Original Article

Dry Eye Among Patients at the Eye Clinic of A Secondary Referral Hospital

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ABSTRACT

Introduction: Dry eye is a common but under-diagnosed problem in the general population. Lack of standardised diagnostic protocol causes prevalence of dry eye varied widely in different populations. Nevertheless, effective management rests largely on the accurate diagnosis and identification of the contributing risk factors. **Methods:** In a cross sectional study, socio-demographic, lifestyle and medical history data were collected from 157 respondents. A validated six-item questionnaire was used to determine the dry eye symptoms. Dry eye was determined by using Schirmer's test. Fluorescein staining test and tear break up time (TBUT) test were performed to characterise the dry eye. **Results:** Using the Schirmer's test, 33.8% of respondents had dry eyes. The likelihood of dry eye increased among Malay females in the seventh decade. The most frequently reported symptom was sensation of dryness of the eye. Although only 22.6% of dry eye cases were symptomatic, up to 47.2% of them may developed surface changes detectable by fluorescein dye test. Ethnicity (p=0.019) and diabetes mellitus (p=0.049) were significantly associated with dry eye. **Conclusion:** Dry eye could be subclinical but clinical tests in potential risk groups can lead to better detection of this condition and allow prescription of appropriate treatment for affected patients.

Keywords: Dry eye symptoms, Dry eye syndrome, Schirmer's test, Tear break-up time (TBUT), Fluorescein staining

INTRODUCTION

Dry eye is a disorder of the tear film due to deficient production or excessive evaporation leading to symptoms and potential damage to the ocular surface. Ocular symptoms such as discomfort, pain, irritation, redness and poor vision can result from dry eye. In severe cases, the patient's ocular and systemic health, general well-being, and quality of life may be affected.

Dry eye can be associated by a variety of factors. Results from a large epidemiological study indicated that the prevalence of symptomatic dry eye in the United States is about 7% in women and 4% in men over the age of 50 years (1). Meanwhile, dry eye prevalence was reported as 17.0% in China (2), 27.5% in Indonesia (3) and 29.2% in India (4). A few studies revealed dry eye were associated with age, cigarette smoking and pterygium (5, 6). Diabetes mellitus can also lead to dry eye through a variety of mechanisms (7). Other systemic diseases such as thyroid disease, rheumatoid arthritis, post-traumatic stress disorder and medications have been reported as risk factors of dry eye.

There seems to be a lack of correlation between the clinical tests and irritative symptoms in dry eyes. This discrepancy can be attributed to the multiple factors such as subjective nature of the disease, pain threshold and cognitive responses of respondents to questions of irritative symptoms. Furthermore, there is no single diagnostic test or certain combination of tests that can be reliably performed for the consistent diagnosis of dry eyes across different populations at different times (8). Nevertheless, more data on epidemiology of dry eyes is required in order to understand the impact of this condition on the ocular and general health of particular populations, including local population.

A few hospital- and population-based dry eye studies have been reported in Malaysia (9-11). Results of these studies noted that around 14.5% of the sample population had dry eye. However, different diagnostic criteria were applied in these studies of dry eye in different sets of population. We investigated dry eye among patients attending the ophthalmology clinic of a secondary referral hospital in Malaysia, determined by using Schirmer's test and compared it with subjective reporting of dry eyes symptoms through a questionnaire.

MATERIALS AND METHODS

Prior approval was obtained from the Medical Research Ethical Committee (MREC), Malaysia and the study was conducted in conformation to the Tenets of Declaration of Helsinki for research involving human subjects. This prospective cross sectional study was carried out from April to August 2014. Based on the reported incidence of dry eye, design of the study and the parameters investigated, a total of 160 patients were recruited into the study in order to obtain a study power of 80%, through systematic randomised sampling. Inclusion criteria were Malaysian patients above 30 years of age who attended the eye clinic and willing to give informed consent. Exclusion criteria included contact lens wearer, patients on topical medications,

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known case of dry eye or other ocular surface pathology such as conjunctivitis, pterygium, previous refractive surgery which could confound the symptoms of dry eye.

