e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(4); 574-577

Original Research Article

Evaluation of Tear Film Biomarkers (Mmp-9 and Il-6) in Patients with Dry Eye Disease and Their Correlation with Clinical Severity

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Received: 01-01-2026 / Revised: 15-02-2026 / Accepted: 21-03-2026

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Conflict of interest: Nil

Abstract

Background: Dry eye disease (DED) is a multifactorial disorder of the ocular surface characterized by tear film instability and inflammation. Recent evidence highlights the role of inflammatory biomarkers such as matrix metalloproteinase-9 (MMP-9) and interleukin-6 (IL-6) in the pathogenesis of DED. Their correlation with clinical severity may aid in early diagnosis and targeted therapy.

Materials and Methods: A cross-sectional study was conducted on 100 participants, including 70 patients with clinically diagnosed DED and 30 healthy controls. Tear samples were collected and analyzed for MMP-9 and IL-6 levels using enzyme-linked immunosorbent assay (ELISA). Clinical severity was assessed using Ocular Surface Disease Index (OSDI), Schirmer test, and Tear Break-Up Time (TBUT). Correlation analysis was performed between biomarker levels and clinical parameters.

Results: Mean MMP-9 and IL-6 levels were significantly elevated in DED patients compared to controls ($p < 0.001$). Higher biomarker levels were observed in moderate and severe DED groups. A strong positive correlation was found between MMP-9 and OSDI scores ($r = 0.71$) and IL-6 and OSDI scores ($r = 0.65$). Negative correlation was observed with TBUT and Schirmer values.

Conclusion: Tear film biomarkers MMP-9 and IL-6 are significantly elevated in DED and correlate well with disease severity. These biomarkers can serve as reliable indicators for diagnosis and monitoring of dry eye disease.

Keywords: Dry eye disease, MMP-9, IL-6, tear film biomarkers and OSDI.

DOI: 10.25258/ijcpr.18.4.95

Introduction

Dry eye disease (DED) is a common ocular disorder affecting millions worldwide and significantly impacting quality of life [1]. It is characterized by tear film instability, hyperosmolarity, and chronic inflammation of the ocular surface [2]. The prevalence of DED is increasing due to environmental factors, aging population, and increased digital screen usage [3].

Inflammation plays a central role in the pathogenesis of DED. Tear film instability leads to epithelial damage and activation of inflammatory pathways, resulting in the release of cytokines and matrix-degrading enzymes [4]. Among these, matrix metalloproteinase-9 (MMP-9) is a key enzyme responsible for extracellular matrix degradation and disruption of corneal epithelial integrity [5].

Interleukin-6 (IL-6) is a pro-inflammatory cytokine that contributes to immune activation and ocular surface inflammation in DED (6). Elevated levels of IL-6 have been reported in tear fluid of patients with dry eye and are associated with disease severity [7]. These biomarkers reflect the underlying inflammatory process and may serve as objective indicators of disease activity.

Traditional diagnostic tests for DED, such as Schirmer test and Tear Break-Up Time (TBUT), have limitations due to variability and lack of specificity [8]. Subjective assessment tools like the Ocular Surface Disease Index (OSDI) provide symptom-based evaluation but may not correlate well with objective findings [9]. Therefore, there is a growing need for reliable biomarkers that can accurately reflect disease severity.

Recent advances in ocular surface research have emphasized the importance of tear film biomarkers in understanding the pathophysiology of DED [10]. MMP-9 and IL-6 have emerged as potential candidates due to their involvement in inflammatory pathways and epithelial damage [11].

This study aims to evaluate the levels of tear film biomarkers MMP-9 and IL-6 in patients with dry eye disease and to correlate these levels with clinical severity parameters. Understanding these relationships may improve diagnostic accuracy and guide targeted therapeutic interventions.

Aim and Objectives

Aim: To evaluate tear film biomarkers (MMP-9 and IL-6) in dry eye disease and correlate them with clinical severity.

Objectives:

1. To measure tear film levels of MMP-9 and IL-6 in DED patients and controls.
2. To assess correlation between biomarker levels and clinical parameters (OSDI, TBUT, Schirmer test).

