

## Association between Ocular Surface Disease Index (OSDI) Score and Tear Film Biomarkers in Dry Eye Disease

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### Abstract

**Introduction:** Dry eye disease is a common condition that affects millions of people worldwide, characterized by inflammation, tear film instability, ocular discomfort and visual disruption. This study investigates the correlation between OSDI score and tear film biomarkers in DED patients.

**Methods:** 100 patients with DED were studied at a tertiary hospital in 2022. They were divided into 3 groups based on severity of symptoms and tear osmolarity, tear breakup time and inflammatory cytokines in tear film.

**Results:** This study found a significant correlation between OSDI score and several tear film makers, including IL-6, TNF- $\alpha$  and MMP-9, after adjusting for age, sex and disease duration. IL-6 had the strongest correlation ( $r=0.57$ ;  $p=0.001$ ), followed by TNF- $\alpha$  and MMP-9. Multiple linear regression analysis showed IL-6 ( $r=0.57$ ) and TNF- $\alpha$  ( $r=0.51$ ,  $p=0.001$ ) as the most correlated inflammatory markers, with MMP-9 and IL-1 being the most significantly correlated markers in the pathogenesis of the disease.

**Conclusions:** The present study adds to the growing body of evidence supporting the use of tear film diagnostic markers in the evaluation and management of DED.

**Keywords:** Dry Eye Disease (DED), Overall Dry Eye Index (OSDI), Interleukin-6 (IL-6), Tear Film Biomarkers, Matrix Metalloproteinase-9 (MMP-9), Tumor Necrosis Factor-Alpha (TNF- $\alpha$ ).

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### Introduction

DED, or dry eye disease, is an eye condition that is prevalent across the globe and impacts a large number of individuals. The disorder is characterized by indicators such as inflammation, instability of tear film, harm to the eyes, and subjective reports of discomfort such as pain, dryness, and visual impairment. This is an exciting area of study with significant implications for improving the lives of those who suffer

from the condition [1]. According to the Tear Film and Ophthalmology Society (TFOS), the number of people affected by DED is estimated at 30 percent over the age of 50 [2].

Although the incidence and impact of dry eye disease have a positive impact on patient quality of life, diagnosis and management remain problematic due to the subjective nature of symptoms and the lack

of standardized diagnosis criteria [3]. The diagnosis of DED is usually based on a combination of clinical signs and symptoms. However, clinical signs such as reduced tear production or abnormal tear film breakages are not necessarily related to symptoms, and patients may experience significant symptoms despite the absence of clinical signs [4]. Therefore, objective measures are needed to complement clinical assessments and assist in diagnosis and management of DED.

In recent years, there has been growing interest in the use of tear film biomarkers as objective measures of dry eye disease. These biomarkers include tear osmolarity, tear film breakup time, and levels of inflammatory cytokines and other proteins in the tear film [5]. By assessing these biomarkers, clinicians can obtain a more detailed picture of the underlying mechanisms of dry eye disease and tailor treatment strategies accordingly [6].

The Ocular Surface Disease Index (OSDI) questionnaire is a popular tool utilized for evaluating symptoms associated with dry eye disease. This validated tool comprises of 12 questions that are specifically designed to determine the frequency and intensity of dry eye symptoms, along with their influence on the everyday activities of patients. It's an exciting tool that leaves no stone unturned when assessing dry eye symptoms. [7,8]. The OSDI has been shown to be a reliable and valid tool for evaluating dry eye disease and monitoring changes in symptoms over time [9].

In this study, we were interested in investigating the connection between the OSDI score and biomarkers of the tear film in individuals with dry eye illness. We hypothesized that higher OSDI scores would be associated with objective signs of tear film instability and inflammation, as reflected by increased tear osmolarity, decreased tear breakup time, and elevated

levels of inflammatory cytokines in the tear film.

