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Research Article

Tear Film and Meibomian Gland Changes among Dry Eye Sub-Groups

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ABSTRACT

Introduction: Dry eye evaluation is crucial for maintaining ocular surface health. Most studies reported dry eyes based on the presence of symptoms and signs; however, those with either symptoms or signs were overlooked. This study evaluated the tear film and Meibomian Gland (MG) morphology among dry eye sub-groups categorized based on signs and symptoms defined by the Dry Eye Workshop-II (DEWS-II) report.

Methods: This cross-sectional study was conducted on 149 subjects who underwent tear film evaluation and meibography and filled out the Ocular Surface Disease Index (OSDI) questionnaire. The subjects were categorised into four groups based on the signs and symptoms no dry eye, pre-clinical dry eye, probable dry eye and dry eye.

Results: It was found that the OSDI scores and Non-Invasive Breakup Time (NIBUT) were significantly different between all the dry eye groups ($p<0.001$). Tear Meniscus Height (TMH) significantly differed between no dry eye and dry eye groups ($p=0.006$). Also, the MG length of the lower lid was significantly lower in the dry eye group compared to other groups ($p=0.01$). Other variables such as Schirmer's test, corneal staining, MG width, loss, and tortuosity score of the upper and lower lid did not significantly differ among the groups ($p>0.05$).

Conclusions: Pre-clinical dry eyes, although expressed symptoms, however, showed no tear film and meibomian gland alterations. A quarter sample showed no symptoms in the presence of clinical signs. Hence, findings from this study may be incorporated into pre-surgical ocular surface evaluation protocols to eliminate post-surgical dry eye signs and symptoms.

Keywords: Pre-clinical dry eye; Probable dry eye; Tear film; Dry eye; Meibography

INTRODUCTION

Dry eye is defined as "*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 increased osmolarity of the tear film and inflammation of the ocular surface*" [1]. It is indicated by the presence of both symptoms and signs. However, according to the DEWS-II report, there are also other considerations of the dry eye that includes the presence of symptoms of the disease without obvious signs suggesting a pre-clinical state or the presence of noticeable signs without any symptoms which can be disposed of in Dry Eye Disease (DED). This might be because the symptoms and signs of dry eye disease do not associate well, as reported in previous studies [2,3]. DED can be detected and diagnosed using various questionnaires and diagnostic tests [4,5].

Studies have also reported a relationship between tear film and meibomian gland dysfunction in dry eyes diagnosed based on symptoms and signs [6,7]. Furthermore, another study reported reduced tear turnover rate among symptomatic dry eyes, [8] whereas, in symptomatic subjects, Non-Invasive Break-Up Time (NIBUT) and Tear Meniscus Height (TMH) differed from normals [9]. In this study, the subjects were grouped as pre-clinical dry eye based on the symptoms alone, assuming that the Indian population has a lower tear break up time when compared to other populations [10]. However, no studies report these changes among dry eyes based on the presence of symptoms or signs as categorised by the DEWS-II report. Hence, there is a need to study if there are any changes in the tear film

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and meibomian gland morphology among the dry eye categories based on the presence of either symptoms or signs to understand the presentation of the disease.

MATERIALS AND METHODS

A prospective cross-sectional study was conducted at the University of Hyderabad's Eye Clinic, Hyderabad, India. The study was approved by the University of Hyderabad Ethics Committee (UH/IEC/2019/148). All the procedures were conducted according to the Declaration of Helsinki. Each subject signed a written informed consent before participating in the study. Subjects aged between 18 and 39 years with no history of ocular dryness, surgery, or contact lens wear were included in the study. Those with ocular or systemic conditions known to cause dry eyes were excluded from the study.

A single examiner performed the non-invasive tear film assessment and meibomian gland morphology imaging using EASYTEAR view+(EASYTEAR S.R.L., Trento, Italy). All the tests were performed on both eyes of each subject on the same day in the given order mention in Table 1. A time interval of 5-10 minutes was given between each test so that the test results were not affected.

