

# Evaluation of Dry Eye, Central Corneal and Epithelial Thickness in Psoriasis Patients: Case Control Study

## Psöriyazisli Hastalarda Kuru Gözün, Santral Korneal ve Epitelyal Kalınlığın Değerlendirilmesi: Olgu Kontrol Çalışması

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**ABSTRACT Objective:** The evaluation of diagnostic tests for dry eye, mean central corneal and epithelial thickness in psoriasis patients. **Material and Methods:** The study was conducted with 54 psoriasis patients and 51 healthy volunteers. Psoriasis was diagnosed based on clinical findings and histopathological examination of the lesions. Those who were under systemic psoriasis treatment drugs were not included in the study. In all cases, in addition to routine eye examination, tear break-up time (TBUT), anesthetized Schirmer test, and corneal fluorescein staining (CFS) score were evaluated. In addition, mean central corneal thickness (CCT), and mean central corneal epithelial thickness (CCET) were measured by anterior segment optical coherence tomography. The study parameters were compared between the two groups. **Results:** The mean age of the psoriasis patients was  $37.85 \pm 12.44$  and the mean age of the control group was  $39.96 \pm 10.11$ . ( $p=0.331$ ) There were 36 (66.7%) women and 18 (33.3%) men in the psoriasis group, and 36 (70.6%) women and 15 (29.4%) men in the control group. ( $p=0.665$ ) TBUT was significantly lower ( $p=0.011$ ) and CFS score was significantly higher ( $p=0.039$ ) in the psoriasis group when compared to the control group. No significant difference was determined in the Schirmer test, CCT, and CCET between the two groups ( $p>0.05$ ). **Conclusion:** Dry eye is common in psoriasis, especially due to impaired tear stability, and could negatively affect the ocular surface. In our study, no statistically significant changes were detected in CCT and CCET. However, we think that new studies are needed on this subject.

**Keywords:** Psoriasis; dry eye; central corneal thickness; central corneal epithelial thickness; anterior segment optical coherence tomography

**ÖZET Amaç:** Bu çalışmanın amacı, psöriyazisli hastalarda kuru göz değerlendirme testlerini, ortalama santral korneal ve epitelyal kalınlığı değerlendirmektir. **Gereç ve Yöntemler:** Psöriyazis tanısı olan 54 hasta ile 51 sağlıklı gönüllü çalışmaya dahil edildi. Psöriyazis tanısı klinik bulgulara ve lezyonların histopatolojik incelemesine dayanılarak konuldu. Psöriyazis nedeniyle sistemik tedavi alan olgular çalışmaya dahil edilmedi. Bütün olgularda rutin göz muayenesine ilaveten göz yaşı kırılma zamanı (GYKZ), anestezi şirmer testi, korneal florescein boyanma (KFB) skoru değerlendirildi. Ayrıca ön segment optik koherens tomografi ile ortalama santral korneal kalınlık (SKK) ve ortalama santral korneal epitelyal kalınlık (SKEK) ölçüldü. Çalışma parametreleri iki grup arasında karşılaştırıldı. **Bulgular:** Psöriyazisli olguların yaş ortalaması  $37,85 \pm 12,44$  ve kontrol grubundaki olguların yaş ortalaması ise  $39,96 \pm 10,11$  idi. ( $p=0,331$ ) Psöriyazis grubunun 36'sı (%66,7) kadın, 18'i (%33,3) erkek, kontrol grubunun ise 36'sı (%70,6) kadın, 15'i (%29,4) erkekti. ( $p=0,665$ ) Psöriyazis grubunda kontrol grubuna kıyasla GYKZ anlamlı derecede düşük ( $p=0,011$ ) ve KFB skoru ise anlamlı derecede yüksek saptandı. ( $p=0,039$ ) Şirmer testi, SKK ve SKEK açısından ise iki grup arasında anlamlı bir fark saptanmadı ( $p>0,05$ ). **Sonuç:** Psöriyaziste kuru göz sık görülen oküler bulgulardandır. Özellikle göz-yaşı stabilitesinin bozulmasına bağlı ortaya çıkan kuru göz oküler yüzeyi olumsuz etkileyebilir. Bizim çalışmamızda SKK ve SKEK'da istatistiksel olarak anlamlı bir değişiklik saptanmamıştır. Ancak bu konuda yeni çalışmalara ihtiyaç olduğunu düşünmekteyiz.