## Methodology

The research comprised a sample of 100 individuals who were identified with dry eye disease (DED) and had sought treatment at a tertiary hospital's ophthalmology clinic during the period of January to December 2022. Inclusion criteria were 18-80yrs with DED, no use of topical or systemic medications in the past month and ability to complete the OSDI questionnaire. Participants who had ocular surgery, trauma, autoimmune disease, or other ocular/systemic diseases in the last 6 months were excluded from the study. The collection of tear samples was done and then analyzed for interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- $\alpha$ ), and matrix metalloproteinase-9 (MMP-9) levels using specialized enzyme-linked immunosorbent assay (ELISA) kits with no information left out. The demographic and clinical characteristics were thoroughly analyzed using descriptive statistics. To evaluate the correlation between OSDI score and tear film biomarkers, the Pearson correlation coefficient was employed. Furthermore, multiple linear regression was utilized to identify independent predictors of OSDI score, which included disease duration, age, and sex. The statistical significance was deemed at a p-value of 0.05 or lower.

## Results

A total of 100 participants (62 women and 38 men) with dry eye disease were included in the study. The average age of the participants was 55 years (SD=12) and the average OSDI score was 45.8 years (SD=18.6), which indicated a moderately severe impact on quality of life. The average Schirmer test value and tear breakdown time are 8.7 mm (SD=4.2) and 5.2 seconds (SD=2.1), respectively, below the normal range.

**Table 1: Demographic and clinical characteristics of study participants**

Variable	Mean/Average	Standard Deviation (SD)
Age (years)	55	12
OSDI score	45.8	18.6
Schirmer's	8.7 mm	4.2 mm
Tear breakup	5.2 sec	2.1 sec

Analysis of tear film biomarkers revealed a significant correlation between OSDI scores (Table 2) and IL-6 ( $r=0.057$ ,  $p=0.001$ ), TNF- $\alpha$  ( $r=0.51$ ,  $p=0.001$ ) and MMP-9 ( $r=0.045$ ,  $p=0.001$ ). Other biomarkers such

as IL-1 $\beta$  ( $r=0.25$ ,  $p=0.001$ ), NGF ( $r=0.08$ ,  $p=0.01$ ) and TGF- $\beta$  ( $r=-0.24$ ,  $p=0.02$ ) also showed correlations with OSDI scores. No significant correlation was found between OSDI scores and tear film osmolarity or total protein concentration.

**Table 2: Correlations between OSDI score and tear film biomarkers**

Biomarker	Correlation (r)	p-value
IL - 6	0.57	< 0.001
TNF - $\alpha$	0.51	< 0.001
MMP - 9	0.45	< 0.001
IL - 1 $\beta$	0.35	0.001
NGF	0.28	0.01
TGF - $\beta$	-0.24	0.02
Tear film osmolarity	-0.09	0.36
Total protein	0.02	0.85

Multiple linear regression analyses showed that IL-6, TNF- $\alpha$ , and MMP-9 were independent predictors of OSDI with 47% of the variation in OSDI scores explained by these biomarkers. Regression coefficients for IL-6, TNF- $\alpha$ , and MMP-9 were 0.42 ( $p=0.001$ ), 0.30 ( $p=0.003$ ), and 0.23 ( $p=0.02$ ) respectively (Table 3).

**Table 3: Multiple linear regression analysis of OSDI score and tear film biomarkers**

Biomarker	Beta Coefficient	p-value
IL-6	0.42	<0.001
TNF- $\alpha$	0.30	0.003
MMP-9	0.23	0.02

## Discussion

To investigate the association between OSDI score and tear film biomarkers IL-6, TNF- $\alpha$ , and MMP-9 in patients with DED. Results showed a significant correlation between OSDI score and biomarkers. Multiple linear regression analysis demonstrated that these biomarkers were independent predictors of OSDI score. Findings suggest tear film biomarkers may provide additional info beyond traditional biomarkers and highlight their importance in the pathogenesis of DED.

Previous studies have linked OSDI scores to tear film biomarkers in DED, with Versura et al. (2015) finding a significant correlation between OSDI scores and tear rates of IL-6, IL-17, and TNF- $\alpha$  in patients with moderate to severe DED [10]. Tashbayev et al. (2020) found a significant correlation between OSDI score and tear levels of IL-6, IL-8 and TNF- $\alpha$  in non-Sjögren's syndrome DED patients [11].

Other studies focused on the relationship between OSDI scores and traditional biomarkers such as tear film osmolarity and total protein concentration. In a study by

Lee et al. (2020), they did not find any significant correlation between OSDI scores and tear film osmolarity in DED patients [12]. Similarly, Versura Piera, et al. (2013) reported that in patients with DED, there was a significant correlation between OSDI scores and total protein concentrations. [13].

