



Original research

Association between dry eye symptoms and signs

Samuel Kyei^{a,*}, Selassie Kojo Dzasimatu^a, Kofi Asiedu^b, Patience Ansomah Ayerakwah^a

^a Department of Optometry and Vision Science, School of Allied Health Sciences, College of Health and Allied Sciences, University of Cape Coast, Cape Coast, Ghana

^b Eye Clinic, Twumasiwaa Medical Center ARS Junction East Legon, Accra, Ghana

Received 16 October 2017; revised 9 May 2018; accepted 15 May 2018

Available online 28 June 2018

Abstract

Purpose: To evaluate the association between subjective dry eye symptoms and the results of the clinical examinations.

Methods: The study was a clinical-based survey involving 215 first-year students selected consecutively during a regular ocular health examination at the University of Cape Coast Optometry Clinic. The data collection process spanned for a period of four months. Out of the 215 students, 212 returned their completed questionnaires and were subsequently included in the study. Dry eye tests including meibomian gland assessment, tear break up time, fluorescein staining, Schirmer test, and blink rate assessment, were performed on each subject after completion of the Ocular Surface Disease Index (OSDI) questionnaire. Shapiro–Wilk test was used to determine the normality of the clinical tests, and Spearman's correlations co-efficient was used to determine the correlations between the clinical test results and dry eye symptoms.

Results: Statistically significant associations were found between OSDI scores and blink rate ($r_s = 0.140$; $P < 0.042$), and associations between OSDI scores and contrast sensitivity scores ($r_s = 0.263$; $P < 0.001$). However, the results of corneal staining ($r_s = -0.006$; $P < 0.926$), Schirmer test ($r_s = -0.033$; $P = 0.628$), tear break up time ($r_s = -0.121$; $P < 0.078$), meibomian gland expressibility ($r_s = 0.093$; $P < 0.180$), and meibomian gland quality ($r_s = 0.080$; $P < 0.244$) showed no significant association with OSDI. The correlation coefficients range from -0.006 to 0.263 showed low to moderate correlation between dry eye symptoms and the results of clinical test.

Conclusion: Associations between dry eye symptoms and clinical examinations are low and inconsistent, which may have implications for the diagnoses and treatment of dry eye disease.

Copyright © 2018, Iranian Society of Ophthalmology. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Keywords: Dry eye; Meibomian gland; Tear break up time; Schirmer test; Contrast sensitivity; Blink rate

Introduction

Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by an increase in tear film osmolarity and ocular surface inflammation.^{1,2}

It is estimated that approximately 3.2 million females and 1.7 million males of age fifty years (50) and older to have dry eye disease in America.³ In Nigeria, the prevalence of dry eye disease was found to be 19.2% and significantly associated with age.⁴ In Ghana, the prevalence of symptomatic dry eye among Ghanaian undergraduate students was found to be 44.3%.⁵ Available data on the cases of dry eye medication has been on the rise from 1.22 million people in 1991 to 1.98 million people in 1998 representing an increase of approximately 57.4% within this period.⁶ Furthermore, the situation is not different today, and cases of dry eye disease are on the rise.⁷ This upsurge in dry eye cases has thus made it a point of concern for researchers.

According to the International Dry Eye WorkShop (DEWS) Report,¹ a major stumbling block in the diagnosis of dry eye

Funding: The authors had no funding from any internal or external sources, but it was self-funded by the authors.

Conflict of interest: The authors declare no known conflict of interest.

* Corresponding author.

E-mail address: skyei@ucc.edu.gh (S. Kyei).

Peer review under responsibility of the Iranian Society of Ophthalmology.

disease has been the reported lack of association between the ocular symptoms experienced by patients and the results of selected clinical tests for dry eye. The most common ocular symptoms of dry eye are feelings of dryness, grittiness or foreign body sensation, and burning sensation. Other reported cases of dry eye have had symptomatology of stringy discharge, transient blurring of vision, redness, and crusting of lids.⁸ Dry eye tests are meant to confirm and quantify the diagnosis of dry eye. The reliability of these tests proves the disease and its severity.⁸ However, studies on the association between dry eye symptoms and dry eye clinical test have been equivocal as some found no correlations between dry eye symptoms and test results,⁹ and others found insignificant correlations between dry eye symptoms and the results of clinical test.¹⁰ All the studies on this subject as reviewed by Bartlett et al. have been done in USA/Canada, South America, Europe, Asia, and jointly in USA/Europe. The other studies involving Africans were conducted in Nigeria, and findings from these previous studies remain conflicting and were conducted in the older generation.^{3,11–15} This study sought to assess the association between dry eye symptoms and clinical examinations among a young African clinical sample.

