseases and medications, symptoms of dry eye (one symptom or more), and evaluation of the tear film and ocular surface integrity including TBUT, TMH, and corneal fluorescein staining. Dry eye was diagnosed by at least one reported symptom or positive clinical sign (TBUT < 5 seconds).²³ History of dry eye symptoms was obtained by reviewing the clinical information records. They included 'dry sensation,' 'itching eye,' 'red eye,' 'blurred vision,' 'foreign body sensation,' 'excess tearing,' 'sensitivity to bright light,' 'eye pain,' and 'eye discharge.' DED was considered based on at least one reported symptom, and 'yes' or 'no' responses were used in the discriminant analysis.²³ The exclusion criteria were chosen because of their impact on corneal sensitivity. Patients who had ocular surgeries or laser treatment within the past 3 months were excluded because they may have changes in corneal sensitivity that contribute to loss of tear flow, goblet cell density, blink rate, and tear film stability.²⁴ Those taking medications that could result in tear film changes, increased evaporation, and dry eye were excluded.²⁵ Patients with rheumatoid arthritis or sarcoidosis may also have altered tear film secretion and were not eligible.²⁶ The results of invasive fluorescein TBUT were observed retrospectively.

Statistical analysis was conducted with IBM SPSS (Version 20.0, IBM Corp. Armonk, NY, USA). In this study, the percentage of patients diagnosed with TBUT was compared with the percentage of patients diagnosed

with symptoms by using descriptive statistics. Prevalence of dry eye was determined from the whole population, and the percentages of dry eye patients were compared with sex and age (< 50 or > 50 years) in each gender. Categorical variables were compared with the X² test or the Fisher exact test between TBUT and gender, symptom and gender, TBUT and age, and symptom and age. Significance was calculated at ($p < 0.05$).

Univariate analysis was carried out to evaluate associations between dry eye symptoms and each of the independent variables. The correlations were measured with Pearson in parametric and Spearman rank in non-parametric data between dry eye symptoms and each variable. The independent variables were age, gender, contact lens wear, TBUT, corneal fluorescein staining, and tear prism.

In multivariate analysis, variables with $p < 0.25$ in the univariate analysis were entered into a general linear model. Significant variables in the final model was determined by the method of backward elimination followed by forward entry, and selected based on optimizing the R² values, which provides an assessment of the ratio of the adjustment accounted for by the model. In the final model, the independent variables were retained if they were significant ($p < 0.05$). Parametric (independent sample t-test) was used to compare the difference between diabetic patients and non-diabetic (controls) and diabetic subjects with dry eye and diabetic subjects without a dry eye.

Results

The medical records of 643 patients were assessed; 314 patients were diagnosed with dry eye and 82 individuals used contact lenses. The prevalence of DED was 48.8%, and of those patients, 97 of 643 (15.1%) reported one or more symptoms of the dry eye syndrome but no clinical signs (Table 1). A total of 172 (26.7%) patient records included a positive clinical sign but not the symptom of a TBUT of <5 seconds, and 45 (7.0%) of 643 patients had both a positive clinical sign and of dry eye symptoms. The prevalence of dry eye signs and symptoms in relation to sex and age are shown in Tables 2 and 3.

Dry eye symptoms were positively associated with contact lens wear ($r = 0.18$, $p = 0.04$) but negatively associated with TBUT ($r = -0.15$, $p = 0.02$). There were no significant associations between age, corneal fluorescein staining, TMH, or dry eye symptoms. Significant univariate relationships were observed between dry eye symptoms and both TBUT and contact lens wear. Patient variables significantly associated ($p < 0.25$) with dry eye symptoms in univariate analysis were used in the adjusted model. In the adjusted model, contact lens wear was associated with higher odds of the outcome of dry eye symptoms versus no contact wear (adjusted OR = 3.4; 95% CI = 1.2–9.3).

Participants with a TBUT of <5 seconds were twice as likely to have the composite outcome of dry eye symptoms compared with the reference category of TBUT \geq 5 seconds (adjusted OR = 2.3; 95% CI = 1.0–5.1, Table 4). Dry eye symptoms were positively associated with TMH ($r = 0.28$, $p = 0.01$). There were no significant associations between TBUT, corneal fluorescein staining, age, contact lens wear, and dry eye symptoms. Univariate analysis showed significant relationships between dry eye symptom with age, TBUT, and TMH, which were then included in the

adjusted model. Participants \geq 50 years of age were twice as likely to have the composite outcome of dry eye symptoms as the reference value of <50 years of age (adjusted OR = 1.9; 95% CI = 1.0–3.6). Those with a TMH \leq 0.2 mm were more likely to have DED symptoms than those with a TMH > 0.2 mm (adjusted OR = 3.8, 95% CI = 2.3–6.3). Participants with low TBUT values did not have increased odds of DED symptoms (adjusted OR = 1.4; 95% CI = 0.8–2.4) (Table 5).