After obtaining informed consent from each respondent, the socio-demographic and past medical data was collected using a *proforma.* This was followed by administration of an interview-based questionnaire (Salisbury Eye Evaluation Questionnaire) adopted from a previous studies,(3, 12) which had a Cronbach's alpha value of 0.61. To minimise bias between interviewers and to ensure the questionnaire would be well-understood by the respondents, a pre-test was conducted by the interviewers prior the study. Respondents were asked to report on the frequency of dry eye symptoms which they had experienced over the previous three months. There were six symptoms investigated and for each symptom the respond could be either 'never', 'seldom', 'sometimes', 'often' or 'always'. A diagnosis of symptomatic respondent was made if they report any of the six symptoms accuring at least as 'often' .

Following the interview, clinical dry eye tests were conducted by two ophthalmologists who were masked to the respondents' socio-demography, medical history and dry eye symptoms. Topical anaesthesia was instilled before all tests were conducted. Tear break-up time (TBUT) test, in which the time between the last blink and the appearance of a random dry eye spot was measured and recorded, was conducted first in order to avoid interference from the other tests. Fluorescein staining of the cornea in the form of superficial punctuate keratopathy (SPK) was observed with a slit lamp with through cobalt blue filter and graded accordingly. For Schirmer's test, the length of the wetting of the test strip paper was measured and recorded at five minutes. These procedures were performed on both eyes and the average readings were taken for analysis.

Training was conducted for all observers involved in the interview and every clinical test before the commencement of data collection in order to standardise the protocols minimise the information and inter-observer biases. Statistical analysis was done using IBM SPSS 21.0 software for Windows. T-test was used to compare means of continuous data. Chi-square ($\lambda 2$) test was used to study the associations between socio-demography, medical history and dry eye symptoms with dry eye. The p value less than 0.05 was considered as statistically significant.

RESULTS

Socio-demography

There were 160 patients recruited but three patients decided not to participate leaving a total of 157 respondents, with response a rate of 98.1%. There were 75 males (47.8%) and 82 females (52.2%). The age was 59.3 ± 11.6 (mean ± standard deviation, SD) years old with the median age for males and female being 64.0 ± 14.0 (mean ± SD) years and 59.0 ± 20.0 (mean ± SD) years old, respectively. Majority of the respondents were Malay (n=77, 49.0%), followed by Chinese (n=57, 36.3%) and Indian (n=23, 14.6%). Most of the respondents attained secondary educational level (n=67, 42.7%), primary education level (n=51, 32.5%), tertiary education (n=28, 17.8%) while another 11 (7.0%) of them did not receive any formal education. With regard to occupation, 76 (48.4%) of the respondents were retiree, 66 (42.0%) respondents worked in low environmental exposure while 15 (9.6%) of them worked in high environmental exposure with excessive exposure to wind, dust, sand and sunlight (Table 1).

Dry eye symptoms

Regardless of the severity, the most commonly reported symptom was sensation of dryness (48.4%) in the eye while the most rarely reported was crusting of eyelashes (25.5%). Majority of the respondents reported 'never' for each of the symptom asked. A variable number of cases responded either 'sometimes', 'often' or 'always' to each of the symptom asked. The responses given by the respondents for each symptom are depicted in Figure 1.

Schirmer's test

The Shirmer's test was 13.26 ± 0.62 mm and 13.54 ± 0.58 mm (mean ± SD) in the right and left eye, respectively. The average Schirmer's test of both eyes were 13.38 ± 0.56 mm (mean ± SD). A patient was classified as a dry eye case when the average Shirmer's test result was less than 10 mm. Based on this criteria, 53 (33.8%) cases were classified as dry eyes.

Symptomatic dry eye

The proportion of the symptomatic dry eye was determined as described in the methodology. Among the dry eye cases (n=53), only 12 (22.6%) of them were found to be symptomatic.

TBUT test

Among the dry eye cases, TBUT test was performed to determine the evaporative component of the dry eye. Abnormal TBUT was detected in 15 (28.3%) cases. This rate was however not significantly higher than the TBUT abnormality among the non-dry eye cases (n=28, 26.9%, p = 0.855).