Table 1: Tests used for assessing tear film and meibomian gland morphology.

Questionnaire	**Ocular Surface Disease Index (OSDI)**
Non-invasive tear film tests	Non-Invasive Break-Up Time (NIBUT)
	Tear Meniscus Height (TMH)
Invasive tear film tests	Schirmer's test
	Corneal staining
Meibomian gland morphology imaging	Meibomian gland length, width, loss and tortuosity

Tear film assessment: NIBUT was assessed as the time taken from the first blink till the appearance of the first breakup in the illuminated grid of the tear film. This procedure was recorded three times, and an average of three readings was taken. TMH was imaged, and these images were further analysed using Image J 1.53 image analysis software (National Institutes of Health, Bethesda, Maryland, USA) [11]. Among invasive tear film tests, Schirmer's test was performed by placing the filter paper in the lower conjunctival fornix at the temporal one-third, and the wetting of the strip was assessed without anaesthesia after 5 minutes. For corneal staining, fluorescein dye was instilled into the eye and the cornea was observed under the blue filter for any staining. This was graded using the Efron grading scale, where grade 0 indicates normal, grade 1 indicates trace staining, grade 2 indicates mild staining, and grade 3 indicates moderate staining and grade 4 indicates severe staining [12]. In addition to invasive and non-invasive tests, all subjects filled out the Ocular Surface Disease Index (OSDI) to assess dry eye symptoms.

Meibomian gland morphology assessment: Meibomian glands of both the upper and lower eyelid were imaged and were further analysed using image J 1.53 image analysis software (national institutes of health, Bethesda, Maryland, USA). The gland length, width, loss and tortuosity were assessed for morphology. The three central glands' length and width were assessed among all the subjects [13]. MG loss was assessed by calculating the total tarsal area divided by the loss area in percentage. Moreover, tortuosity was evaluated by calculating the bent angle of the twisted glands, which is more than 45 degrees, which was graded using a 3-point scale [14]. Where grade 0 indicates no distortion, grade 1 indicates 1 to 4 distorted glands, and grade 2 indicates five or more distorted glands. The methodology published in the previous article has been adopted here [9].

Dry eye grouping: All the subjects were categorised into four sub groups as per the DEWS-II definition of dry eye based on signs and symptoms.

- No dry eye as having an OSDI score <13 and with NIBUT of ≥ 10 sec.
- Pre-clinical dry eye as the presence of symptoms represented by an OSDI score of ≥ 13 with the absence of clinical signs indicated with NIBUT of ≥ 10 sec.
- Probable dry eye as the presence of signs such as NIBUT <10 sec without symptoms (OSDI <13).
- Dry eye as the presence of both signs and symptoms, wherein OSDI score is ≥ 13 and NIBUT of <10 seconds.

Statistical analysis: Statistical analysis was performed using SPSS software version 25 (SPSS Inc., Chicago, USA). Normality was analysed using the Kolmogorov-Smirnov test. Kruskal Wallis H test was performed to compare the tear film and MG morphology among the dry eye groups. Post hoc tests were performed using the Mann-Whitney U test to study the significance between individual groups. The significance value was set as less than 0.05.

RESULTS

This study included 149 subjects with a median age of 22 years (IQR 21-23); 78 were males, and 71 were females. Measurements from the right eye were taken for all the subjects for analysis. Table 2 shows the descriptive statistics of the variables studied among the subjects. In groups discussed as per the DEWS-II definition of dry eye based on signs and symptoms above, 47

subjects were categorised as no dry eye, 29 as pre-clinical dry eye, 37 as probable dry eye, and 36 as dry eye.

Table 2: Descriptive statistics for the study variables.