Table 1. Dry Eye Symptoms Assessment in Number (and Percentage)

One or more dry eye symptom	Subjects N (%)
Yes*	97 (15.1%)
No	546 (84.9%)

*Dry eye symptoms were included 'dry sensation,' 'eye itching,' 'red eye,' 'blurred vision,' 'foreign body sensation,' 'excess tearing,' 'sensitivity to bright light,' 'eye pain,' and 'eye discharge.'

Table 2. Prevalence (%) of Sign and Any Symptoms of Dry Eye by Gender

Variable	Male (n = 244) n(%)	Female (n = 399) n(%)	Total n (%)	p^*
Based on TBUT (sign) or \geq one dry eye symptom	118 (48.4)	196 (49.1)	314 (48.8)	0.85
Based on \geq one dry eye symptom	31 (12.7)	112 (28.1)	172 (26.7)	0.33
Based on TBUT (sign)	60 (24.6)	66 (16.5)	97 (15.1)	0.18

*Gender difference by chi-square test was used to compare proportions (categorical data); significant correlation at $p < 0.05$

Table 3. Prevalence (%) of Sign and Any Symptoms of Dry Eye by Age

Variable	Female (n = 399)		p^*	Male (n = 244)		p^{\wedge}
	< 50 years (n = 323) n (%)	\geq 50 years (n = 76) n (%)		< 50 years (n = 178) n (%)	\geq 50 years (n = 76) n (%)	
Based on TBUT (sign) or \geq one dry eye symptom	139 (43.0)	52 (68.4)	0.01	80 (44.9)	37 (56.1)	0.12
Based on \geq one dry eye symptom	47 (14.6)	19 (25.0)	0.02	24 (13.5)	7 (10.6)	0.55
Based on TBUT (sign)	92 (28.5)	39 (51.3)	0.04	56 (31.5)	30 (45.5)	0.01

*Female age difference by chi-square test was used to compare proportions (categorical data)

\wedge Male age difference by chi-square test was used to compare proportions (categorical data); significant correlation at $p < 0.05$

Table 4. Multivariate Logistic Regression Model to Identify Predictors of the Dry Eye Symptoms in Males

Variable	Multivariate analysis		p^*
	OR	95%CI	
CL wear			
No	1	1.2–9.3	0.02
Yes	3.4		
TBUT			
\geq 5 (sec)	1	1–5.1	0.04
<5 (sec)	2.3		

*Significant correlation at $p < 0.05$

Table 5. Multivariate Logistic Regression Model to Identify Predictors of the Dry Eye Symptoms in Females

Variable	Multivariate analysis		p*
	OR	95%CI	
Age		SS	
<50 years	1	1.0–3.6	0.04
≥50 years	1.9		
TMH			
>0.2 mm	1	2.3–6.3	0.01
≤0.2 mm	3.8		
TBUT			
≥5 (sec)	1	0.8–2.4	0.19
<5 (sec)	1.4		

*Significant correlation at ($p < 0.05$)

Discussion

The overall prevalence of DED in this study was 48.8%, which is higher than the estimated 7% to 34% global prevalence.^{3,8} The high prevalence might have been related to the relatively high percentages of participants with diabetes mellitus (13.7%), contact lens wearers (12.6%), and women >50 years of age (19.0%).^{2, 7, 10} In a previous prospective UMMC study, the prevalence of dry eye symptoms and positive clinical signs in 200 outpatients was 14.5%¹⁶ compared with the 48.8% in this study. Variation in the estimated prevalence of dry eye might be caused by differences in diagnostic criteria, objective dry eye test cut-off values, the definitions of dry eye/tear film disorders, demographics, and population age range and lifestyle. The current retrospective study has the advantages of being shorter, easier, and cheaper to conduct, and not prone to loss of follow-up. They also can be initial studies that generate hypotheses to be tested in subsequent studies. This study, using a yes or no response for discriminant analysis, found that 15% of the patients reported one or more DED symptoms. This is in line with previous studies in Asia that reported a prevalence of dry eye symptoms of 21% to 73.5%.^{3,5}

TBUT is effective for the identification and diagnosis of early stage and mild DED.²⁷ A TBUT score of ≤5 seconds has a higher sensitivity (98%) than most other objective tests used to distinguishing abnormal cases.²³ In this study, the TBUT value was consistent with previous reports from Oman and China^{28,29} but not with those from Japan and Saudi Arabia.^{30,31} The prevalence of the dry eye diagnosed with both signs and symptoms was higher in women than in men (Table 2). This might have been related to the difference in the size of the lacrimal gland acini in men and women, which could account for a greater tear volume in men.³² In both men and women, the prevalence of dry eye was higher in participants who were >50 years of age than those who were younger. The difference might have been caused by changes in tear function with increasing age.¹⁰ The study results are consistent with those of Din et al.³³

who reported that post-menopausal women on hormone replacement therapy with oestrogen therapy were at increased risk of DED.

