An Innovative Meibography Approach for Assessing Meibomian Gland Structure and Function in Dry Eye Disease

ABSTRACT

Background and Aims: Dry eye disease (DED) is a multifactorial condition affecting the tear film and ocular surface, leading to discomfort, visual impairment, and ocular surface damage. Meibomian gland dysfunction (MGD) is the primary cause of evaporative dry eye, significantly contributing to DED pathophysiology. This study aimed to evaluate meibomian gland structure and function using an innovative meibography approach and correlate gland loss with DED severity.

Methods: This cross-sectional comparative study was conducted at a tertiary healthcare center from September 2023 to August 2024. Ethical approval and informed consent were obtained. A total of 260 patients were recruited, with 130 diagnosed with DED and 130 age-matched controls. Clinical assessments included tear breakup time (TBUT), Schirmer's Test I (SCH I), and meibography using transillumination techniques. Meibomian gland loss was graded using Arita et al.'s [5] classification. Statistical analyses were performed using SPSS v25, with a p-value <0.05 considered significant.

Results: The mean age was 53.2 ± 12.8 years. Females constituted 66.9% of the study group. Evaporative dry eye was predominant (68.46%). Gland loss correlated significantly with age (P = 0.000), TBUT (P = 0.002), and SCH I (P = 0.001). Severe DED was present in 55.2% of eyes with grade 3 gland loss.

Conclusion: We concluded that meibography is an effective, non-invasive tool for assessing MGD-related DED. Gland loss is strongly associated with DED severity, emphasizing the need for early intervention.

Keywords: Dry Eye Syndrome; Meibography; Meibomian Gland Dysfunction; Tear Film; Ocular Surface Disease

INTRODUCTION

Dry eye disease (DED) stands as the most common ophthalmological diagnosis globally and is characterized as a disorder of the tear film and ocular surface. It manifests through symptoms of discomfort, visual disturbances, and tear film instability, all of which can lead to potential damage to the ocular surface [1,2]. Additionally, DED is accompanied by increased osmolarity of the tear film and ocular surface inflammation, as outlined by the International Dry Eye Workshop (DEWS) in 2007 [3]. The disease results primarily from a decrease in tear film volume or an imbalance in the composition of the tear film, which can further contribute to the pathophysiology of DED [4]. Etiologically, DED is categorized into two main types: evaporative dry eye and aqueous-deficient dry eye. Among these, evaporative dry eye is the more commonly encountered form in clinical practice [5].

Meibomian gland dysfunction (MGD), a major contributor to evaporative dry eye, is a chronic, diffuse abnormality affecting the meibomian glands. It is primarily characterized by terminal duct obstruction or qualitative and quantitative changes in glandular secretion, as detailed by the International Workshop on MGD. MGD is considered the most frequent cause of evaporative dry eye [5]. An important diagnostic tool for evaluating DED is the determination of tear film osmolarity, which has been established as the "gold standard" test for diagnosing the disease [6]. In cases of MGD, the meibomian glands become obstructed, causing the lipids within to stagnate, thicken, and become saturated. This leads to alterations in gland morphology and can even result in gland atrophy [7,8].

Meibography, an imaging technique for visualizing meibomian glands through the conjunctival side of the tarsal plate, was initially described by Tapie in 1977 [9]. It is a non-invasive method that provides valuable insights into the structure of meibomian glands, allowing for early detection of glandular changes that may be indicative of MGD. This study aims to assess the morphological characteristics of meibomian glands in various dry eye conditions, specifically focusing on identifying any loss of glands, evaluating the functionality of the remaining

glands, and exploring the relationship between the anatomical structure of the glands, their function, and the severity of DED.

MATERIAL AND METHODS

Study Design and Setting

This cross-sectional comparative study was conducted at a tertiary healthcare center from September 2023 to August 2024. The study received approval from the Institutional Ethics Committee, and informed consent was obtained from all participants.

Study Population and Sample Size

A total of 260 patients were included in this study, with 130 patients diagnosed with dry eye disease (DED) in the study group and 130 age-matched controls without dry eye symptoms in the control group. The sample size was calculated with a 95% confidence level, 80% power, and 6% absolute precision, as per the methodology of Rege et al. [11], which resulted in a sample size of 130 in each group.