Variable		Median (IQR)†
‡OSDI score, grade		10.41 (4.16-18.75)
Non-invasive break up time, sec		9 (10-11)
Tear meniscus height, mm		0.26 (0.23-0.31)
Schirmer's test, mm		25 (20-35)
Upper lid	§MG length, mm	5.93 (5.41-6.57)
	§MG width, mm	0.42 (0.38-0.48)
	§MG loss, %	6.24 (1.50-13.37)
Lower lid	§MG length, mm	2.54 (2.21-2.99)
	§MG width, mm	0.54 (0.49-0.61)
	§MG loss, %	11.03 (6.66-16.24)

Note: †Interquartile range; ‡Ocular surface disease index; §Meibomian gland

Tear film changes among the dry eye groups: OSDI scores significantly differed between the four dry eye groups (Kruskal Wallis H=110.20, p=0.0001) (Figure 1A). Post hoc comparisons showed a statistically significant difference between no dry eye and pre-clinical dry eye (test statistic= -6.83, p=0.0001); probable dry eye and dry eye groups (test statistic= -7.90, p=0.0001); probable dry eye and preclinical dry eye (test statistic=7.00, p=0.0001); no dry eye and dry eye groups (test statistic=-7.79, p=0.0001); with high scores among the pre-clinical dry eye and dry eye groups and low scoring in the probable dry eye and the no dry eye groups. Other comparisons did not significantly differ, including no dry eye *vs.* probable dry eye (test statistic=0.56, p=0.99) and pre-clinical dry eye *vs.* dry eye groups (test statistic=0.45, p=0.99).

Similarly, NIBUT was significant between the four dry eye groups (Kruskal Wallis H=114.99, p=0.0001) (Figure 1B). Post hoc comparisons showed a statistically significant difference between no dry eye and dry eye groups (test statistic=8.47, p=0.0001); dry eye and pre-clinical dry eye groups (test statistic=6.52, p=0.0001); probable dry eye and pre-clinical dry eye groups (test statistic=6.28, p=0.0001); probable dry eye and no dry eye groups (test statistic=8.23, p=0.0001); where the NIBUT was reduced among probable dry eye and dry eye groups followed by pre-clinical dry eye and no dry eye groups. Other comparisons, such as pre-clinical dry eye *vs.* no dry eye groups (test statistic=1.05, p=0.99) and dry eye *vs.* probable dry eye groups (test statistic=0.28, p=0.99), did not significantly differ.

TMH also showed statistical significance for comparison between the four groups (Kruskal Wallis H=10.74, p=0.013) (Figure 1C). Post hoc comparisons showed a statistically significant difference for comparisons between dry eye and no dry eye groups (test statistic=2.81, p=0.024), pre-clinical dry eye and dry eye groups (test statistic=2.77, p=0.033), where the TMH was lesser in the dry eye group when compared to other groups. However, comparisons between other groups showed no statistical significance (p>0.05).

Other tear film variables, such as Schirmer's test (Kruskal Wallis H=3.22, p=0.35) and corneal staining (Kruskal Wallis H=2.60, p=0.45), showed no significant difference between the four groups compared.

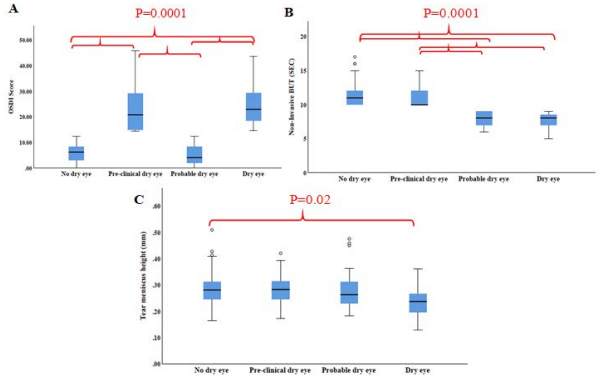

Figure 1: Tear film changes among the dry eye groups.

