Ocular surface changes in moderate-to-severe acne vulgaris

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Abstract

- **AIM:** To investigate ocular surface disorders and tear function changes in patients with acne vulgaris and explore the potential relationship between acne vulgaris and dry eye.
- **METHODS:** This cross-sectional study included right eyes of 53 patients with acne vulgaris and 54 healthy controls. The participants completed the Ocular Surface Disease Index (OSDI) questionnaire. The following ocular surface-related parameters were measured: tear meniscus height (TMH), noninvasive tear breakup time (NIBUT), Schirmer I test (SIT), lipid layer thickness (LLT) score of the tear film, meibum score, meibomian gland orifice obstruction score, the ratio of meibomian gland loss, conjunctival hyperemia score, and corneal fluorescein staining (CFS) score.
- **RESULTS:** The stability of the tear film decreased in acne vulgaris patients. In the acne group, the TMH and NIBUT were lower, whereas the OSDI, meibum score, meibomian gland orifice obstruction score, ratio of meibomian gland loss, and conjunctival hyperemia score were higher compared with controls (P<0.05). There were no significant differences between OSDI, SIT, and CFS score (P>0.05). In two dry eye groups, the TMH, NIBUT, and LLT score were lower in the acne with dry eye (acne-DE) group, and the meibum score, meibomian gland orifice obstruction score, ratio of meibomian gland loss and conjunctival hyperemia score in the acne-DE group were higher (P<0.05). There were no significant differences between OSDI, SIT, and CFS score (P>0.05).
- **CONCLUSION:** Patients with moderate-to-severe acne vulgaris are more likely to experience dry eye than those without acne vulgaris. Reduced tear film stability and meibomian gland structure dysfunction are more pronounced in patients with moderate-to-severe acne and dry eye.
- **KEYWORDS:** acne vulgaris; meibomian gland dysfunction; dry eye; tear film

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INTRODUCTION

Dry eye is a chronic ocular surface disease that can damage patients’ vision and affect their quality of life¹, with a prevalence ranging from 5% to 50% in the global adult population (13.5%-31.4% in China) and increasing with age²-³. Dry eye can be caused by multiple factors. Furthermore, the relationship between skin diseases and dry eye has been reported in a few studies⁴-⁵. Acne vulgaris is a chronic inflammatory skin disease of the pilosebaceous unit that tends to occur in adolescence and primarily affects the face⁶. As a chronic inflammatory skin disease involving sebaceous glands, acne vulgaris may affect a special type of sebaceous glands—meibomian glands. Meibomian glands produce a lipid layer in the tear film and maintain the tear film stability. A change in their structure and function will increase tear evaporation, affect tear film stability, and lead to evaporative dry eye⁷. Isotretinoin has demonstrated effectiveness in treating acne vulgaris, but the majority of studies have also discovered that isotretinoin can result in a variety of ocular surface adverse effects⁸-¹¹. Only a small number of studies have shown that patients with acne...
vulgaris have clinical manifestations of dry eye and meibomian gland dysfunction (MGD)\textsuperscript{[12-15]} . However, no relationship between acne vulgaris and dry eye in the Chinese population has been reported, and the difference between dry eye patients with acne vulgaris and those without acne vulgaris has not been clarified.

This study aimed to investigate ocular surface changes in patients with moderate-to-severe acne vulgaris. Furthermore, the difference in ocular surface parameters between dry eye patients with and without acne vulgaris was explored to identify typical ocular surface manifestations in patients with acne vulgaris.

**SUBJECTS AND METHODS**

**Ethical Approval** This cross-sectional study was approved by the Ethics Committee of the First Affiliated Hospital of Kunming Medical University (No.LSL2023013). Written informed consent was obtained from all the subjects. This study adhered to the tenets of the Declaration of Helsinki. The methods were carried out in accordance with the relevant guidelines and regulations.

**Study Population** The right eyes of 53 patients with moderate-to-severe acne vulgaris (acne group) and 54 healthy individuals (nonacne group) were included in this study. All participants underwent dermatological examination to confirm the diagnosis of acne vulgaris by the same dermatologist at the Department of Dermatology, the First Affiliated Hospital of Kunming Medical University\textsuperscript{[6,16]} . The diagnostic criteria for dry eye were based on the Expert Consensus on Dry Eye in China: Examination and Diagnosis (2020)\textsuperscript{[17]} . The exclusion criteria included: 1) a history of eye surgery, eye trauma, or infectious eye disease; 2) any systemic disease (such as Sjögren’s syndrome that may affect the ocular surface) or any skin disease other than acne vulgaris; 3) the use of topical or systemic drugs within the past 2wk (such as antiandrogens, antidepressants, and antihistamines); 4) previous oral administration of isotretinoin; 5) the use of contact lenses, eye makeup, eyelash implants, eyeliner tattoos, and any other eye cosmetic operations; 6) pregnant and lactating women.