Methods

This study was a clinic-based survey. Questionnaires were handed out to consecutive participants to retrieve information on dry symptoms and dry eye symptom severity. These symptoms were verified by the performance of dry eye tests. This study involved first-year students of the University of Cape Coast. Subjects were included in the study if they were capable of completing the questionnaires, were non-contact lens wearers, and were previously not on any dry eye medication. Consent was obtained from all of the participants before the commencement of the study. The study was approved by the Institutional Review Board of the University of Cape Coast with ethical clearance number UCCIRB/CHAS/2017/04.

The data collection process was performed in two major phases. The first process involved provision of questionnaires to the study participants to be completed and returned on an agreed date. The Ocular Surface Disease Index (OSDI) was used in this study.¹⁶

Phase two involved the performance of dry eye tests on the participants who had completed the questionnaires, to confirm or not the existence of dry eye. This stage was solely done in the clinic. These tests were non-invasive examinations causing no harm to the participants. The examination involved the performance of six dry eye assessment techniques on each patient.

Participants were asked to read the letters from the visual acuity chart within a period of 60 s. The number of blinks within this period was then noted either by observation or by video recording. In order to eliminate the effect of visual crowding, the logMAR chart was used in addition to the benefit of providing enough lettering to be read off during the stipulated time frame. All refractive errors were corrected before the reading of the letters.

Contrast sensitivity of the participants was determined using the Macushield contrast sensitivity chart (MacuVision Europe Limited, UK). The chart contained different shapes of different contrasts, and participants were asked to identify the faintest of the shapes. Each of the shapes had a label attached which was used to determine the contrast sensitivity of the participant (1–3 poor, 4–6 moderate, and 7–10 normal).

The tip of a wetted (with a single drop of normal saline) fluorescein strip was gently applied into the inferior cul-de-sac. The time from normal blinking to the first occurrence of a dark spot in the tear film was determined using a stopwatch as the timer. The test was repeated three times, and the average of the three measurements was recorded as the break up time.

Following the measured tear break up time, corneal staining was graded using the Modified Oxford Grading Scales (0-absent i.e. no staining; 1- minimal i.e. dot count per sector of up to 10; 2- mild i.e. dot count per sector up to 32; 3- moderate i.e. dot count per sector up to 100; 4- marked i.e. dot count per sector up to 316; 5- severe i.e. count per sector greater than 316) under cobalt blue filter.

Meibomian gland expressibility was done by applying the required pressure using the lid expresser. The central 8 glands of the lower lid and the number of glands yielding lipid secretion were observed under the slit-lamp biomicroscope and graded as follows: (0) all glands expressible (normal), (1) 3–4 glands expressible, (2) 1–2 glands expressible, and (3) no glands expressible.¹⁷

The quality of expressed oil was considered for clarity and viscosity, and graded as follows: (0) clear (normal), (1) cloudy, (2) cloudy with particles, and (3) inspissated (gel-like). The highest score for any of the expressed glands was designated as the quality score.¹⁷

OSDI was used to diagnose dry eye symptomatology. The OSDI is a proficient means of diagnosing dry eye symptomatology based on the subject responses. Each response is then scored on a scale, summing up to an OSDI score ranging from 0 to 100. The twelve questions on the OSDI questionnaire were scored on a scale of 0–4: (0) none of the time, (1) some of the time, (2) half of the time, (3) most of the time, and (4) all of the time. The total OSDI score was computed for each subject based on the formula: the sum of scores of all items answered multiplied by twenty-five divided by the total number of items answered.¹⁶

All analyses were performed using the SPSS 21 statistical package. For 95% confidence level, $P < 0.05$ was considered statistically significant. The mean values of the clinical test scores were also determined. Shapiro–Wilk test was used to determine the normality of the clinical tests, and Spearman's correlations co-efficient (r_s) was used to determine the correlations between the clinical test results and dry eye symptoms.

