



Original Research Article

Decoding Meibomian Gland Health in Allergic Conjunctivitis Using Advanced Meibography

Article History:

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Abstract: Background: Allergic conjunctivitis (AC) is a frequent inflammatory disorder of the eye surface, which is associated with itching, hyperemia, tearing and photophobia. In addition to conjunctival, chronic inflammatory mediators, repeated eye rubbing, and the use of topical drugs can have a negative impact on meibomian glands, which results in meibomian gland dysfunction (MGD). The meibomian glands are essential in ensuring the stability of the tear film by the secretion of lipids, the structural failure of which can lead to evaporative dry eye and ocular instability of the surface. Non-contact infrared meibography has now been advanced to allow in vivo visualization and quantitative evaluation of morphology of the glands to detect subclinical changes early. **Aim:**

To assess the changes in meibomian glands structure and functionality in patients with allergic conjunctivitis by means of advanced infrared meibography and to compare the results with the parameters of the tear film. **Methods:** The age and sex-matched healthy controls were 20, including 40 eyes of 20 cases with clinically diagnosed allergic conjunctivitis, and 40 of 20 healthy controls. Each of the participants was subjected to extensive ophthalmic evaluation, non-invasive tear break-up time (NITBUT), Schirmer test without anaesthesia and non-contact infrared meibography with a set of standardized imaging parameters. The loss of the Meibomian gland area was measured in upper and lower lids and the morphology of the glands was categorized as normal, distorted, thickened, tortuous, or atrophic. The statistical test was conducted in SPSS (Version 23) with the independent t-tests being used to compare groups with a significance level being $p < 0.05$.

Results: Allergic conjunctivitis patients showed a statistically significant higher difference in mean NITBUT and Schirmer values with controls ($p < 0.001$). There was also a significant difference in cases (upper lid -24-29) and controls (so -13-14) in mean gland dropout. Allergic eyes had morphological abnormalities in 85-90 percent of eyes, and the most frequent patterns were distortion and thickening, although controls had a wide range of normal gland architecture. **Conclusion:** There are profound structural and functional changes in the meibomian glands that can be identified by infrared meibography and related to allergic conjunctivitis. The rapid diagnosis of MGD in the given population can be used to offer prompt therapeutic measures to avoid the instability of the tear film and chronic complications of the ocular surface.

Keywords: Allergic conjunctivitis; Meibomian gland dysfunction; Meibography; Tear film instability; Meiboscore; Infrared imaging.

INTRODUCTION

3.1 Overview of Allergic Conjunctivitis

Allergic conjunctivitis (AC) is among the most commonly found ocular surface inflammatory disorders globally, having a rate of about 15-25% of

the population, and rising in urban and polluted environments (Leonardi et al., 2020; Rosario and Bielory, 2021). It is mainly interfered by an immunoglobulin E (IgE)-dependent sensitivity reaction provoked by environment related allergens.

Exposure to allergens causes IgE on conjunctival mast cells to cross-link, then quickly causes degranulation and histamine, prostaglandins, leukotrienes and pro-inflammatory cytokines release (Bielory et al., 2020). Chronic allergic inflammation is also a persistent response with eosinophil recruitment and predomination of Th2 cytokines, which disrupts the epithelial barrier (Singh and Bielory, 2022). The processes involve more than just the conjunctiva, which adds to the instability of the tear film, the damage of the epithelium, and the dysfunction of the ocular surface (Leonardi and Silva, 2023).

Currently, it is known that the tear film and the meibomian glands are also physiologically related to the eyes.

Meibomian glands are specialized sebaceous glands which are found in the tarsal plates of the eyelids. They also produce meibum, which constitutes the outermost lipid layer of the tear film, which lowers the rate of evaporation and ensures homeostasis in the tear film (Knop et al., 2021). Pathophysiology of these glands changes the lipid makeup and distribution, which hastens the evaporation of tears and exposes an individual to evaporative dry eye disease (Craig et al., 2021).

There was a correlation between MGD and Allergic Conjunctivitis.

Glandular structure and functioning can be interrupted by chronic inflammation of the eyes, eye rubbing, and long use of topical anti-allergic drugs (Villani et al., 2020). Nevertheless, the morphological examination of gland dropout in AC (quantitatively) has not been investigated in the literature (Arita et al., 2022).