MG morphology changes among the dry eye groups: MG length of the lower lid showed a statistical significance for comparison between the four groups (Kruskal Wallis H=10.56, p=0.014) (Figure 2A). Post hoc comparisons showed a statistically significant between dry eye and probable dry eye groups (test statistic=3.21, p=0.008), where the MG length of the lower lid was lesser in the dry eye group compared to the probable dry eye group. Comparisons between other groups showed no statistically significant difference (p>0.05) between

the dry eye groups. Comparison of other variables such as MG length of the upper lid (Kruskal Wallis H=3.29, p=0.34), MG width (lower lid: Kruskal Wallis H=5.69, p=0.12; upper lid: Kruskal Wallis H=3.55, p=0.31) (Figure 2B), MG loss (lower lid: Kruskal Wallis H=3.44, p=0.32; upper lid: Kruskal Wallis H=0.27, p=0.96) (Figure 2C) and tortuosity score (lower lid: Kruskal Wallis H=0.48, p=0.92; upper lid: Kruskal Wallis H=1.53, p=0.67) of both upper and lower lid were not significantly different between the four groups.

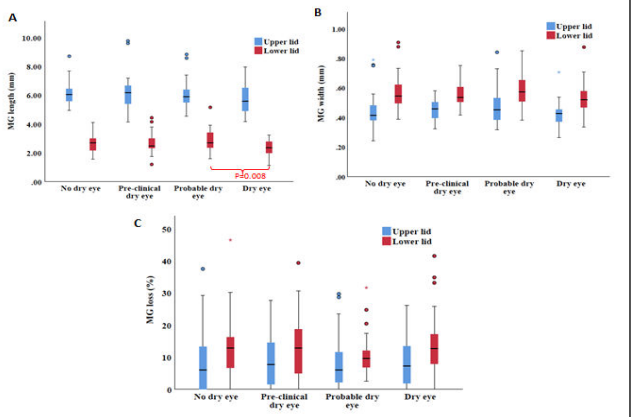

Figure 2: MG morphology changes among the dry eye groups.

DISCUSSION

In this study, the tear film and MG morphological changes among dry eye groups based on the presence of signs and symptoms defined by the DEWS-II report were categorised and analysed. Almost half of the subjects in the sample had pre-clinical dry eye and probable dry eye based on the DEWS-II definition, which was also seen in another study [15]. With respect to the changes in the tear film, a significant difference was found for OSDI scores, NIBUT and TMH but not for Schirmer's test and corneal staining. For MG morphological changes, only the MG length of the lower lid was significantly different between the dry eye groups.

Among all the tear film variables, OSDI score and NIBUT significantly differed between the dry eye groups, followed by TMH, indicating that NIBUT is a sensitive test in detecting dry eye changes [16]. It was found that NIBUT was significantly different between no dry eye and probable dry eye groups; however, no difference was seen between any dry eye and pre-clinical dry eye groups, indicating that the presence of symptoms alone might not indicate the presence of signs. However, it must be noted that there are other tests for detecting dry eye, such as tear osmolarity, which is also one of the key underlying factors for dry eye apart from tear instability [17]. In addition, there was also a significant difference in TMH between no dry eye and dry eye groups, although the values fall within the normal range.

For MG morphology, the MG length of the shorter lid was found to be a sensitive indicator, where it was found shorter in the dry eye group when compared to the other groups; however, significance was only seen for the probable group. This finding is similar to what has been reported previously [18] among evaporative dry eyes, where only the MG length was shortened in evaporative dry eyes compared to healthy controls. The MG length was, however, similar between no dry eye, pre-clinical dry eye and probable dry eye groups. Similarly, other variables, such as MG loss, MG width, and tortuosity score, did not differ among the dry eye groups.

This study can be extended by comparing dry eye symptoms with other signs, such as hyper osmolarity and studying other tear biomarkers. It is also worth studying the functional changes of the meibomian gland along with the structural changes and the correlation between them.

CONCLUSION

Subjects with pre-clinical dry eyes, represented by the presence of symptoms, behaved similar to normals without dry eyes and showed no tear film changes or MG alterations. Similarly, the probable dry eye group represented by the presence of signs alone also showed no alterations in the MG morphology. However, their behaviour might change over time, which needs to be evaluated. Hence, it is equally important to evaluate both signs and symptoms of dry eye to understand the course of the disease and its development further and to avoid consequences post-cataract or corneal surgery.