**Study Design** All participants were evaluated using the ocular surface disease index (OSDI) questionnaire. The following ocular surface-related parameters were measured: tear meniscus height (TMH), noninvasive tear breakup time (NIBUT), Schirmer I test (SIT), lipid layer thickness (LLT) score of the tear film, meibum score, meibomian gland orifice obstruction score, the ratio of meibomian gland loss, conjunctival hyperemia score, and corneal fluorescein staining (CFS) score. Baseline information which was related to dry eye\textsuperscript{[18-20]} , including age, gender, body mass index (BMI), sleep time, video display terminal (VDT) use time, were recorded for all participants to reduce bias on the results.

Statistical differences in all parameters between the acne and nonacne groups were analyzed. Furthermore, all the above-mentioned parameters were compared between participants with dry eye in the acne group (acne-DE group) and nonacne group (nonacne-DE group).

**Clinical Examinations** All participants were evaluated using the OSDI questionnaire (Allergan, Irvine, CA, USA) before the examination to obtain subjective complaints related to the ocular surface. The patients marked the frequency of their complaints in 3 subscales. The final score was calculated and interpreted as follows: 0-12, normal; 13-22, mild dry eye disease; 23-32, moderate dry eye disease; >33, severe dry eye disease\textsuperscript{[21-22]} .

TMH, NIBUT, LLT score of the tear film, and conjunctival hyperemia score were measured using the Kanghua Dry Eye Analyzer (DED-1L, Kanghua Ruiming, Chongqing, China). SIT was performed without anesthesia, a standard Schirmer test strip (Tianjin Jingming New Technology Development Co., Ltd., China) was placed at the one-third lateral conjunctival fornix avoiding any contact with the cornea, and the amount of wetting was recorded in 5min. The extent of corneal epithelial damage was evaluated using a fluorescein sodium test paper (Tianjin Jingming New Technology Development Co., Ltd., China), and the CFS score, which was recorded with the 4-quadrant 12-point technique, was used to describe the results.

The eyelid margins were examined with a slit-lamp biomicroscope and an anterior segment camera system of the same device (DED-1L, Kanghua Ruiming, Chongqing, China). The meibomian gland orifice obstruction score of each eyelid was assessed using the following scoring system\textsuperscript{[23]} : 0 points, unobstructed opening; 1 point, the meibomian gland orifice is film-like and bulges on the surface of the skin; 2 points, the meibomian gland is blocked in the orifice, protruding on the surface of the skin; 3 points, severe blockage of the meibomian gland orifice.

Besides, the meibum quality was evaluated by squeezing the middle part of the lower and upper eyelids, and the meibum score was measured in five meibomian glands using the following scoring method\textsuperscript{[24]} : 0 points, clear and transparent liquid; 1 point, turbid liquid; 2 points, turbid granular discharge; 3 points, thick toothpaste-like secretions; 4 points, no secretion. The total score for each eyelid ranged from 0 to 20 points. Furthermore, infrared meibography images of the everted upper and lower eyelids of right eyes were captured (DED-1L, Kanghua Ruiming, Chongqing, China). The ratio of meibomian gland loss was calculated from these images using Image J (Vision1.46r) computer graphics software (Figure 1).

**Statistical Analysis** All data were analyzed using the IBM SPSS Statistics 26 software (SPSS Inc. Chicago, IL, USA)
and expressed as the mean±standard deviation. The sex composition ratio was based on Chi-square test results. The basic subject characteristic data of each group were tested for normality. A t-test using the mean comparison of two independent samples following the normal distribution was performed. The Mann-Whitney U test was employed if the normal distribution was violated, and \( P<0.05 \) denoted a statistically significant difference.

RESULTS

Demographic Characteristics  A total of 107 participants (107 eyes) were included in this study: 53 participants (53 eyes) in the acne group and 54 participants (54 eyes) in the nonacne group. There were no significant differences in important non-experimental factors, such as age, sex, and BMI between the two groups (Table 1).