**Anahtar Kelimeler:** Psöriyazis; kuru göz; santral korneal kalınlık; santral korneal epitelyal kalınlık; anterior segment optik koherens tomografi

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Psoriasis is a chronic inflammatory skin disease characterized by scaly erythematous plaques. It develops due to abnormal differentiation and proliferation of keratinocytes and infiltration of inflammatory cells into the papillary regions of the epidermis and dermis.<sup>1</sup> It affects about 2-4% of the global population.<sup>2</sup> Although its etiology has not been clarified, it was suggested that psoriasis could be an autoimmune disease where various environmental factors stimulate T-lymphocytes and lead to inflammation in individuals with a genetic predisposition. Beyond a skin disease, it is a systemic inflammatory disease. Systemic inflammation could affect the entire body, causing arthritis, obesity, metabolic syndrome, diabetes, hypertension, and atherosclerotic disease.<sup>3</sup> The most common ocular symptoms include blepharitis, conjunctivitis, dry eye, and anterior uveitis.<sup>4</sup> These symptoms are due to the direct impact of psoriatic plaques on the ocular surface, systemic inflammation affecting the ocular structures, and side effects of drugs and phototherapy used in the treatment of psoriasis.

Dry eye is a common ocular symptom in psoriasis. Various studies demonstrated that psoriasis patients had meibomian gland dysfunction (MGD), their tear lipid layer was affected, tear osmolarity increased, the number of goblet cells decreased in impression cytology, and they developed conjunctival squamous metaplasia.<sup>5-8</sup> These factors reduced tear stability, leading to dry eye and ocular surface degeneration.

In psoriasis, both the inflammation inherent in the disease and common eyelid and tear film pathologies could affect the cornea. Various studies demonstrated that corneal anatomical and biomechanical properties [such as central corneal and epithelial thickness, corneal hysteresis (CH), and corneal resistance factor (CRF)] were altered in psoriasis patients.<sup>9-12</sup> There are few studies in the literature regarding the effects of psoriasis on the cornea. Therefore, this study was planned to evaluate the effects of psoriasis on the cornea and changes in corneal thickness.

The present study aimed to evaluate diagnostic tests for dry eye [tear break-up time (TBUT), Schirmer test, corneal fluorescein staining (CFS)

score], and central corneal and epithelial thickness measured with anterior segment-optical coherence tomography (AS-OCT) in psoriasis patients.

## MATERIAL AND METHODS

This case-control study consisted of 54 psoriasis patients without systemic treatment and 51 healthy volunteers, which was performed in dermatology and ophthalmology departments of the Elazığ Fethi Sekin City Hospital between June 2023 and October 2023. The study was performed with the approval of the Fırat University Non-Invasive Research Ethics Committee (date: June 8, 2023; 2023/08-32), and all procedures were in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients.

Psoriasis was diagnosed by the dermatologist based on clinical findings and histopathological examination of the lesions. Those who were under systemic psoriasis treatment drugs, who previously underwent ocular surgery, with a history of trauma, eyelid and ocular surface pathologies, who used contact lenses, with other eye pathologies such as glaucoma and uveitis, who were under systemic anticholinergic and antihistamine treatments, who had systemic diseases other than psoriasis (e.g., diabetes, goiter), with high refractive defects (3 diopter cylindrical, 6 diopter spherical), and who used artificial tear drops during the previous month were not included in the study.

All patients underwent a complete ophthalmological examination, including best-corrected vision, intraocular pressure, and anterior and posterior segments. Furthermore, TBUT, anesthetized Schirmer test, CFS score, mean central corneal thickness (CCT), and mean central corneal epithelial thickness (CCET) were recorded as study parameters. The right eyes of the patients were used for analysis in the study.