Fluorescein test

The fluorescein test was abnormal in 25 (47.2%) of dry eye cases, which was higher compared to the fluorescein abnormality rate among the non-dry eye cases (n= 36, 34.6%). However, these figures were not significant in difference (p=0.08). Figure 2 summarises the abnormality associated with dry eye.

Factors associated with dry eye

The socio-demographic profile and medical history data were examined to determine their associations with dry eye. The only factors found to be significantly associated with dry eyes were ethnicity (p=0.019) and diabetes mellitus (p=0.049). Symptoms of eye redness was albeit marginally, not significantly associated with dry eye (p=0.052). The statistical results of all the association factors investigated in this study is summarised in Table 2.

Table 1: The socio-demography and medical characteristics of the respondents.

Characteristics	**Mean ± SD**
Age (years)	59.3 ± 11.6
Schirmer's test	
Right eye (mm)	13.26 ± 0.62
Left eye (mm)	13.54 ± 0.58
Average (mm)	13.38 ± 0.56
TBUT test	
Right eye (s)	13.98 ± 0.52
Left eye (s)	13.48 ± 0.51
Average (s)	13.67 ± 0.48
	n (%)
Age group (N=157)	
Up to 40 years	11 (7.0)
41-50 years	26 (16.6)
51-60 years	40 (25.5)
61-70 years	47 (29.9)
above 70 years	33 (21.0)
Elderly status (N=157)	
Up to 60 years	77 (49.0)
Above 60 years	80 (51.0)
Education level (N=157)	
No formal education	11 (7.0)
Primary	51 (32.5)
Secondary	67 (42.7)
Tertiary	28 (17.8)
Occupation (N=157)	
Retiree	76 (48.4)
Occupation with low exposure to wind and sunlight	66 (42.0)
Occupation with high exposure to wind and sunlight	15 (9.6)
Diabetes mellitus (N=157)	
No	87 (55.4)
Yes	70 (44.6)
Rheumatoid arthritis (N=157)	
No	150 (95.5)
Yes	7 (4.5)
Thyrotoxicosis (N=157)	
No	149 (94.9)
Yes	8 (5.1)
Other systemic disease (N=157)	
No	142 (90.4)
Yes	15 (9.6)
Hypercholestrolaemia (N=157)	
No	131 (83.4)
Yes	26 (16.6)
Hypertension (N=157)	
No	100 (63.7)
Yes	57 (36.3)

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Characteristics	Mean ± SD
Smoker (N=157)	
No	133 (84.7)
Yes	24 (15.3)
Menopause status (N=82)	
No	27 (32.9)
Yes	55 (67.1)
Hormonal replacement therapy (N=55)	
No	52 (94.5)
Yes	3 (5.5)

*Occupation with lower environmental exposure to excessive wind and sunlight included housewife, office staff, clerk, business man, lawyer, doctor, teacher/lecturer and facility manager.
¥Occupation with high environmental exposure to excessive wind and sunlight included driver, mechanic, welder, security guard and construction site worker.

Table 2: The association between socio-demography and medical characteristics with dry eye.

Association factors	Dry eyes, n (%)		Λ2	p
	Yes	No		
Gender			0.12	0.914
Male	25 (33.3)	50 (66.7)		
Female	28 (34.1)	54 (65.9)		
Age group			5.85	0.210
Up to 40 years	6 (54.5)	5 (45.5)		
41-50 years	8 (30.8)	18 (69.2)		
51-60 years	17 (42.5)	23 (57.5)		
61-70 years	11 (23.4)	36 (76.6)		
above 70 years	11 (33.3)	22 (66.7)		
Elderly status			2.857	0.091
Up to 60 years	31 (40.3)	46 (59.7)		
Above 60 years	22 (27.5)	58 (72.5)		
Ethnicity			7.961	0.019
Malay	31 (40.3)	46 (59.7)		
Chinese	20 (35.1)	37 (64.9)		
Indian	2 (8.7)	21 (91.3)		
Education level			4.217	0.239
No formal education	2 (18.2)	9 (81.8)		
Primary	16 (31.4)	35 (68.6)		
Secondary	28 (41.8)	39 (58.2)		
Tertiary	7 (25.0)	21 (75.0)		
Occupation			0.219	0.896
Retiree	27 (35.5)	49 (64.5)		
Occupation with low exposure to wind and sunlight	21 (31.8)	45 (68.2)		
Occupation with high exposure to wind and sunlight	5 (33.3)	10 (66.7)		
Diabetes mellitus			3.324	0.049
No	24 (27.6)	63 (72.4)		
Yes	29 (41.4)	41(58.6)		
Rheumatoid arthritis			0.271	0.439
No	50 (33.3)	100 (66.7)		
Yes	3 (42.9)	4 (57.1)		