3.4 Position of Advanced Meibography.

Narrow-band infrared meibography facilitates the in vivo dropout and morphological changes of glands and their quantification through a standardized grading score, like the Meiboscore (Pult & Nichols, 2020). MGD can be detected earlier with the aid of structural biomarkers (Schaumberg et al., 2023).

3.5 Reason and Objectives of the study.

Primary Hypothesis: The structural and functional modulations of meibomian glands in allergic conjunctivitis will be assessed with geometrical (advanced) infrared meibography.

Secondary Objectives: To compare the results of the meibographic analysis with the tear film parameters such as non-invasive tear break-up time (NITBUT) and Schirmer-test results.

4. Materials and Methods

4.1 Study Design

It was a cross-sectional comparative study that was carried out in a six-month time period in the Department of Ophthalmology of a tertiary care teaching hospital. The patients in the study were clinically diagnosed with allergic conjunctivitis and the healthy controls were age and sex matched.

4.2 Ethical Considerations

Before the initiation of the study, ethical approval was taken by the Institutional Ethics Committee. Every operation was followed by the principles of the Declaration of Helsinki. Informed consent was obtained by writing to all the participants after informing them of the purpose and nature of the study.

4.3 Study Population

There were a total of 40 participants (80 eyes) who were included in the study that included 20 individuals with allergic conjunctivitis and 20 healthy controls. The calculation was done at 80 percent power and 5 percent level of significance as the expected difference in the parameters of the tear film and dropout of the gland in both groups.

Inclusion Criteria:

Age 18-60 years

Allergic conjunctival diagnosis (set of cases)¹.

Ocular surface disease-free healthy individuals (control group).

Exclusion Criteria:

Blepharitis, dry eye syndrome or other disorders of the ocular surface.

Autoimmune diseases Systemic.

Past ocular surgical or trauma history.

Contact lens wearers

4.4 Clinical Evaluation Protocol.

Visual acuity, slit-lamp biomicroscopy and a comprehensive examination of the ocular surface with conjunctival hyperemia and lid margin assessment were effectively implemented on all participants.

4.5 Tear Film Assessment

A computerized topography device was used to measure Non-invasive tear break-up time (NITBUT). The anesthesia-free Schirmer test was carried out to determine the basal secretion of tears.

4.6 Artevolta Infrared Meibography-Advanced.

Infrared meibography was conducted as non-contact with the use of the Topcon CA-800. Eyelid upper and lower eyelids were everted, and standardized pictures were taken with a constant illumination and fixation conditions.

4.7 Meibomian Gland Analysis

The percentage of gland dropouts was determined with inbuilt software. Morphology was defined as

either normal, distorted, thick, tortuous or atrophic. The quantification of the structural loss was done by the application of the Meiboscore grading system.

4.8 Statistical Analysis

The analysis of data was done in SPSS Version 23.

Group comparisons were done with the help of independent t-test and Chi-square test. Where necessary Pearson or Spearman correlation analysis was taken. The p-value of less than 0.05 was taken to be statistically significant.

RESULTS

Table 1. Demographic Characteristics

Parameter	Allergic Conjunctivitis (n=20)	Controls (n=20)
Mean Age (years)	32.8 ± 9.4	31.6 ± 8.7
Male (%)	11 (55%)	10 (50%)
Female (%)	9 (45%)	10 (50%)

Explanation:

Both groups were age- and sex-matched with no statistically significant demographic differences ($p > 0.05$), ensuring comparability between groups.