Inclusion and Exclusion Criteria

Inclusion Criteria:

1. Patients diagnosed with dry eye disease.
2. Age-matched controls without any dry eye symptoms.
3. Both males and females aged more than 18 years.

Exclusion Criteria:

1. Patients with dry eye complaints during the immediate postoperative period.
2. Patients with keratitis or epithelial defects.
3. Any systemic or ocular condition that could interfere with dry eye diagnosis.
4. Contact lens wearers.

Clinical Examination and Assessment

All patients underwent a comprehensive clinical evaluation, including:

1. **History**: Detailed patient history was taken, focusing on symptoms of dry eye and associated factors.
2. **Vision Tests**: Distant vision was assessed using Snellen's chart, and near vision was tested using Jaeger's chart.
3. **Anterior Segment Examination**: Slit-lamp examination was performed to assess the anterior segment, with special attention to the meibomian glands.
4. **Fundus Examination**: Fundus examination was performed using both direct and indirect ophthalmoscopy to rule out any ocular abnormalities.

Meibography and Meibomian Gland Morphology

The primary focus of the study was to evaluate the meibomian gland morphology in both groups. The procedure followed was:

1. **Meibomian Gland Assessment**: Both upper and lower eyelids were examined after everting the lids under magnification. The meibomian glands were assessed using a slit lamp and transillumination with a small red LED bulb. This allowed visualization of gland morphology through the palpebral conjunctival surface.
2. **Transillumination Meibography**: A red LED bulb was applied to the cutaneous side of the everted eyelid, and the gland appearance, duct dilation, and percentage of gland loss or dropout were analyzed.
3. **Meiboscore**: The meiboscore for both upper and lower eyelids was calculated by summing the scores from each eyelid. A photograph was taken for documentation. Arita et al. grading was followed to grade the area of meibomian gland loss [5].

Tear Film Function Assessment

Tear film function was evaluated using:

1. **Tear Breakup Time (TBUT)**: To assess the stability of the tear film. Based on TBUT, the severity of dry eye was graded as follows (Table 1):
    - **Mild**: >8–10 s
    - **Moderate**: 6–8 s
    - **Severe**: ≤5 s

2. **Schirmer's Test I (SCH I)**: To assess aqueous tear secretion. Based on SCH I, the severity of aqueous deficient dry eye was classified (Table 2):
    - **Mild**: 11–15 mm
    - **Moderate**: 6–10 mm
    - **Severe**: ≤5 mm
3. **Schirmer's Test II (SCH II)**: Performed only in patients with abnormal SCH I results to assess the secretion of tears under stimulation.

Statistical Analysis

The data were analyzed using SPSS version 25. Descriptive statistics were calculated for demographic characteristics and clinical parameters. Student's unpaired t-test was used to compare continuous variables between the study and control groups, while Chi-square test was applied to compare categorical variables. A p-value of < 0.05 was considered statistically significant.

Merits of Meibography in this Study

In this study, meibography was performed using the Auto Refracto-Keratometer (ARK), which is commonly available in most ophthalmological settings. The red LED bulb used for transillumination is widely available in electronic stores, making this technique both cost-effective and easy to implement in routine clinical practice without additional costs for equipment. The use of meibography allows for a non-contact, non-invasive method to visualize and document meibomian gland morphology in patients with dry eye disease.