Participants in the acne and nonacne groups who met the diagnostic criteria for dry eye were included in the acne-DE and nonacne-DE groups, respectively. There were no statistically significant differences in basic features of the two dry eye groups (Table 2).

Ocular Surface Discomfort in Acne Vulgaris  We analyzed the OSDI scores of the two groups to explore whether there was any difference in ocular surface discomfort between the participants with or without acne vulgaris. The OSDI scores in the acne and nonacne groups were 23.11±17.15 and 15.43±12.13, respectively (\( P<0.05 \); Figure 2A). Furthermore, we classified OSDI scores into four grades: grade 1, 0-12 points; grade 2, 13-22 points; grade 3, 23-32 points; and grade 4, 33-100 points. The proportions of different OSDI grades in the acne and nonacne groups are shown in Table 3 and Figure 2B. Compared to the nonacne group, the acne group had a greater proportion of participants with higher OSDI values.

Ocular Surface Changes in Moderate-to-Severe Acne Vulgaris  We analyzed the tear film water layer and stability parameters (TMH, NIBUT, and SIT), tear film lipid layer and meibomian gland parameters (LLT score, meibum score, meibomian gland orifice obstruction score, and the ratio of meibomian gland loss), conjunctival hyperemia score, and CFS score of all participants to explore the differences in ocular

![Figure 1](image1.png) Methods for measuring the ratio of meibomian gland loss.

![Figure 2](image2.png) Comparison of ocular surface discomfort in participants

A: Comparison of OSDI scores between acne and nonacne groups: participants with acne vulgaris showed more significant ocular surface discomfort than those without acne vulgaris. B: Stacked column chart showing the detailed distribution of different symptom grades among participants. In comparison to the nonacne group, the acne group had a greater proportion of participants with higher OSDI values. OSDI: Ocular Surface Disease Index. \(^{1}\)\( P<0.01 \). Error bar: Standard deviation.

<table>
<thead>
<tr>
<th>Table 1 Demographic characteristics of the subjects</th>
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<td>Parameters</td>
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<td>Age (y)</td>
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<td>Sex ratio</td>
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<td>BMI (kg/m(^2))</td>
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<td>Sleep time (h/d)</td>
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<td>VDT use time (h/d)</td>
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BMI: Body mass index; VDT: Video display terminal.

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<th>Table 2 Demographic characteristics of acne-DE and nonacne-DE groups</th>
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<td>Parameters</td>
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<td>BMI (kg/m(^2))</td>
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<td>Sleep time (h/d)</td>
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<td>VDT use time (h/d)</td>
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DE: Dry eye; BMI: Body mass index; VDT: Video display terminal.
Ocular surface characteristics between the acne and nonacne groups (Figures 3-5).

Compared with the nonacne group, patients with moderate-to-severe acne vulgaris showed significant changes in the ocular surface: TMH (0.18±0.05 vs 0.22±0.06 mm), first NIBUT (NIBUTf; 3.90±2.38s vs 4.64±2.25s), and average NIBUT (NIBUTav; 6.29±2.89s vs 7.66±2.66s) were lower in the acne group, whereas the meibum score (2.89±3.42 vs 1.46±2.45), the ratio of upper eyelid meibomian gland loss (0.26±0.11 vs 0.20±0.09), the ratio of lower eyelid meibomian gland loss (0.31±0.15 vs 0.21±0.15), upper eyelid meibomian gland orifice obstruction score (0.85±0.95 vs 0.33±0.64), lower eyelid meibomian gland orifice obstruction score (1.02±0.95 vs 0.44±0.72), and conjunctival hyperemia score (1.56±0.28 vs 1.42±0.29) were higher ($P<0.05$). There was no significant difference in CFS score (1.26±2.03 vs 1.77±2.94), SIT (16.24±9.92 vs 18.50±9.95) and LLT score (3.74±1.13 vs 4.31±1.41) between the two groups ($P>0.05$).

The results showed that tear film stability in the acne-DE group was worse than that in the nonacne-DE group ($P<0.05$; Figure 6).

### Table 3 The portion of different ocular symptom grades in each group

<table>
<thead>
<tr>
<th>Group</th>
<th>0-12</th>
<th>13-22</th>
<th>23-32</th>
<th>33-100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acne group</td>
<td>28.4</td>
<td>22.6</td>
<td>24.5</td>
<td>24.5</td>
</tr>
<tr>
<td>Nonacne group</td>
<td>46.3</td>
<td>33.3</td>
<td>9.3</td>
<td>11.1</td>
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</tbody>
</table>

**Dry Eye and Acne Vulgaris** According to the Chinese Dry Eye Expert Consensus: Examination and Diagnosis (2020), there were 38 patients with dry eye in the acne group (71.70%) and 26 patients with dry eye in the nonacne group (48.15%). The proportion of dry eye patients in the acne group was significantly higher than that in the nonacne group ($P<0.05$; Figure 6).