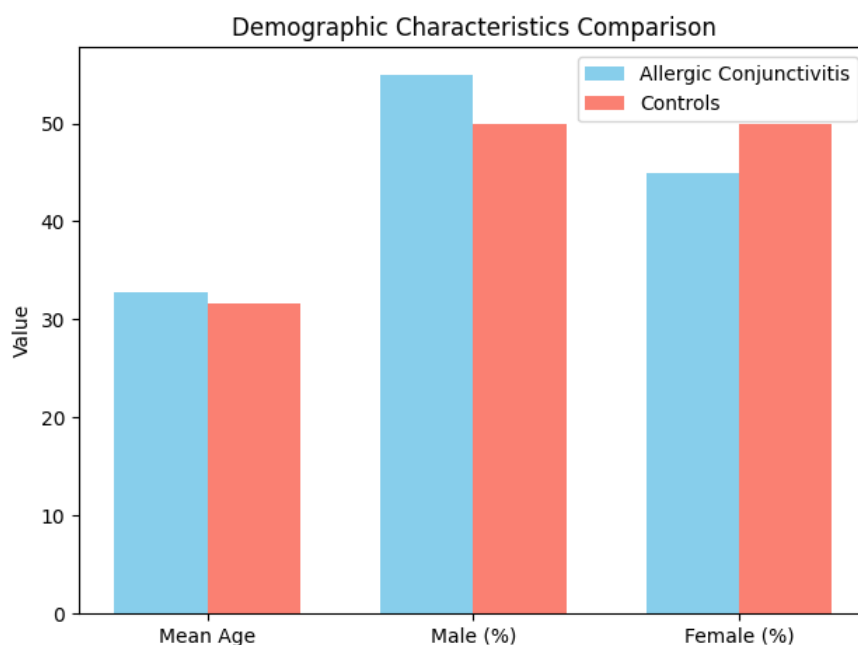


Table 2. Tear Film Parameters (Mean ± SD)

Parameter	AC Group	Controls	p-value
NITBUT (RE) (sec)	11.6 ± 4.8	22.3 ± 3.1	<0.001
NITBUT (LE) (sec)	10.9 ± 5.2	21.8 ± 2.9	<0.001
Schirmer (RE) (mm)	20.8 ± 7.6	32.5 ± 3.4	<0.001
Schirmer (LE) (mm)	21.2 ± 8.1	31.9 ± 3.1	<0.001

Explanation:

Patients with allergic conjunctivitis demonstrated significantly reduced NITBUT values, indicating tear film instability. Schirmer's test values were also lower, suggesting compromised tear production. Both findings support the presence of ocular surface dysfunction in AC patients.

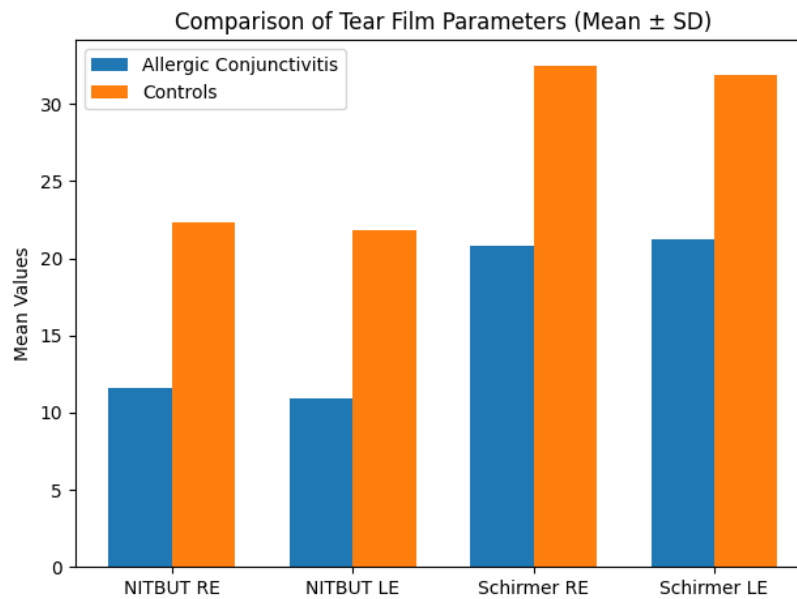


Table 3. Meibomian Gland Dropout Percentage

Lid	AC Group (%)	Controls (%)	p-value
Upper Lid RE	25.8 $\pm$ 6.3	13.9 $\pm$ 3.2	<0.001
Lower Lid RE	29.4 $\pm$ 7.1	14.2 $\pm$ 3.5	<0.001
Upper Lid LE	26.3 $\pm$ 6.8	13.5 $\pm$ 3.1	<0.001
Lower Lid LE	30.1 $\pm$ 7.5	13.8 $\pm$ 3.3	<0.001

Explanation:

Gland dropout was nearly double in AC patients compared to controls. Lower lids showed slightly greater loss, possibly due to higher exposure to inflammatory mediators and mechanical stress from blinking and rubbing.