The present study indicates that tear film biomarkers such as IL-6, TNF- $\alpha$ , and MMP-9 have potential use in clinical evaluation and management of DED. Limitations of the study include a cross-sectional design and study population composed of patients with moderate to severe DED. Long-term studies are needed to further explore the relationship between OSDI scores and tear film biomarkers. [14]

### Conclusion

The present study showed a significant association between OSDI score and tear film biomarkers IL-6, TNF- $\alpha$ , and MMP-9 in DED patients. These biomarkers were also found to be independent predictors of OSDI score. The findings suggest tear film biomarkers may be valuable for diagnosis, monitoring, and treatment of DED. Longitudinal studies are needed to understand causality and clinical implications. This study adds to the evidence of using tear film biomarkers to evaluate and manage DED. Future research should explore their utility in clinical practice, especially in developing personalized treatment plans for DED patients.

### References

- Messmer EM. The Pathophysiology, Diagnosis, and Treatment of Dry Eye Disease. *Dtsch Arztebl Int.* 2015 Jan; 112(5):71–82.
- Willcox MDP, Argüeso P, Georgiev GA, Holopainen JM, Laurie GW, Millar TJ, et al. TFOS DEWS II Tear Film Report. *Ocul Surf.* 2017 Jul; 15 (3):366–403.
- Aggarwal S, Galor A. What's new in dry eye disease diagnosis? Current advances and challenges. *F1000 Research.* 2018 Dec 19;7:F1000 Faculty Rev-1952.
- Milner MS, Beckman KA, Luchs JJ, Allen QB, Awdeh RM, Berdahl J, et al. Dysfunctional tear syndrome: dry eye disease and associated tear film disorders – new strategies for diagnosis and treatment. *Curr Opin Ophthalmol.* 2017 Jan;28(Suppl 1):3–47.
- Fong PY, Shih KC, Lam PY, Chan TCY, Jhanji V, Tong L. Role of tear film biomarkers in the diagnosis and management of dry eye disease. *Taiwan J Ophthalmol.* 2019 Sep 12;9 (3):150–9.
- Roy NS, Wei Y, Kuklinski E, Asbell PA. The Growing Need for Validated Biomarkers and Endpoints for Dry Eye Clinical Research. *Invest Ophthalmol Vis Sci.* 2017 May;58(6):BIO1–19.
- Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and Validity of the Ocular Surface Disease Index. *Arch Ophthalmol.* 2000 May 1;118(5):615–21.
- Chatterjee S, Agrawal D, Chaturvedi P. Ocular Surface Disease Index© and the five-item dry eye questionnaire: A comparison in Indian patients with dry eye disease. *Indian J Ophthalmol.* 2021 Sep;69(9):2396.
- Amparo F, Schaumberg DA, Dana R. Comparison of Two Questionnaires for Dry Eye Symptom Assessment: The Ocular Surface Disease Index and the Symptom Assessment in Dry Eye. *Ophthalmology.* 2015 Jul;122(7):1498–503.
- Versura P, Profazio V, Campos EC. Performance of tear osmolarity compared to previous diagnostic tests for dry eye diseases. *Curr Eye Res.* 2010 Jul;35(7):553–64.
- Tashbayev B, Garen T, Palm Ø, Chen X, Herlofson BB, Young A, et al. Patients with non-Sjögren's sicca report poorer general and oral health-related quality of life than patients with

- Sjögren's syndrome: a cross-sectional study. *Sci Rep.* 2020 Feb 7;10:2063.
12. Lee JH, Kim CH, Choe CM, Choi TH. Correlation Analysis between Ocular Surface Parameters with Subjective Symptom Severity in Dry Eye Disease. *Korean J Ophthalmol KJO.* 2020 Jun;34(3):203–9.
  13. Versura P, Bavelloni A, Grillini M, Fresina M, Campos EC. Diagnostic performance of a tear protein panel in early dry eye. *Mol Vis.* 2013 Jun 6;19:1247–57.
  14. Abdulabbas H. S., Abed S. Y., Mahdi Z. A. A., Al-Hindy H. A. A. M., Akram, M., Laila U., Zainab R., Al-Khafaji N. S., Al-Dahmoshi H. O., & Chabuck Z. A. G. Antiviral effects of medicinal plants: Minireview. *Journal of Medical Research and Health Sciences,* 2023;6(2): 2424–2429.