The absence of a significant correlation of age and DED symptoms might be a consequence of the study population, which comprised a broad age range rather than a selected elderly population. Contact lens wearers are also five times more susceptible to dry eye than glasses wearers.³⁴ As most contact lens wearers are young, it is not surprising that there was no significant association between age and dry eye symptoms. Previous epidemiological studies that found symptoms increased with age were performed in older populations.^{35,36}

Dryness is the most frequently reported symptom in contact lens wearers. An early survey of contact lens-associated dryness by Brennan and Efron³⁷ found that 75% of contact lens wearers reported dryness. A self-administered questionnaire administered in the UK by Young et al.³⁸ reported that 44% of 932 contact lens wearers experienced dry eye symptoms. It was not surprising to see that contact lens wear was significantly associated with dry eye symptoms in this study. Moss et al.³⁹ found that 15.3% of contact lens wearers reported dry eye symptoms, whereas only 12.8% of non-wearers had dry eye symptoms. In this study, the use of contact lenses was significantly associated with the risk of dry eye symptoms, and wearers had 3.4 times higher risk of developing dry eye symptoms than non-wearers. This is consistent with a previous epidemiological study from Singapore⁷ that found that wearing contact lenses increased the risk of dry eye symptoms 2.9 times. The odds ratio was higher in this study, but the results were comparable.

A significant association was found between more symptoms and lower TBUT in men, which suggests that tear film instability of the ocular surface plays a role in the presence of dry eye symptoms. This finding could have resulted from a decrease in aqueous tear production, Meibomian gland disease that led to lipid tear deficiency,

or another undetermined cause.⁴⁰ Previous studies have also reported reduced TBUT values in symptomatic dry eye patients.⁷ Patients with TBUT values <5 seconds had a 2.3 times higher risk of developing dry eye symptoms than those with TBUT values \geq 5 seconds (Table 4). Han et al., found that patients with abnormal TBUTs had a 0.9 times increased risk of developing dry eye symptoms. The difference between studies might be the result of differences in the definition of an abnormal TBUT.

A significant association was found between more symptoms and higher TMH values in women, but many studies have reported significantly decreased TMH in patients with DED.^{41, 42} In the current study, TMH was measured immediately after eye opening, as previously described, but other studies delayed the time of measurement.⁴³ This indicates that a reduction in reflex tearing occurs with delayed blinking. TMH has also been found greater early in the day and to steadily decrease towards the end of the day.⁴⁴ Therefore, variation in the time of TMH measurement may be responsible for the reported differences in the association of dry eye symptoms and TMH. Lamberts et al.⁴⁵ found that TMH was influenced by several variables such as tear flow, the location of the punctum, lid length, and location of the grey line that limits the anterior extension of tears on the lid margin. The palpebral aperture height also affected TMH. This study found that dry eye symptoms in women were significantly associated with a TMH \leq 0.2 mm in women with an odds ratio of 3.8 with a TMH > 0.2 mm. To our knowledge, no previous study has reported a similar significant association of dry eye symptoms and TMH. The current study revealed a higher percentage of dry eye in Kuantan than in Kuala Lumpur, the capital city of Malaysia, which is located in the middle of the Malaysia Peninsula. The humidity in Kuantan, on the east coast of the peninsula, is lower than in Kuala Lumpur. This result is in line with a report by Lee et al.⁴⁶ that low humidity increased the frequency of dry eye symptoms.

The east coast of the peninsula includes rural areas, in which the prevalence of DED is higher than urban areas.⁶ The proportion of patients with a TBUT of <5 seconds or one or more dry eye symptom was higher in women than in men and in patients \geq 50 than in those <50 years of age. Contact lens wear and TBUT were both significantly associated with dry eye symptoms in men; TMH was the only variable found to be associated with symptoms in women. Other variables including age, corneal staining, and TMH were not associated with symptoms in men. Age, contact lens wear, TBUT, and corneal staining were significantly associated with symptoms in women. Contact lens wear, a TBUT of <5 seconds, and age \geq 50 years increased the risk of symptomatic DED in men, in addition to a TMH \leq 0.2 mm in women. These new estimates of the prevalence

of DED and its risk factors in Malaysia will serve to inform the eye care community and assist its practitioners in advising and improving the management of their patients.

The prevalence of DED varies with local conditions, type of clinical examination, and study methods and population. Prospective studies of dry eye symptoms and clinical signs in the three states on the east coast of the Peninsular Malaysia, Kuantan, Terengganu and Kelantan that include the three resident races, Malay, Chinese, and Indian, are recommended. Future studies should include a larger sample size, a highly reliable clinical test such as TearLab osmolarity,⁴⁷ tear function tests, and TBUT as well as recording the type of contact lenses worn, i.e. soft or hard. The effect of the contact lens material and the duration of lens wear would increase the understanding of the aetiology, diagnosis, and treatment of DED. Few data comparing the effects of contact lens material and prolonged contact lens wearing on corneal physiology are available. Additional research on the relationship between those variables and normal corneal physiology are warranted.

Conclusions

To the best of our knowledge, this is the first study to report the prevalence of dry eye disease in the east coast of Peninsular Malaysia (one of the states). This new information on the prevalence of DED and its risk factors in Malaysia will serve to inform the eye-care community and assist its practitioners in advising and managing their patient more suitably. We suggest a further prospective investigation to identify the relationship between factors such as diabetes mellitus, race, haze, visual display terminal and dry eye.

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Conflict of Interest Statement

None declared.

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