Results

Out of the 215 first-year students who accepted the questionnaires, 212 successfully completed and returned the questionnaires. All 212 (100%) indicated their gender; 107 (50.5%) were female, and 105 (49.5%) were male. The

mean age \pm standard deviation was 22.5455 ± 6.599 . The mean age of the females and males was 22.16 ± 4.93 and 21.7 ± 2.884 , respectively. All 212 had their eyes tested clinically for dry eye (Table 1). The OSDI scores were then compared to the results from the clinical tests performed. The mean OSDI score from Table 1 shows that on average, the 212 participants had mild to moderate dry eye disease (if the classification is based on patient symptomatology without the performance of the clinical tests). The mean blink rate of the participants (9.171 ± 6.5076) was lower than the normal blink rate of 10 blinks per minute (Table 1). The mean tear break up time (6.774 ± 2.514) was also lower than the expected 10 s.⁸ The mean Schirmer test results [19.364 ± 11.550]; was within the expected normal range of 10 mm–35 mm and the mean contrast sensitivity scores (8.594 ± 1.685) were also within the high contrast sensitivity range of 7–10 using the Macus Shield contrast sensitivity chart. Finally, the corneal staining test results (using the Oxford grading scale) showed that most of the participants had the dry eye disease (4.995 ± 2.780).

Table 2 also describes the relationship between the clinical test results and the OSDI scores of the subjects. The Spearman's correlation coefficient, (r_s) describes the correlation between the clinical test results and the OSDI scores. The negative correlation coefficient describes a negative correlation between clinical test results and the OSDI scores. This was observed in relationships between tear break up time, Schirmer test, and Oxford grading scale. This negative correlation between tear break up time and the OSDI scores meant that whilst the tear break up time results increased or became better, the OSDI scores decreased or showed less dry eye symptoms. The correlation coefficient between Schirmer test results and the OSDI scores meant that while the Schirmer test results increased or became better, the OSDI scores decreased or revealed fewer symptoms.

Positive correlation coefficients were observed for the other clinical tests other than the above two. The positive correlation coefficients meant that as the results from the clinical tests increased, the OSDI scores also increased, and signifying dry eye symptomatology.

Statistical significance was obtained for only two (Blink rate and contrast sensitivity), out of the seven clinical tests performed.

Table 1
Summary of clinical tests and Ocular Surface Disease Index (OSDI) scores.

	N	Mean	Standard deviation (SD)	Range
Age of subject	211	21.88	3.77	17–35
The blink rate of participant	211	9.17	6.51	1–33
Tear break up time	212	6.77	2.51	1–21
Schirmer test	212	19.36	11.55	1–35
Contrast sensitivity	212	8.59	1.68	0–10
Meibum quality	211	0.92	3.08	0–24
Meibum expressibility	212	0.37	0.89	0–3
Oxford grading scale	212	4.99	2.78	0–12
OSDI score	212	59.62	21.8	0–100

OSDI: Ocular Surface Disease Index.

Table 2
Relationship between clinical test results and Ocular Surface Disease Index (OSDI) scores.

	N	r_s	P-value	Significance
Oxford grading scale	212	−0.006	0.926	No Sig
Schirmer test	212	−0.036	0.628	No Sig
Tear break up time	212	−0.121	0.078	No Sig
Blink rate	211	−0.140	0.042	Sig
Meibum expressibility	211	0.093	0.180	No Sig
Meibum quality	212	−0.080	0.244	No Sig
Contrast sensitivity	212	−0.263	0.001	Sig
OSDI scores	212	1.000		

Correlation is significant at 0.05 level (2-tailed). Sig: Significance, No Sig: No significance, N = Total number of participants, OSDI: Ocular Surface Disease Index.

Discussion

To the best of our knowledge, studies on the associations between dry eye clinical test results and dry eye symptoms among a youthful population are non-existent in Ghana and Africa at large. The various dry eye clinical tests are less than perfect in the diagnoses of dry eye.¹⁸ Clinician's inability to sufficiently link dry eye symptoms with dry eye clinical results has been the reason for the difficulties in diagnosing dry eye.¹ Bartlett et al. reviewed the literature on the association between dry eye symptoms and signs and found low to moderate correlation.¹⁹ The difference between Bartlett's findings and this study was that, unlike Bartlett's review that rather compared results from 75 other studies, this study was conducted independently among a youthful population and obtained a low correlation between signs and symptoms of dry eye. A poor correlation was also observed between some of the dry eye test results and the symptoms. This was consistent with the results obtained by Nichols et al.¹⁰ However, unlike Nichol et al. who rather utilized 75 participants, this study used 212 participants. This study also had an entry criterion before the clinical tests were performed, unlike Nichol's study. The majority of studies have observed no significant correlations between dry eye tests and dry eye symptoms.¹⁰ This study had only two significant correlations between the dry eye signs and symptoms. Dry eye patients spend more time with their eyes closed than normal patients.²⁰ Blink rate was significantly related to the OSDI scores of the subjects. The correlation coefficient meant that as the blink rate scores increased the OSDI scores of the participants also decreased. In other words, low blink rates meant more susceptibility to dry eye symptoms. This finding was not consistent with several studies on the association between blink rate and dry eye symptoms.²¹