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Association factors	Dry eyes, n (%)		Λ2	p
	Yes	No		
Thyrotoxicosis			0.994	0.319
No	49 (32.9)	100 (67.1)		
Yes	4 (50.0)	4 (50.0)		
Other systemic disease			1.236	0.266
No	46 (32.4)	96 (67.6)		
Yes	7 (46.7)	8 (53.3)		
Hypercholestrolaemia			2.941	0.086
No	48 (36.6)	83 (63.4)		
Yes	5 (19.2)	21 (80.8)		
Hypertension			0.190	0.663
No	35 (35.0)	65 (65.0)		
Yes	18 (31.6)	39 (68.4)		
Smoker			0.267	0.605
No	46 (34.6)	87 (65.4)		
Yes	7 (29.2)	17 (70.8)		
Menopause status			2.545	0.111
No	6 (22.2)	21 (77.8)		
Yes	22 (40.0)	33 (60.0)		
Hormonal replacement therapy			0.059	0.808
No	21 (40.4)	31 (59.6)		
Yes	1 (33.3)	2 (66.7.3)		

*Occupation with lower environmental exposure to excessive wind and sunlight included housewife, office staff, clerk, business man, lawyer, doctor, teacher/lecturer and facility manager.
ϒOccupation with high environmental exposure to excessive wind and sunlight included driver, mechanic, welder, security guard and construction site worker.

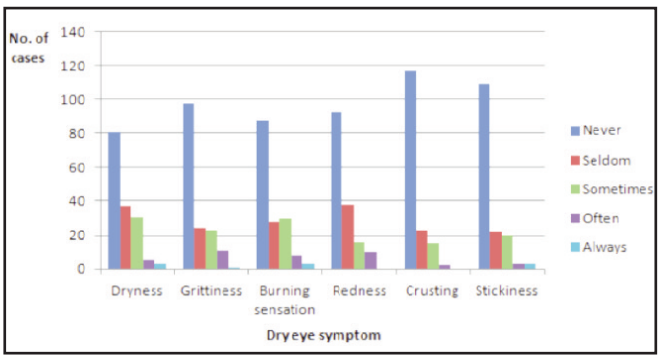

Figure 1: Histogram showing the responses regarding the presence and frequency of dry eye symptoms among the cases.

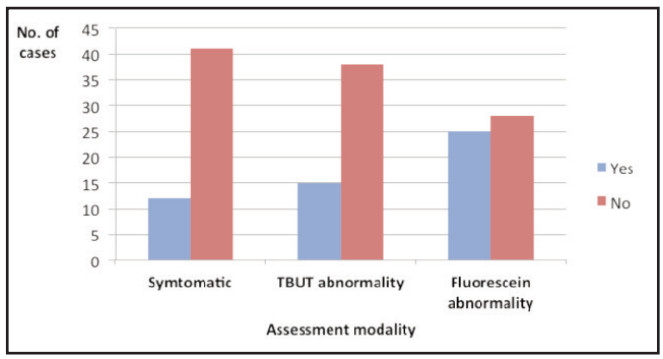

Figure 2: Histogram showing the cases with abnormality of different assessments among the Shirmer's test-proven dry eye (TBUT, tear break-up time).

DISCUSSION

The proportion of dry eye, determined by the average Schirmer's test of both eyes of less than 10 mm, in this study was 33.8%. This rate was in line with the rates between 5.5% and 34.0% reported in other studies (1, 11, 13-18). What caused the wide range in dry eye prevalence stems mainly from the different definition of dry eye, lack of consensus of the cut-off value of the various objective tests and different study population in different studies. With regards to hospital-based studies on the dry eye, the prevalence reported was from 14.5% to 34.0% (19-21), whereas, our dry eye prevalence of 33.8% was among the highest.