**Ocular Surface Changes in Acne Vulgaris Patients with Dry Eye** We analyzed tear film stability parameters, meibomian gland parameters, conjunctival hyperemia score, and CFS score of the acne-DE and nonacne-DE groups to compare the differences in ocular surface changes in dry eye participants with or without acne vulgaris.

Compared with the nonacne-DE group, TMH (0.18±0.05 mm vs 0.22±0.06 mm), NIBUTf (3.43±2.03s vs 4.39±1.94s), NIBUTav (5.69±2.65s vs 7.14±2.52s), and LLT score (3.74±1.13 vs 4.31±1.41) were lower in the acne-DE group, whereas the meibum score (2.68±2.52 vs 1.77±2.94), upper eyelid meibomian gland orifice obstruction score (1.03±0.97 vs 0.50±0.71), lower eyelid meibomian gland orifice obstruction score (1.08±0.97 vs 0.54±0.76), the ratio of upper eyelid meibomian gland loss (0.26±0.10 vs 0.20±0.11), the ratio of lower eyelid meibomian gland loss (0.32±0.15 vs 0.23±0.17), and conjunctival hyperemia score (1.51±0.27 vs 1.33±0.24) increased ($P<0.05$). There was no significant difference in CFS score (1.55±2.21 vs 1.38±1.83) and SIT (16.24±9.92 vs 18.50±9.95) between the two groups ($P>0.05$).

The results showed that tear film stability in the acne-DE group was worse than that in the nonacne-DE group. The structural and functional changes in the meibomian glands were especially obvious based on all ocular surface parameters (Figures 7-9).
DISCUSSION

Patients with dry eye typically experience eye discomfort, which has become a common reason for patient visits. In our study, we found that participants with acne vulgaris showed more significant ocular surface discomfort than those without acne vulgaris. By analyzing the dry eye index of participants to explore the causes of eye discomfort, we found that the stability of the tear film decreased in the acne group, which was consistent with previous studies [12-14]. The SIT of the participants in the two groups did not show any difference, but the structural and functional changes of meibomian glands were obvious in the acne group, suggesting
that changes in the meibomian glands might be the primary factor causing ocular surface changes and related symptoms. Abnormalities of meibomian glands can be related to the damaged lipid layer of the tear film, resulting in increased evaporation of the aqueous layer and tear film instability.

As the largest sebaceous gland in the body, the meibomian glands are found in the meibomian plate of the upper and lower eyelids, opening directly at the eyelid edge. Meibomian glands release meibum, which forms the lipid layer of the tear film and can prevent tear evaporation, reduce surface tension, and stabilize the tear film.\(^{[25]}\) Consistent with the results of previous studies\(^{[14]}\), we discovered that acne vulgaris patients had higher levels of meibomian gland orifice obstruction, meibomian gland atrophy, and meibum score and increased meibum viscosity. At the same time, we compared the indicators of dry eye patients in the two groups and found that the structural and functional damage to the meibomian glands was more pronounced in the acne-DE group. Propionibacterium acnes, a key player in acne vulgaris, may be associated with these changes. Meibomian glands and eyelid margins may also be...
affected by *Propionibacterium acnes* in patients who suffer from acne vulgaris, and the glycocalyx complex secreted by overmultiplying *Propionibacterium acnes* might cause alterations in meibium viscosity and obstruct meibomian gland openings[26]. Zhang *et al*[27] compared differences in ocular surface bacteria between patients with or without MGD and found that the positive rate of anaerobic bacteria culture in the MGD group significantly increased, among these anaerobic bacteria, *Propionibacterium acnes* accounted for the highest proportion, reaching 75%, which showed that *Propionibacterium acnes* was crucial to the development of MGD. At the same time, obstruction of the meibomian gland opening hinders meibum secretion, the pressure in meibomian gland ducts increases, and toxins or proteases released by bacteria in the meibum damage epithelial cells of the gland, eventually leading to meibomian gland atrophy[25,27]. Blockage of the meibomian gland opening in MGD can result in a hypoxic environment and promote the growth of anaerobic bacteria[27]. Therefore, MGD and *Propionibacterium acnes* may be mutually causative in patients with acne vulgaris: *Propionibacterium acnes* overgrowth causes meibomian gland opening obstruction and changes the meibum, which, in turn, promotes anaerobic bacteria growth. This inference also corroborates our findings that ocular surface indicators showed greater changes in the acne-DE group than in the nonacne-DE group. Therefore, meibomian gland examination should be emphasized in dry eye patients with moderate-to-severe acne vulgaris.