In dry eye, low contrast sensitivity will result from a central superficial punctate keratitis (SPK).²² This implies that severe states of dry eye will cause a reduction in contrast sensitivity.²² Most dry eye patients will achieve a better corrected visual function²³; however, low visual function may be difficult to ascertain using conventional visual acuity methods, hence the need for contrast sensitivity tests.²² The results obtained revealed a significant correlation between the contrast

sensitivity scores of the subjects and the OSDI scores. The correlation coefficient also revealed that the contrast sensitivity scores were negatively correlated with the OSDI scores. This meant that as the contrast sensitivity scores increased, the OSDI scores also decreased. This was consistent with the findings of Koh et al.²²

As there is no gold standard in diagnosing dry eye,²⁴ Oxford grading scores are appropriate for as a reference values for dry eye severity.¹ There was no significant correlation between the Oxford grading scale scores and the OSDI scores. The results obtained meant that as the patient's dry eye symptoms improve, the Oxford grading scale provided results show that the condition was worsening but this correlation was not statistically significant. This finding was inconsistent with other findings which suggested the use of corneal staining in detecting dry eye severity.²⁵

The Schirmer test is the most commonly used test to evaluate aqueous tear production.²⁶ The results obtained from the Schirmer test results reveal that there is no association between Schirmer test results and the OSDI scores this is consistent with findings of by Onwubiko and colleagues.¹³ However, the Spearman's correlation coefficient interprets a relationship whereby as the Schirmer test results increases or becomes better, the OSDI scores of the patient also become better.¹

An unstable tear film is the most common sign of dry eye proven by tear break up time being the most common dry eye test performed in the clinic.²⁷ There was no significant relationship between tear break up time and the OSDI scores. However, the correlation coefficient revealed that as the scores from the tear break up time increased or improved, the results from the OSDI scores also decreased or became better. This was consistent with several studies assessing the role of tear break up time in diagnosing dry eye.²⁸

Meibomian gland dysfunction is clinically significant in the diagnoses of dry eye.⁷ Meibum quality scores and meibomian gland secretion scores were not significantly correlated to OSDI scores. The Meibum quality and OSDI scores were positively correlated, in that as the Meibum quality scores increased, the OSDI scores also increased. This meant that as the Meibum quality of the participants worsened, the symptoms of a dry eye also worsened.²⁹ Meibum expressibility and OSDI scores were positively correlated. What it meant was that as the Meibum expressibility scores increased, the OSDI scores also increased. In summary, this study shows that there is a low and inconsistent association between dry eye symptoms and dry eye clinical tests among a youthful clinical sample, this implies that utilizing clinical tests alone in the diagnosis of dry may be problematic. Therefore, diagnosis of a dry eye should be focused on symptoms assessment along with the clinical test results.

Acknowledgment

The authors are grateful to Francisca Akpene for proof-reading the manuscript.