Against the Schirmer's test result, the questionnaire was calculated to have a sensitivity of 22.64% (95% confidence interval, CI = 12.28% to 36.21%) and a specificity of 74.04% (95% CI = 64.52 to 82.14%). The questionnaire's positive predictive value was 30.77% (95% CI = 17.02 to 47.57%) while the negative predictive value was 65.25% (95% CI = 73.78%). These findings underlined the fact that the historical data from

the questionnaire alone has low capability to diagnosed dry eye with reliable accuracy. They also reflect on the existence of various dry eyes questionnaires and any one should not be used solely as a clinical diagnostic tool (8).

In the association part of the study, it was revealed that only ethnicity was statistically significantly associated with the dry eye (p=0.019). Dry eye was shown to be most prevalent among Malay (40.3%) patients, followed by Chinese (35.1%) and Indian (8.7%). This was in contrast to a previously reported local study (11) which showed higher prevalence of dry eye in Chinese ethnicity. Dry eye association with ethnicity was also reported by Schaumberg et al who reported higher prevalence among the Hispanics and Asian women when compared to that of the Caucasians (1). In contrast, there was no association found between dry eye prevalence and ethnicity among males (22). The inconsistent and contrasting relation between dry eye and ethnicity is not fully understood and deservingly warrant further study.

Several large scale epidemiological studies had reported that prevalence of dry eye increased with age and age was shown to be a significant association for dry eye (1, 3, 15, 18, 23). This could be explained by the fact that older patients are prone to have reduction in tear production, tear film instability and increased prevalence of meibomian gland anomalies (24). Furthermore, older age group was also associated with higher frequency of medical illnesses such as the diabetes, hypertension and hypercholesterolaemia, and the post-menopausal status in women. However, age group (p=0.210) and elderly status (p=0.091) were not significantly associated with dry eye in this study.

In this study, gender was not a significant association of dry eyes (p=0.914). This was in agreement with a previously reported local study (11). Nevertheless, a few studies had shown the prevalence of dry eyes was higher in female compared to male gender (15, 18, 19, 23). Androgen regulates meibomian gland function, improves the quality and/or quantity of lipids produced by this tissue, and promotes the formation of the tear film's lipid layer.(25) Reduction in androgen contributes to an increased in dry eye was supported by increased prevalence of dry eye in female and older patient.

Dry eye was more likely occurring among respondents with lower education (21) and those with occupation with high environmental exposure. The higher likelihood of respondents with lower education level to engage in excessive exposure occupation might be the explanation for these findings. However, there were no significant associations found between highest education level and type of occupation with dry eye in our study. The small sample size could be the reason that contributed to the absence of significant association between education level and occupation with dry eye.

Diabetic cases had a significantly higher prevalence of dry eye compared to non-diabetic cases. Among the diabetics, the TBUT and Schirmer's tests were test significantly lower in those with history longer than 10 years (26). Moss et al. reported that systemic diseases such as diabetes mellitus, rheumatoid arthritis and thyroid disease were associated with dry eye (27). Cigarette smoking was reported to be significantly associated with dry eye in the Riau Eye Study (3) and the Beaver Dam Eye Study (13). However, except for diabetes mellitus, the other factors mentioned did not show statistically significant associations with dry eye in this study, believed due to the small sample size.

Menopause status and postmenopausal hormonal replacement therapy were found not significantly associated with dry eye in our study. However, a few studies have suggested that sex hormones could affect the secretion of tears and meibomian gland function (28-30). Lin et al. reported that women taking sex hormones tend to have a higher rate of dry eye symptoms.(31) Contrary to this, Din et al. reported that post-menopausal women on HRT had lower prevalence of dry eye compared to post-menopausal women not on HRT regime. These conflicting results could be due to the different types of HRT regime consumed and the variable degree of dry eye severity in the post-menopausal elderly female population.