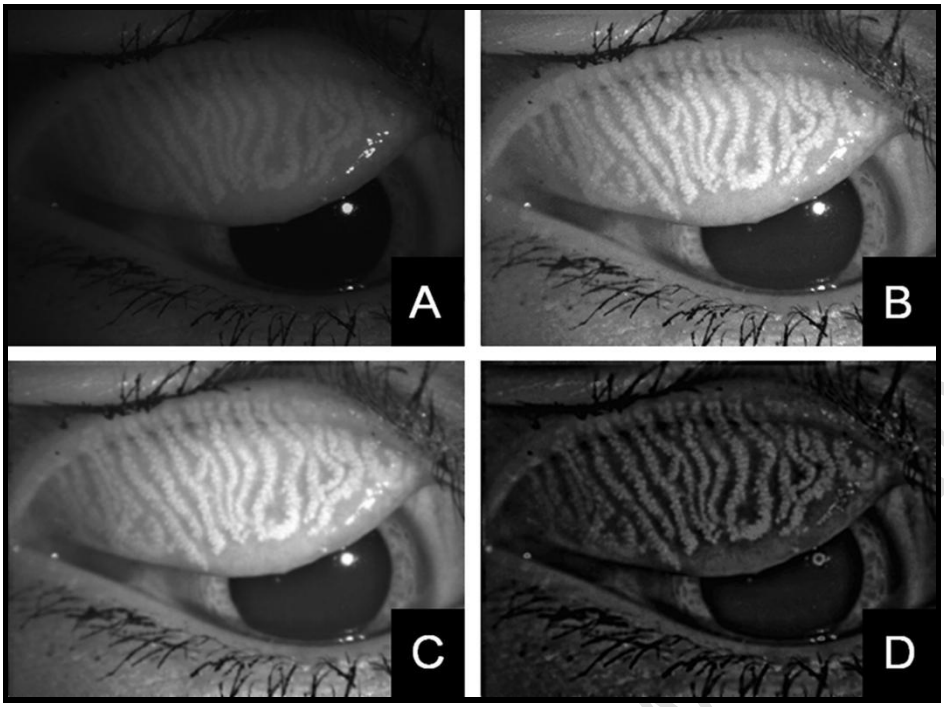


Figure: Objective image analysis of the meibomian gland area [5]

Documentation

Non-contact meibography images were captured using ARK, ensuring accurate and consistent documentation of meibomian gland structure and function.