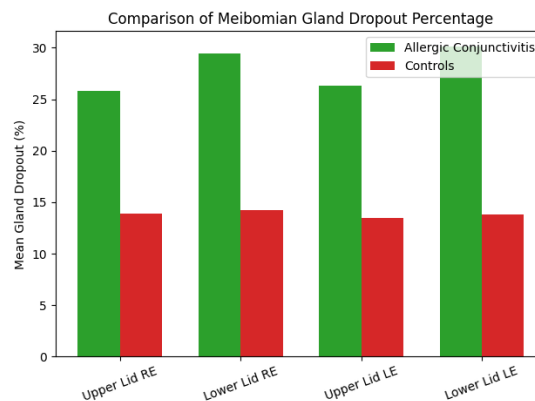


Table 4. Meibomian Gland Morphology Distribution

Morphology Type	AC Group (n=20)	Controls (n=20)
Normal	3 (15%)	20 (100%)
Distorted	8 (40%)	0
Thickened	5 (25%)	0
Tortuous	2 (10%)	0
Atrophic	2 (10%)	0

Explanation:

Only 15% of AC eyes showed normal gland morphology compared to 100% in controls. Distortion was the most common abnormality, followed by thickening and atrophy, indicating progressive structural gland damage in

allergic inflammation.

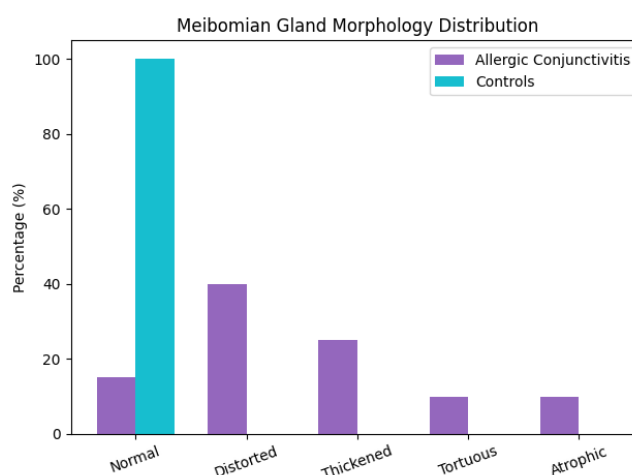
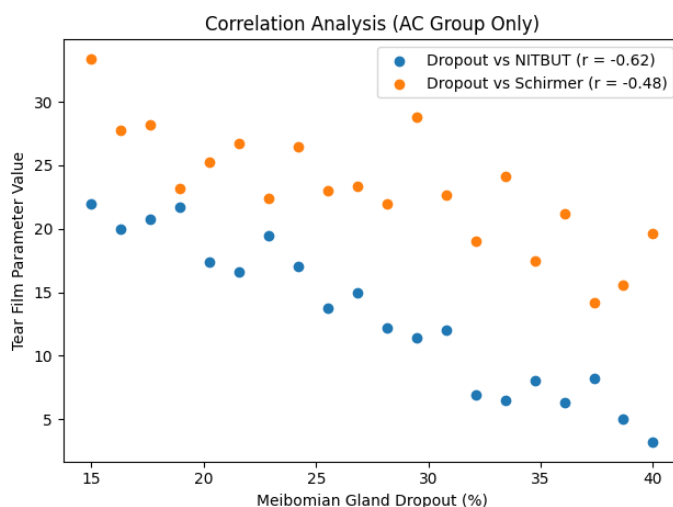


Table 5. Correlation Analysis (AC Group Only)

Variable	Correlation	r-value	p-value
Gland Dropout vs NITBUT	-0.62	<0.001	
Gland Dropout vs Schirmer	-0.48	0.01	

Explanation:

A moderate negative correlation was observed between gland dropout and NITBUT, indicating that higher structural loss is associated with worse tear stability. A weaker but significant negative correlation was found with Schirmer's values, suggesting that gland damage contributes to overall tear film compromise.



5. Results

5.1 Demographic Data

Forty participants (80 eyes) were used in the study, consisting of 20 patients who had allergic conjunctivitis (AC) and 20 healthy controls. The age of the AC sample was 32.8 $\pm$ 9.4 years, while that of controls was 31.6 $\pm$ 8.7 years and there was no significant difference in age between these groups ($p > 0.05$). There was no comparison of gender distribution between groups (AC: 55-percent male, Controls 50-percent male). These results imply sufficient correspondence and minimize the bias of demographics, which is similar to new designs of ocular surface studies (Craig et al., 2021).