The cross sectional design of this study precluded us from explaining the temporal sequence of events between associated factors and dry eye. Since this was a hospital-based study, the result cannot be extrapolated to, and therefore may not represent the general population. There was also non-respond bias when sampled respondents refused to be assessed on dry eye symptoms and signs. Time constrain had limited the sample size. Because of this limitation, we did not find significant associations of dry eye with several factors that have been reported previously such as age, gender, occupation, menopause status and postmenopausal oestrogen therapy.

CONCLUSION

In conclusion, Shirmer's test revealed 33.8% of cases had dry eye and 28.3% of them were of the evaporative type. Female Malays in their sixties were more likely to develop dry eye. Majority of the dry eye cases were asymptomatic but up to 47.2% of them may developed surface changes detectable by fluorescein dye test. Apart from ethnicity and diabetes, no other socio-demographic or medical factor was significantly associated with dry eye. In certain likely groups, Shirmer's test is recommended to detect evaporative dry eyes. A larger population base study is recommended to precisely elicit the magnitude and associations of dry eye in Malaysia.

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REFERENCES

1. Schaumberg DA, Sullivan DA, Buring JE, Dana MR. Prevalence of dry eye syndrome among US women. Am J Ophthalmol. 2003;136(2):318-26.
2. Liu NN, Liu L, Li J, Sun YZ. Prevalence of and risk factors for dry eye symptom in mainland china: a systematic review and meta-analysis. J Ophthalmol. 2014; 2014: 748654. doi(2014 Oct 15):10.1155/2014/748654.
3. Lee AJ, Lee J, Saw SM, Gazzard G, Koh D, Widjaja D, *et al.* Prevalence and risk factors associated with dry eye symptoms: a population based study in Indonesia. Br J Ophthalmol. 2002;86(12):1347-51.
4. Gupta N, Prasad I, Jain R, D'Souza P. Estimating the prevalence of dry eye among Indian patients attending a tertiary ophthalmology clinic. Ann Trop Med Parasitol. (10):2010 Apr;104(3):247-55.
5. Galor A, Feuer W, Lee DJ, Florez H, Carter D, Pouyeh B, *et al.* Prevalence and risk factors of dry eye syndrome in a United States veterans affairs population. Am J Ophthalmol. (10):2011 Sep;152(3):377-384.e2.
6. Uchino M, Nishiwaki Y, Michikawa T, Shirakawa K, Kuwahara E, Yamada M, *et al.* Prevalence and risk factors of dry eye disease in Japan: Koumi study. Ophthalmology. 2011 Dec; 118(12):2361-7. doi(2011 Sep 1): 10.1016/j.ophtha.2011.05.029.
7. Alves Mde C, Carvalheira JB, Modulo CM, Rocha EM. Tear film and ocular surface changes in diabetes mellitus. Arq Bras Oftalmol. 2008;71(6 Suppl):96-103.
8. The Epidemiology of Dry Eye Disease: Report of the Epidemiology Subcommittee of the International Dry Eye WorkShop (2007). The Ocular Surface. 5(2):93-107.
9. Mohd-Ali B, Fee LS, Abdul-Mutalib H, Mohidin N. Incidence of dry eye in a sample population in Kuala Lumpur. International Journal of Collaborative Research on Internal Medicine and Public Health. [Article]. 2011;3(11):839-45.
10. Din NM, Sa'aid SHB, Shen LC, Shu YS, Rahman MBA, Azmi ABM, et al. Hormone Replacement Therapy and Dry Eye in Post Menopausal Women: Study in a Tertiary Centre in Malaysia 2013.
11. Jamaliah R, Fathilah J. Prevalence of dry eye in University Malaya Medical Centre. Med J Malaysia. 2002;57(4):390-7.