Materials and Methods

A hospital-based cross-sectional study was conducted in the department of Ophthalmology, Parbhani Medical College and R P Hospital and Research Institute over a period of 12 months. A total of 100 participants were enrolled, including 70 patients diagnosed with dry eye disease and 30 age-matched healthy controls. Diagnosis of DED was based on symptoms and clinical tests including OSDI score (>13), TBUT (<10 seconds), and Schirmer test (<10 mm).

Tear samples were collected using microcapillary tubes under aseptic conditions. Levels of MMP-9 and IL-6 were quantified using ELISA kits following standard protocols. Clinical severity was graded into mild, moderate, and severe based on OSDI scores.

Inclusion Criteria:

- Adults aged 20–65 years
- Clinically diagnosed dry eye disease
- Willing to participate

Exclusion Criteria:

- Ocular infections or allergies
- Contact lens users
- Recent ocular surgery
- Systemic autoimmune diseases

Statistical analysis was performed using SPSS software. Mean values were compared using t-test and ANOVA.

Pearson correlation coefficient was used to assess relationships. $p < 0.05$ was considered statistically significant.

Results

Table 1: Biomarker Levels in Study Groups

Parameter	DED Patients (n=70)	Controls (n=30)	p-value
MMP-9 (ng/mL)	145 ± 25	65 ± 15	<0.001
IL-6 (pg/mL)	38 ± 10	15 ± 5	<0.001

Significantly higher levels of MMP-9 and IL-6 were observed in DED patients compared to controls.

Table 2: Biomarker Levels vs Severity

Severity	MMP-9	IL-6
Mild	110 ± 20	25 ± 8
Moderate	150 ± 18	38 ± 7
Severe	180 ± 22	50 ± 9

Biomarker levels increased progressively with severity of DED.

Table 3: Correlation with Clinical Parameters

Parameter	MMP-9 (r)	IL-6 (r)
OSDI	+0.71	+0.65
TBUT	-0.60	-0.55
Schirmer	-0.58	-0.50

Strong positive correlation with symptom severity (OSDI) and negative correlation with tear function tests.

Discussion

The present study highlights the significant role of inflammatory biomarkers in the pathogenesis and severity assessment of dry eye disease. Elevated levels of MMP-9 and IL-6 in DED patients indicate ongoing inflammation at the ocular surface, consistent with previous studies [11,12]. MMP-9 plays a crucial role in epithelial barrier disruption by degrading tight junction proteins, leading to increased corneal permeability [13]. The significantly higher levels observed in this study support its role as a marker of epithelial damage and inflammation. Sambursky et al. reported

similar findings, demonstrating increased MMP-9 levels in DED patients [14].

IL-6 is a multifunctional cytokine involved in immune regulation and inflammatory responses. Elevated IL-6 levels observed in this study indicate activation of inflammatory pathways in DED. Previous studies have also shown increased IL-6 levels correlating with disease severity [15].

The strong positive correlation between biomarker levels and OSDI scores suggests that these markers reflect patient-reported symptoms. The negative correlation with TBUT and Schirmer test indicates that higher inflammation is associated with decreased tear stability and production.

These findings are in agreement with studies by Pflugfelder et al., which highlighted the inflammatory basis of dry eye disease [11]. Traditional diagnostic methods lack sensitivity and specificity, whereas biomarkers provide objective assessment of disease activity.

The progressive increase in biomarker levels from mild to severe DED suggests their potential role in grading disease severity. This could be particularly useful in monitoring treatment response and guiding therapy.

Limitations of the study include its cross-sectional design and relatively small sample size. Longitudinal studies are needed to establish causality and evaluate changes with treatment.

Conclusion

This study demonstrates that tear film biomarkers MMP-9 and IL-6 are significantly elevated in patients with dry eye disease and correlate strongly with clinical severity. These biomarkers reflect the underlying inflammatory processes and provide an objective measure of disease activity.

The strong correlation with OSDI scores and inverse relationship with TBUT and Schirmer test highlight their clinical relevance. Incorporating biomarker analysis into routine clinical practice may improve diagnostic accuracy and enable early detection of disease.

MMP-9 and IL-6 can serve as valuable tools for monitoring disease progression and response to therapy. Their use may facilitate personalized treatment strategies targeting inflammation.

Further large-scale and longitudinal studies are recommended to validate these findings and explore their role in clinical management.

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