Moreover, since the inflammatory response is present throughout the pathogenesis of acne vulgaris, the involvement of ocular surface inflammation might also be one of the causes of the decrease in tear film stability. Lipase and toxins produced by bacteria may cause ocular surface cell damage and instability of the tear film, leading to ocular surface inflammation and irritation[28]. The instability of the tear film triggers a series of inflammatory cascades on the ocular surface, which can damage goblet cells and mucus, cause epithelial cell death, and even lead to punctate epithelial lesions[28-30]. In our study, we found a higher degree of conjunctival hyperemia in patients with moderate-to-severe acne vulgaris than in those without acne vulgaris. However, there was no significant difference in CFS scores between the groups, indicating that the decline in tear film stability and changes in meibomian glands in patients with acne vulgaris did not cause corneal epithelial lesions. The conjunctival epithelium is one of the earliest altered and most reactive structures in dry eye patients. Lesions in the conjunctival epithelium frequently occur before those in the corneal epithelium[28,31]. Prior research on inflammation and damage of the ocular surface in acne vulgaris patients has caused a debate. Similar to our study, Muhafiz *et al*[34] found no significant difference between the acne vulgaris and control groups when conjunctival cells were evaluated by impression cytology. However, Koca and Oral[31] found that the staining score assessed by the Oxford scale was significantly higher in the acne group. Therefore, whether patients with acne vulgaris experience damage to the ocular surface and the characteristics of ocular surface changes requires further exploration.

According to the diagnostic criteria of dry eye in the Chinese Dry Eye Expert Consensus, we found that the proportion of dry eye in the acne group was significantly higher than that in the nonacne group. Previous studies did not investigate the difference in the proportion of dry eye population, and only Ozdemir *et al*[32] found that the number of participants with abnormal TBUT, low Schirmer value, and subjective complaints significantly increased in the acne group. Therefore, people with moderate-to-severe acne vulgaris are more likely to experience dry eye.

Excessive secretion of lipids by the sebaceous glands is considered a prerequisite for acne vulgaris[32]. Various dietary factors can cause excessive secretion of lipids. Specifically, studies have shown that the onset and worsening of acne vulgaris are associated with high-sugar and high-fat diets[33-35]. Studies also show that people with acne vulgaris tend to have diets higher in fat and sugar than those without the acne vulgaris[33]. Additionally, high-sugar and high-fat diets are also external risk factors for MGD[30] and might lead to a decrease in tear film stability. Studies have demonstrated that a high-fat diet can result in pathological changes in lacrimal acini and induce a chronic inflammatory response in meibomian glands[37-38]. Hence, eating habits might be an important bridge connecting acne vulgaris and dry eye, and people suffering from acne vulgaris usually have dietary habits that are rich in sugar and fat, which affect the stability of the tear film. Therefore, attention should also be paid to dietary modifications in acne vulgaris individuals who have ocular surface changes.

Oral isotretinoin is an important treatment for moderate-to-severe acne vulgaris[16], but studies showed that patients treated with oral isotretinoin have an increased risk of meibomian gland atrophy, corneal epithelial detachment, and other signs of ocular surface damage[5,11]. However, there is currently no effective clinical treatment for meibomian gland atrophy[39], and if the condition persists, it might even cause varying degrees of ocular surface damage. Thus, early diagnosis of ocular surface alterations in acne vulgaris patients is essential before starting isotretinoin therapy.

Patients with moderate-to-severe acne vulgaris are more likely to suffer from dry eye than those without acne, and reduced tear film stability and impaired meibomian gland structure
Ocular surface changes in acne vulgaris

and function are also important reasons for ocular surface changes. Ocular surface changes were also more pronounced in dry eye patients with moderate-to-severe acne vulgaris than those without acne vulgaris. Early assessment of the ocular surface status and prevention and treatment of dry eye in patients with moderate-to-severe acne vulgaris is necessary.

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REFERENCES

25 Knop E, Knop N, Millar T, Obata H, Sullivan DA. The international workshop on meibomian gland dysfunction: report of the