CONFLICTS OF INTEREST

None.

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REFERENCES

1. Craig JP, Nichols KK, Akpek EK, Caffery B, Dua HS, Joo CK, et al. TFOS DEWS II definition and classification report. Ocul Surf. 2017;15(3):276-283.
2. Schein OD, Tielsch JM, Munoz B, Bandeen-Roche K, West S. Relation between signs and symptoms of dry eye in the elderly: A population-based perspective. Ophthalmol. 1997;104(9):1395-1401.
3. McCarty CA, Bansal AK, Livingston PM, Stanislavsky YL, Taylor HR. The epidemiology of dry eye in Melbourne, Australia. Ophthalmol. 1998;105(6):1114-1119.
4. Wolffsohn JS, Arita R, Chalmers R, Djalilian A, Dogru M, Dumbleton K, et al. TFOS DEWS II diagnostic methodology report. Ocul Surf. 2017;15(3):539-574.
5. Okumura Y, Inomata T, Iwata N, Sung J, Fujimoto K, Fujio K, et al. A review of dry eye questionnaires: measuring patient-reported outcomes and health related quality of life. Diagnostics. 2020;10(8):559.
6. Pult H. Relationships between meibomian gland loss and age, sex, and dry eye. Eye Contact Lens. 2018;44:S318-S324.

7. Pult H, Riede-Pult B, Nichols J. Relation between upper and lower lids' meibomian gland morphology, tear film, and dry eye. Optom Vis Sci 2012;89:E310-E315.
8. Sorbara L, Simpson T, Vaccari S, Jones L, Fonn D. Tear turnover rate is reduced in patients with symptomatic dry eye. Cont Lens Anterior Eye. 2004;27(1):15-20.
9. Fatima A, Vadla P, Konda N. Changes in the tear film and meibomian gland morphology between preclinical dry eye and normal subjects represented by ocular surface disease index scores. Exp Eye Res. 2022;222:109188.
10. Mishra P, Srivastava D, Misra R, Malik VK, Trivedi V. Assessment of tear secretions in healthy Indian volunteers. Indian J Physiol Pharmacol. 2014;58(2):137-140.
11. Garcia-Resua C, Pena-Verdeal H, Lira M, Oliveira ME, Giraldez MJ, Yebra-Pimentel E. Comparison between three methods to value lower tear meniscus measured by image software. In 8th Iberoamerican Optics Meeting and 11th Latin American Meeting on Optics, Lasers, and Applications 2013;8785:1603-1610.
12. Efron N. Grading scales for contact lens complications. Ophthalmic Physiol Opt. 1998;18(2):182-186.
13. Ban Y, Shimazaki-Den S, Tsubota K, Shimazaki J. Morphological evaluation of meibomian glands using noncontact infrared meibography. Ocul Surf. 2013;11(1):47-53.
14. Arita R, Itoh K, Maeda S, Maeda K, Tomidokoro A, Amano S. Association of contact lens related allergic conjunctivitis with changes in the morphology of meibomian glands. Jpn J Ophthalmol. 2012;56:14-19.
15. Noor NA, Rahayu T, Gondhowiardjo TD. Prevalence of dry eye and its subtypes in an elderly population with cataracts in Indonesia. Clin Ophthalmol. 2020:2143-150.
16. Mengher LS, Pandher KS, Bron AJ. Non-invasive tear film break-uptime: Sensitivity and specificity. Acta ophthalmologica. 1986;64(4):441-444.
17. Foulks GN, Lemp M, Jester J, Sutphin J, Murube J, Novack GJ. Report of the international Dry Eye Workshop (DEWS). Ocul Surf. 2007;5(2):65-204.
18. Crespo-Trevino RR, Salinas-Sanchez AK, Amparo F, Garza-Leon M. Comparative of meibomian gland morphology in patients with evaporative dry eye disease versus non-dry eye disease. Scientific Reports. 2021;11(1):20729.