References

1. The epidemiology of dry eye disease: report of the epidemiology subcommittee of the international dry eye workshop. *Ocul Surf.* 2017;5(2): 119–205.
2. The definition and classification of dry eye disease: report of the definition and classification subcommittee of the international dry eye workshop (DEWS). *Ocul Surf.* 2007;5(2):75–92.
3. Schein OD, Hochberg MC, Muñoz B, et al. Dry eye and dry mouth in the elderly: a population-based assessment. *Arch Intern Med.* 1999;159(12): 1359–1363.
4. Onwubiko SN, Eze BI, Udeh NN, Arinze OC, Onwasigwe EN, Umeh RE. Dry eye disease, prevalence, distribution and determinants in a hospital based population. *Contact Lens Anterior Eye.* 2014;37(3):157–161.
5. Asiedu K, Kyei S, Boampong F, Ocansey S. Symptomatic dry eye and its associated factors: a study of university undergraduate students in Ghana. *Eye Contact Lens.* 2017;43(4):262–266.
6. Ellwein LB, Urato C. Use of eye care and associated charges among the medicare population: 1991–1998. *Arch Ophthalmol.* 2002;120(6): 804–811.
7. Miljanovic B, Dana MR, Sullivan DA, Schaumberg DA. Prevalence and risk factors for dry eye syndrome among older men in the United States. *Investig Ophthalmol Vis Sci.* 2007;48(13):4293.
8. Kanski J, Bowling B. *Clinical Ophthalmology. A Systemic Approach.* 7th ed. Elsevier Saunders; 2011.
9. Begley CG, Chalmers RL, Abetz L, et al. The relationship between habitual patient-reported symptoms and clinical signs among patients with dry eye of varying severity. *Investig Ophthalmol Vis Sci.* 2003;44(11): 4753–4761.
10. Nichols KK, Nichols JJ, Mitchell GJ. The lack of association between signs and symptoms in patients with dry eye disease. *Cornea.* 2004;23(8): 762–770.
11. Bekibele C, Baiyeroju A, Ajaiyeoba A, Akang E, Ajayi B. Tear function and abnormalities of ocular surface: relationship with subjective symptoms of dry eye in Ibadan, Nigeria. *Middle East Afr J Ophthalmol.* 2008; 15(1):12–15.
12. Bekibele CO, Baiyeroju AM, Ajaiyeoba A, Akang EE, Ajayi BG. Case control study of dry eye and related ocular surface abnormalities in Ibadan, Nigeria. *Int Ophthalmol.* 2010;30(1):7–13.
13. Onwubiko SN, Eze BI, Udeh NN, Onwasigwe EN, Umeh RE. Dry eye disease: concordance between the diagnostic tests in African. *Eye Contact Lens.* 2016;42(6):395–400.
14. Schein O, Muñoz B, Tielsch JM, Bandeen-Roche K, West S. Prevalence of dry eye among the elderly. *Am J Ophthalmol.* 1997;124(6):723–728.
15. 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):1096–1101.
16. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the ocular surface disease. *Arch Ophthalmol.* 2000;118(5):615–621.
17. Tomlinson A, Bron AJ, Korb DR, Amano S, Paugh JR, Pearce EI. The international workshop on meibomian gland dysfunction: report of the diagnosis subcommittee. *Investig Ophthalmol Vis Sci.* 2011;52(4): 2006–2049.
18. Savini G, Prabhawat P, Kojima T, Grueterich M, Espana E, Goto E. Challenge of dry eye diagnosis. *Clin Ophthalmol.* 2008;2(1):31–55.
19. Bartlett JD, Keith MS, Sudharshan L, Snedecor SJ. Association between signs and symptoms of dry eye: a systemic review. *Clin Ophthalmol.* 2015;9:1719–1730.
20. Ousler 3rd GW, Abelson MB, Johnston PR, Rodriguez J, Lane K, Smith LM. Blink patterns and lid contact times in dry eye and normal patients. *Clin Ophthalmol.* 2014;8:869–874.
21. Lee SY, Tong L. Lipid-containing lubricants for dry eye: a systematic review. *Optom Vis Sci.* 2012;89(11):1654–1661.
22. Koh S, Maeda N, Ikeda C, et al. The effect of ocular surface regularity on contrast sensitivity and straylight in dry eye. *Investig Ophthalmol Vis Sci.* 2017;58(5):2647–2651.

23. Goto E, Yagi Y, Matsumoto N. Impaired functional visual acuity of dry eye patients. *Am J Ophthalmol*. 2002;133(2):181–186.
24. Sullivan BD, Whitmer D, Nichols KK, et al. An objective approach to dry eye disease severity. *Investig Ophthalmol Vis Sci*. 2010;51(12):6125–6130.
25. 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. *Clin Exp Ophthalmol*. 2003;31(3):229–232.
26. Schirmer O. Studies on the physiology and pathology of tear secretion and tear drainage. *Albrecht Von Graefes Arch Ophthalmol*. 1903;56:497–500.
27. Lemp MA. Breakup of the tear film. *Int Ophthalmol Clin*. 1973;13(1):97–102.
28. Cuevas M, González-García MJ, Castellanos E, et al. Correlations among symptoms, signs, and clinical tests in evaporative-type dry eye disease caused by meibomian gland dysfunction. *Curr Eye Res*. 2012;37(10):855–863.
29. Amano S, Inoue K. Estimation of prevalence of meibomian gland dysfunction in Japan. *Cornea*. 2017;36(6):684–688.