The dry eye was analyzed with the TBUT and Schirmer test, and the ocular surface was analyzed based on the CFS score. In the TBUT test, 2% fluorescein drops were instilled into the eye. The time from the last blink until the first dry spot was recorded, this process was repeated three times, and

the mean duration was calculated. The CFS score was recorded 5 minutes after fluorescein was instilled based on the Oxford scale. Based on this scale, corneal staining was graded between 0 (no staining) and 5 (severe), and Grades 1 and 2 were classified as mild, Grade 3 was classified as moderate, and Grades 4 and 5 were classified as severe.<sup>13</sup> In the Schirmer test, local anesthetic drops were instilled and a Schirmer strip was placed on the lower fornix. Five minutes later, aqueous tear secretion was determined based on strip wetness. AS-OCT was conducted initially to prevent the impact of invasive procedures on corneal epithelium. Mean CCT and CCET were measured in the central 5 mm distance to the cornea with Spectral-Domain AS-OCT (OCT HS100, Canon, Australia). The above-mentioned parameters were compared between the two groups.

### STATISTICAL ANALYSIS

Statistical analyses were conducted on SPSS v 25.0 (IBM Corp., USA). The Kolmogorov-Smirnov test was employed to determine the normal distribution of the numerical data. Descriptive statistics of normally distributed variables are presented as mean±standard deviation, and non-normally distributed variables are presented as medians (minimum-maximum). Variables that exhibited normal distribution were compared with the independent samples t-test. Variables that did not exhibit normal distribution were compared with the Mann-Whitney U test. Categorical variables are presented with frequencies and percentages and compared with the chi-square test.  $p < 0.05$  was accepted as statistically significant.

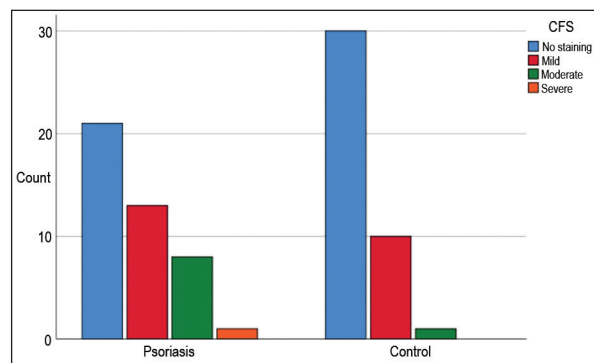
### RESULTS

The mean age of 54 psoriasis patients [36 (66.7%) female, 18 (33.3%) male] was  $37.85 \pm 12.44$  and the mean age of 51 healthy volunteers in the control group [36 (70.6%) female, 15 (29.4%) male] was  $39.96 \pm 10.11$ . The age and gender distributions were similar in the 2 groups ( $p = 0.331$ ,  $p = 0.665$ , respectively). TBUT was statistically significantly lower in the psoriasis group when compared to the control group ( $p = 0.011$ ). There were no statistically significant differences in the Schirmer, CCT, and CCET findings of the two groups ( $p = 0.141$ ,  $p = 0.930$ ,  $p = 0.294$ , respectively) (Table 1).

**TABLE 1:** Demographics characteristics and clinical findings of psoriasis and control group.

	Psoriasis (n=54)	Control (n=51)	p value
Age (year)	37.85±12.44	39.96±10.11	0.331*
Gender (female/male)	36/18	36/15	0.665*
TBUT (sec)	8 (3-20)	12 (4-20)	<b>0.011#</b>
Schirmer (mm)	15 (2-25)	15 (5-25)	0.141#
CCT (micron)	538.76±29.41	539.31±27.72	0.930*
CCET (micron)	54.02±2.36	53.31±3.65	0.294*

\*Independent samples t-test; #Mann-Whitney U test; \*Chi-square test; TBUT: Tear break up time; CCT: Central corneal thickness; CCET: Central corneal epithelial thickness.



**FIGURE 1:** CFS scores of psoriasis and control group.

CFS: Corneal fluorescein staining.