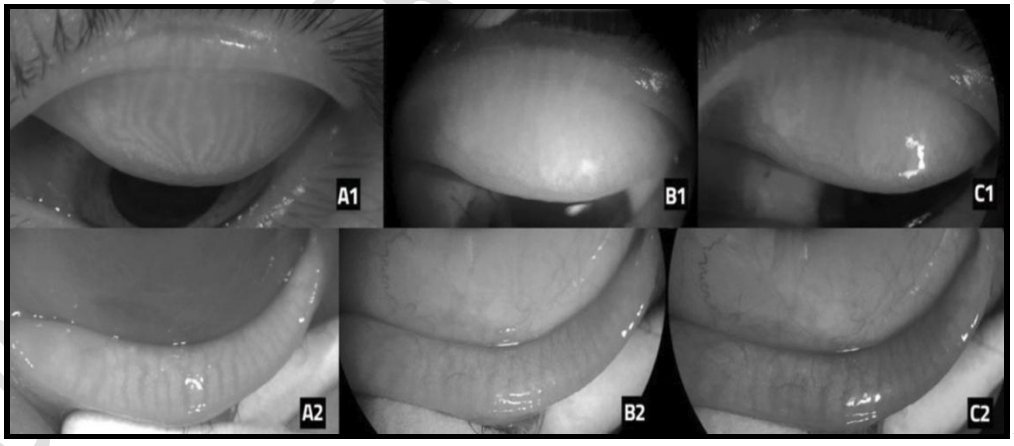


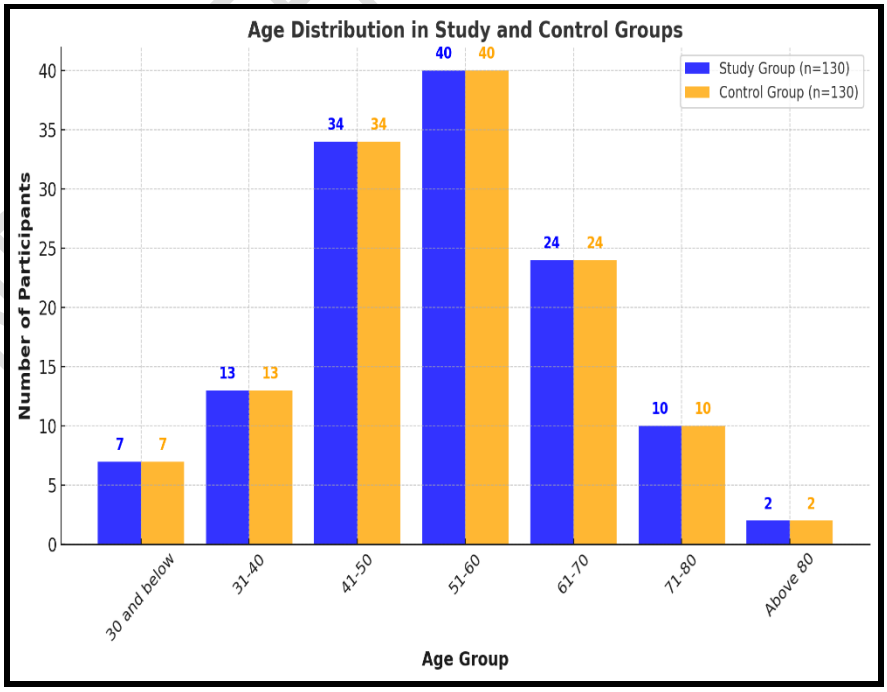
Figure: Red filter meibography by smartphones in patients with meibomian gland dysfunction [15]

RESULTS

The age distribution in both the study and control groups showed a higher prevalence of participants in the 41–60 age range, accounting for 56.92% of the total population. The least representation was in the above 80 category, with only 1.54% of participants in each group, indicating that dry eye disease (DED) is more commonly observed in middle-aged and older individuals, as shown in **Table 1**.

Table 1: Age Distribution in Study and Control Groups

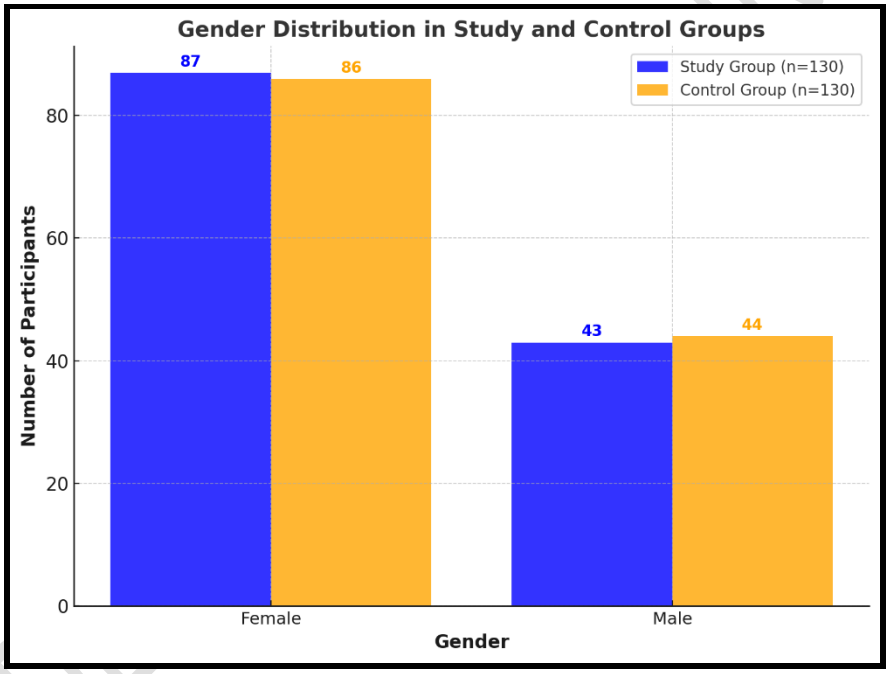
Age Group	Study Group (n=130)	Control Group (n=130)
30 and below	7 (5.38%)	7 (5.38%)
31-40	13 (10.00%)	13 (10.00%)
41-50	34 (26.15%)	34 (26.15%)
51-60	40 (30.77%)	40 (30.77%)
61-70	24 (18.46%)	24 (18.46%)
71-80	10 (7.69%)	10 (7.69%)
Above 80	2 (1.54%)	2 (1.54%)



Females comprised a larger proportion in both the study (66.9%) and control (66.2%) groups, indicating a higher prevalence of dry eye disease among women. This finding aligns with previous studies linking hormonal influences to meibomian gland dysfunction and tear film instability, as shown in **Table 2**.