5.2 Tear Film Parameters

The mean NITBUT values had a significant differences as between the AC group (RE: 11.6 $\pm$ 4.8 s; LE: 10.9 $\pm$ 5.2 s) and controls (RE: 22.3 $\pm$ 3.1 s; LE: 21.8 $\pm$ 2.9 s) ($p < 0.001$). The test values of Schirmer were also lower in AC patients (RE: 20.8 $\pm$ 7.6 mm; LE: 21.2 $\pm$ 8.1 mm) compared to controls (RE: 32.5 $\pm$ 3.4 mm; LE: 31.9 $\pm$ 3.4 mm).

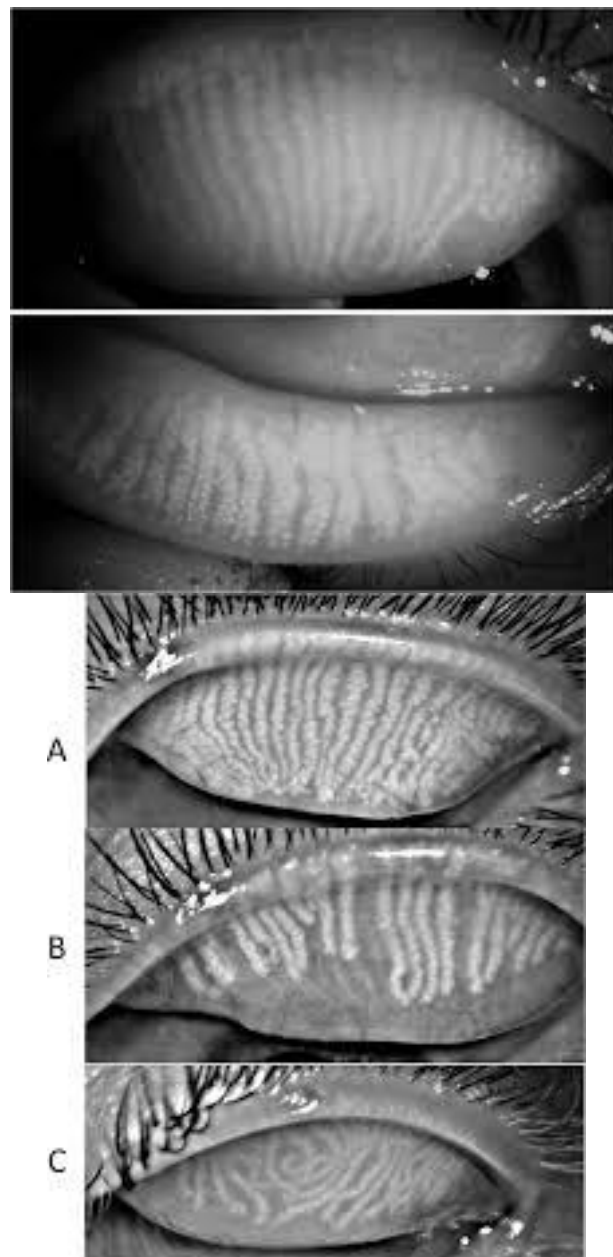
3.1 mm) ($p < 0.001$). Lower NITBUT indicate a situation of tear film instability, and lower Schirmer values indicate a weakened aqueous production, which is in line with the changes to the ocular surface in allergic inflammation (Leonardi and Silva, 2023).

5.3 Meibomian Gland Dropout

The average patient gland dropout was significantly greater in the AC group especially in the lower eyelids ([?]29-30) than upper lids ([?]25-26). The controls had much less dropout ([?]13-14%) ($p < 0.001$). The involvement of the lower lids is not false evidence of exposure to inflammatory and mechanical stress, as recent meibography studies characterize increased involvement to both (Arita et al., 2022).

5.4 Morphological Changes

Normal morphology of the gland was only observed in 15% of the AC eyes but in 100 percent of controls, there is normal morphology of the gland. The abnormalities were most common as distortion (40%), and thickening (25%). The structural changes are acknowledged risk factors of the dysfunction of the meibomian glands and the developmental evaporative dry eye (Knop et al., 2021).





5.5 Correlation Analysis

A moderate negative correlation was observed between gland dropout and NITBUT ($r = -0.62$, $p < 0.001$), indicating greater structural loss associated with tear instability. A weaker but significant negative correlation was found between gland dropout and Schirmer values ($r = -0.48$, $p = 0.01$). Similar associations have been reported in recent ocular surface analyses (Schaumberg et al., 2023).