The CFS score was significantly higher in the psoriasis group when compared to the control group ( $p = 0.039$ , chi-square test) (Figure 1).

### DISCUSSION

Psoriasis is a systemic inflammatory disease that involves multiple organs. Previous studies reported that ocular involvement was observed in about 10% of psoriasis patients.<sup>14,15</sup> However, since most patients are asymptomatic, it could be suggested that eye involvement is more common than observed. Recently, thanks to advances in imaging methods, studies demonstrated that ocular findings were observed in more than half of the patients.<sup>16,17</sup> Psoriasis generally affects anterior segment structures such as eyelids, conjunctiva, cornea, and anterior uvea. Dry eye is among the most common symptoms.

Tear includes mucin, aqueous, and lipid components, and interference with one of these components leads to dry eye. The pathophysiology of dry eye ex-

acerbated by psoriasis has not yet been clarified. Karabulut et al. reported that TBUT was significantly lower in psoriasis patients when compared to the control group, and there was no significant difference in the Schirmer test. In the same study, conjunctival impression cytology demonstrated that squamous metaplasia was significantly high in psoriasis.<sup>8</sup> Demirci et al. reported that TBUT was lower, Ocular Surface Disease Index (OSDI) and corneal staining scores, and tear osmolarity were higher in psoriasis patients, and there was no significant difference in the Schirmer test.<sup>6</sup> Her et al. reported that TBUT was lower and corneal staining score was higher in psoriasis patients, there were no significant differences in the Schirmer test and meibomian gland function, epithelial cell morphology was altered in impression cytology, and the number of goblet cells decreased.<sup>7</sup> Kemeriz et al. demonstrated that TBUT was lower, OSDI and corneal staining scores were higher, MGD was common, meibomian gland loss increased in psoriasis patients when compared to the control group, and there was no significant difference in the Schirmer test.<sup>18</sup> Taheri et al. determined that TBUT and Schirmer test were lower in psoriasis patients, and a significant degree of meibomian gland atrophy was observed in meibography; however, there was no significant difference in the SM tube test (Echo Electricity, Japan), another test employed to analyze aqueous secretion.<sup>19</sup> Aragona et al. demonstrated that the OSDI score, TBUT, Schirmer test, lipid layer thickness, corneal and conjunctival staining, squamous metaplasia in impression cytology, corneal esthesiometry findings, and MGD score were significantly worse in psoriasis patients, and there was no significant difference in the meibomian gland secretion in meibography.<sup>5</sup> Studies generally reported low TBUT and high corneal and conjunctival staining scores, and variable Schirmer test results. This could be due to the fact that dry eye is induced by high tear evaporation and low tear stability due to MGD and goblet cell loss, rather than a lack of aqueous secretion in psoriasis. Thus, TBUT, a measure of tear film stability, was affected rather than the Schirmer test, a measure of aqueous tear secretion. Furthermore, the sensitivity and specificity of the Schirmer test are lower in dry eye diagnosis, and TBUT and ocular sur-

face staining are more accurate. In our study, it was determined that TBUT was lower and CFS score was higher in the psoriasis group; however, there was no significant difference in the Schirmer test.

The impact of dry eye on corneal and conjunctival epithelial thickness has not been evidenced. Erdélyi et al. reported that CCET was thinner in dry eye cases, and Cui et al. reported that corneal epithelium was thinner in the superior region; however, CCET was not different.<sup>20,21</sup> Fabiani et al. reported that CCET increased in the dry eye-induced mice model, and Kanellopoulos and Asimellis suggested that high CCET could be a clinical indicator of dry eye.<sup>22,23</sup> Gumus and Pflugfelder demonstrated that there was no significant difference in the bulbar conjunctival epithelium and CCET in dry eye cases, and Liang et al. reported that bulbar conjunctival epithelial thickness increased but CCET remained the same.<sup>24,25</sup> The difference between the studies could be due to patient groups with different ages and races, variable dry eye severity and duration, the presence of other comorbid systemic diseases, and differences between the employed devices. Corneal epithelial thickness could be affected due to the high dry eye incidence and ocular surface inflammation in various rheumatic diseases. Studies that investigated corneal epithelial thickness with AS-OCT in rheumatoid arthritis and Sjögren's syndrome patients demonstrated that superior corneal epithelial thickness decreased but CCET remained the same.<sup>26,27</sup> We reviewed 2 studies in the literature that investigated ocular surface epithelium with AS-OCT in psoriasis. Güneş et al. reported that CCET was significantly lower in psoriasis patients when compared to the control group. In the study, the mean CCET for the central 2 mm of the cornea was calculated and psoriasis cases with dry eye were not included in the study.<sup>10</sup> Ersan et al. reported that TBUT and Schirmer test were significantly lower in psoriasis patients, but there was no significant difference in the central corneal and bulbar conjunctival epithelial thicknesses. In the study, corneal epithelium was measured manually from a single focus in the central cornea.<sup>9</sup> In our study, the mean epithelial thickness of the central 5 mm area of the cornea was analyzed, and no significant difference was determined between the psoriasis and control groups.