Table 2: Gender Distribution in Study and Control Groups

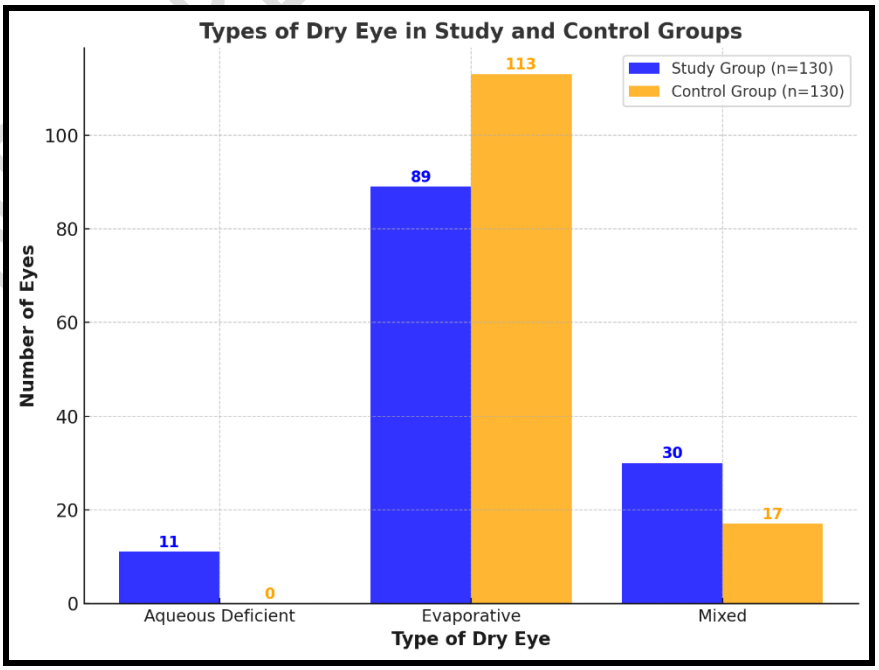
Gender	Study Group (n=130)	Control Group (n=130)
Female	87 (66.9%)	86 (66.2%)
Male	43 (33.1%)	44 (33.8%)



Evaporative dry eye was the most prevalent form in both groups, affecting **68.46% of the study group and 86.92% of the control group**. Mixed dry eye was observed in **23.08% of study participants**, while aqueous-deficient dry eye was present in **8.46%** of cases, with no occurrences in the control group. These findings reinforce the dominant role of meibomian gland dysfunction in dry eye pathophysiology, as shown in **Table 3**.

Table 3: Types of Dry Eye in Study and Control Group

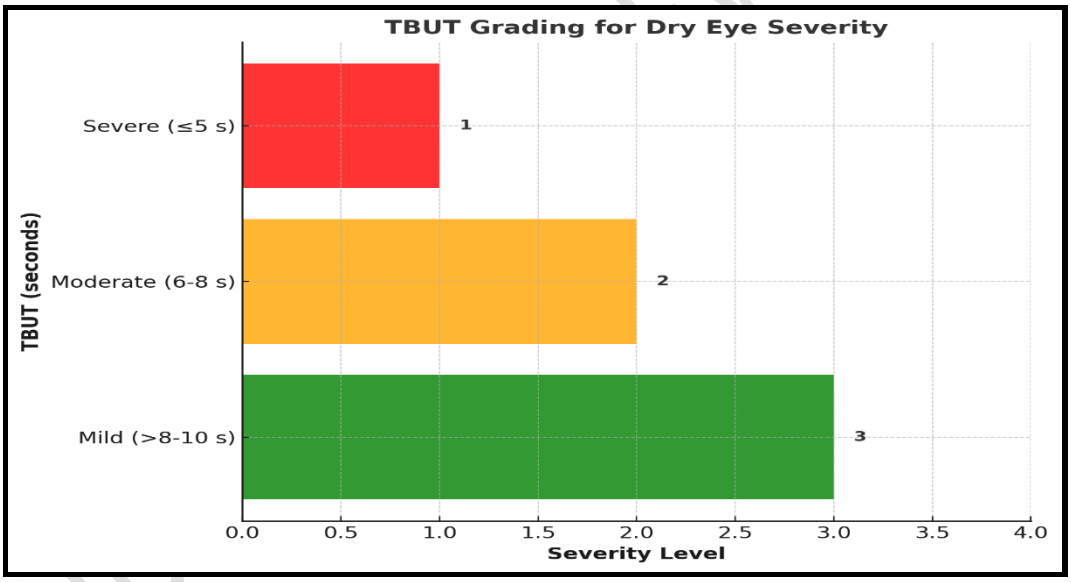
Type of Dry Eye	Study Group (n=130) - Number of Eyes	Study Group (n=130) - Percentage (%)	Control Group (n=130) - Number of Eyes	Control Group (n=130) - Percentage (%)
Aqueous Deficient	11	8.46%	0	0.00%
Evaporative	89	68.46%	13	86.92%
Mixed	30	23.08%	17	13.08%