12. Schein OD, Munoz B, Tielsch JM, Bandeen-Roche K, West S. Prevalence of dry eye among the elderly. Am J Ophthalmol. 1997;124(6):723-8.
13. Moss SE, Klein R, Klein BE. Prevalence of and risk factors for dry eye syndrome. Arch Ophthalmol. 2000;118(9):1264-8.
14. Paulsen AJ, Cruickshanks KJ, Fischer ME, Huang GH, Klein BE, Klein R, *et al.* Dry eye in the beaver dam offspring study: prevalence, risk factors, and health-related quality of life. Am J Ophthalmol. 2014 Apr;157(4):799-806. doi(2014 Jan 2):10.1016/j.ajo.2013.12.023.
15. Chia EM, Mitchell P, Rochtchina E, Lee AJ, Maroun R, Wang JJ. Prevalence and associations of dry eye syndrome in an older population: the Blue Mountains Eye Study. Clinical and Experimental Ophthalmology. 2003;31(3):229-32.
16. Uchino M, Nishiwaki Y, Michikawa T, Shirakawa K, Kuwahara E, Yamada M, *et al.* Prevalence and risk factors of dry eye disease in Japan: Koumi study. Ophthalmology. 2011;2011 Dec; 118(12):2361-7. doi(2011 Sep 1):10.1016/j.ophtha.2011.05.029.
17. Uchino Y, Uchino M, Dogru M, Ward S, Yokoi N, Tsubota K. Changes in dry eye diagnostic status following implementation of revised Japanese dry eye diagnostic criteria. Jpn J Ophthalmol. 2012;2012 Jan; 56(1): 8-13. doi(2011 Nov 15):10.1007/s10384-011-0099-y.
18. Jie Y, Xu L, Wu YY, Jonas JB. Prevalence of dry eye among adult Chinese in the Beijing Eye Study. Eye (Lond).2009 Mar;23(3):688-93. doi(2008 Feb 29): 10.1038/sj.eye.6703101.
19. Sahai A, Malik P. Dry eye: prevalence and attributable risk factors in a hospital-based population. Indian J Ophthalmol. 2005;53(2):87-91.
20. Lekhanont K, Rojanaporn D, Chuck RS, Vongthongsri A. Prevalence of dry eye in Bangkok, Thailand. Cornea. 2006;25(10):1162-7.
21. Onwubiko SN, Eze BI, Udeh NN, Arinze OC, Onwasigwe EN, Umeh RE. Dry eye disease: prevalence, distribution and determinants in a hospital-based population. Cont Lens Anterior Eye.2014 Jun;37(3): 157-61. doi(2013 Oct 11):10.1016/j.clae.2013.09.009.
22. Schaumberg DA, Dana R, Buring JE, Sullivan DA. Prevalence of Dry Eye Disease among US Men: Estimates from the Physicians' Health Studies. Arch Ophthalmol. 2009;127(6):763-8.
23. McCarty CA, Bansal AK, Livingston PM, Stanislavsky YL, Taylor HR. The epidemiology of dry eye in Melbourne, Australia. Ophthalmology. 1998;105(6):1114-9.
24. Sharma A, Hindman HB. Aging: A Predisposition to Dry Eyes. Journal of Ophthalmology. 2014;2014:8.
25. Sullivan DA, Sullivan BD, Evans JE, Schirra F, Yamagami H, Liu M, et al. Androgen Deficiency, Meibomian Gland Dysfunction, and Evaporative Dry Eye. Ann N Y Acad Sci. 2002;966(1):211-22.
26. Akinci A, Cetinkaya E, Aycan Z. Dry eye syndrome in diabetic children. Eur J Ophthalmol. 2007;17(6):873-8.
27. Moss SE, Klein R, Klein BE. Incidence of dry eye in an older population. Arch Ophthalmol. 2004;122(3):369-73.
28. Mathers WD, Stovall D, Lane JA, Zimmerman MB, Johnson S. Menopause and tear function: the influence of prolactin and sex hormones on human tear production. Cornea. 1998;17(4):353-8.
29. Krenzer KL, Dana MR, Ullman MD, Cermak JM, Tolls DB, Evans JE, et al. Effect of androgen deficiency on the human meibomian gland and ocular surface. J Clin Endocrinol Metab. 2000;85(12):4874-82.
30. Connor CG, Flockencier LL, Hall CW. The influence of gender on the ocular surface. J Am Optom Assoc. 1999;70(3):182-6.
31. Lin PY, Tsai SY, Cheng CY, Liu JH, Chou P, Hsu WM. Prevalence of dry eye among an elderly Chinese population in Taiwan: the Shihpai Eye Study. Ophthalmology. 2003;110(6):1096-101.