Infiltration of the corneal stroma into inflammatory cells in rheumatic diseases and ocular surface inflammation induced by the comorbid dry eye leads to an increase in pro-inflammatory cytokines in the stroma and tears.<sup>28,29</sup> Thus, the increased catabolic activation could lead to corneal degradation, affecting corneal stromal thickness and biomechanical properties of the cornea. Various studies reported a significant decrease in CH and/or CRF in rheumatoid arthritis patients without a significant change in CCT.<sup>30-32</sup> Contrary to these findings, other studies reported that CCT was significantly low in rheumatoid arthritis and ankylosing spondylitis.<sup>33,34</sup> There are a limited number of studies that investigated corneal thickness and biomechanical properties of the cornea in psoriasis patients. Celik et al. reported that CH and CRF were significantly low in psoriasis patients, there was no significant difference in the CCT measurements determined with ultrasonic pachymetry; however, there were positive correlations between CCT with CH and CRF.<sup>11</sup> Edris et al. reported that CRF decreased significantly in psoriasis patients, and although there was a decrease in CCT measured with AS-OCT and CH, it was not statistically significant.<sup>12</sup> Ersan et al. reported that CCT measured with AS-OCT was significantly higher in psoriasis patients when compared to the control group.<sup>9</sup> As a result of these studies, it was revealed that corneal biomechanical properties were affected in various rheumatic diseases, even if no significant difference was detected in CCT. This shows us that the corneal morphology could alter without affecting the corneal thickness. In our study, similar to literature no statistically significant difference was determined in the CCT.

There are some limitations to this study. First, evaluation of the meibomian glands is important in determining the type of dry eye. However, the structure and functions of the meibomian glands were not evaluated in this study. Second, relatively small num-

ber of patients was used in this study. Larger groups and more comprehensive investigations are needed for acquiring more information.

## CONCLUSION

Dry eye is a common ocular symptom in psoriasis. Dry eye in psoriasis is mostly induced by the deterioration of tear film stability rather than lack of aqueous secretion and affects the ocular surface. Therefore, patients with psoriasis should be followed up and examined regularly. Adequate treatment should be started before ocular surface complications develop due to dry eye. Studies involving electron microscopy or confocal microscopy investigating cell morphology are needed to demonstrate corneal changes in psoriasis. We also think that new studies can be planned with larger patient groups.

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*During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.*

### Conflict of Interest

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

### Authorship Contributions

**Idea/Concept:** Elif Yusufoglu, Neşe Göçer Gürok; **Design:** Elif Yusufoglu, Neşe Göçer Gürok; **Control/Supervision:** Elif Yusufoglu; **Data Collection and/or Processing:** Elif Yusufoglu, Neşe Göçer Gürok; **Analysis and/or Interpretation:** Elif Yusufoglu; **Literature Review:** Elif Yusufoglu, Neşe Göçer Gürok; **Writing the Article:** Elif Yusufoglu; **Critical Review:** Elif Yusufoglu; **References and Fundings:** Elif Yusufoglu, Neşe Göçer Gürok; **Materials:** Elif Yusufoglu.

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