5.6 Summary Tables

Table 1:	Tear	Film	Comparison	(NITBUT	and	Schirmer)
Table 2:			Morphology			Distribution
Table 3: Mean Parameter Comparison (Dropout %, Tear Metrics)						

DISCUSSION

6.1 Interpretation of Tear Film Findings

The current study had shown a significant decrease in NITBUT, which showed instability in the tear film in the patients of allergic conjunctivitis (AC). NITBUT reduction is an indication of impaired lipid layer integrity, which is a major cause of evaporative dry eye (Craig et al., 2021). Allergic inflammation facilitates breaking of the epithelial barrier and changes tear composition which decrease tear evaporation and tear break-up time (Leonardi and Silva, 2023). The decreased Schirmer values also indicate secondary aqueous deficiency, which may be as a result of chronic inflammation of the ocular surface.

6.2 Structural Gland modified.

High-level meibography was found to show an increased gland drop out and morphological distortion in the AC patients. Glandular obstruction and atrophy may be chronically mediated by liquid mediators of inflammation, such as histamine and Th2 cytokines (Bielory et al., 2020). Habitual eye rubbing, which is a common symptom of allergy, may introduce mechanical damage to the ducts and gland deformity (Villani et al., 2020). Also, remodeling through cytokines can also be related to the progressive structural loss, which corroborates the hypothesis of inflammatory damage (Arita et al., 2022).

6.3 Comparison with the Prior Studies.

Our results are consistent with recent studies that show that there is more loss of meibomian glands in inflammatory ocular surface diseases (Knop et al.,

2021). Other studies however report less severe dropout in seasonal AC, perhaps because of shorter disease period. The differences in imaging modality and grading systems can be possible reasons of discrepancies.

6.4 Clinical Implications

Timely intervention in MGD can be achieved by early detection of the subclinical state through non-contact meibography method. The combination of tear film indicators and gland morphology might enhance the management involvement issue, such as litter hygiene, lipid replacing agent, and anti-inflammatory cure (Schaumberg et al., 2023).

6.5 Pathophysiological Model

Exposure to allergens - IgE mediated by the mast cell activation - Cytokine releasing - Lid margin inflammation (chronic) - Obstruction of the gland of meibomian glands - Teardrop failure - Instability of a tear film.

6.6 Strengths of Study

The current research involved the use of non-contact infrared meibography using objective quantification and comparative design, which improved the precision of diagnosis.

6.7 Limitations

This is because the cross-sectional nature does not allow causal inference. The sample size was small, and no lipid layer thickness and inflammatory biomarkers were measured.

6.8 Future Research Directions

Recovery of glands, use of AI to measure glands, cytokine profiling, and pediatric AC measurements should be investigated using longitudinal studies.

7. Conclusion

The current research shows that allergic conjunctivitis (AC) is not confined to conjunctival inflammation but has a tremendous impact on the structure and functioning of meibomian glands. AC patients demonstrated more gland dropout, as well as structural distortion of infrared meibography, lower values of NITBUT and Schirmer with evidence of tear film instability. These results are in line with the emerging evidence that chronic allergic inflammation can spread to the eye margin of the eyelid and affect the integrity of the meibomian glands (Leonardi and Silva, 2023; Arita et al., 2022).

Notably, meibography allowed one to visualize the changes in the glands even in those cases where clinical symptoms of dry eye were not so severe. Non-contact infrared imaging has been suggested to be very valuable in diagnosing advanced evaporative dry eye through early structural distortion and partial loss of glands (Knop et al., 2021). The connection between gland dropout and the lack of tear stability is also consistent with current knowledge regarding the effect of the lipid layer that helps to avoid tear evaporation (Craig et al., 2021).

These results support the idea that patients with allergic conjunctivitis should have integrated ocular surface assessment. The assessment of tear film (NITBUT, Schirmer test) and objective meibography could be used to detect the dysfunction of the meibomian glands before the onset of the clinical manifestation. Early therapeutic interventions, such as lid hygiene, lipid-based tear substitutes and potential anti-inflammatory therapy, could possibly avoid the development of a chronic cases of ocular surface disease (Schaumberg et al., 2023).

To sum up, it is necessary to note that allergic conjunctivitis is a multifactorial disease of the surface of the eye and participants of the conjunctiva and meibomian glands. Implementing meibography as part of clinical assessment on a regular basis can enhance disease classification, allow for earlier treatment and improve longer-term complications of the ocular surface.

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