Tear Breakup Time (TBUT) assessment is a crucial indicator of tear film stability, with shorter TBUT values reflecting greater **tear film instability and severity of dry eye disease**. In this study, dry eye severity was categorized as **mild (>8-10s), moderate (6-8s), and severe (≤5s)**, highlighting the progressive deterioration of tear film integrity in affected individuals, as shown in **Table 5**.

Table 5: TBUT Grading for Dry Eye Severity

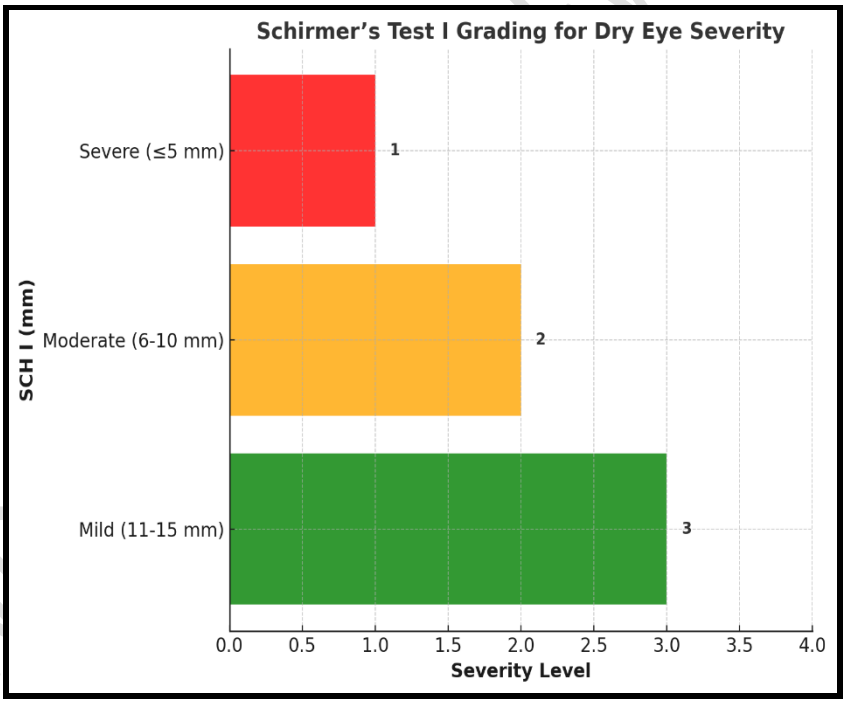
TBUT (seconds)	Severity of Dry Eye
>8-10 s	Mild
6-8 s	Moderate
≤5 s	Severe



Schirmer's Test I (SCH I) evaluates **aqueous tear production**, with lower values indicating **greater tear deficiency and more severe dry eye disease**. In this study, dry eye severity was categorized as **mild (11–15 mm), moderate (6–10 mm), and severe (≤5 mm)**, highlighting the progressive decline in tear secretion associated with disease severity, as shown in **Table 6**.

Table 6: Schirmer's Test I Grading for Dry Eye Severity

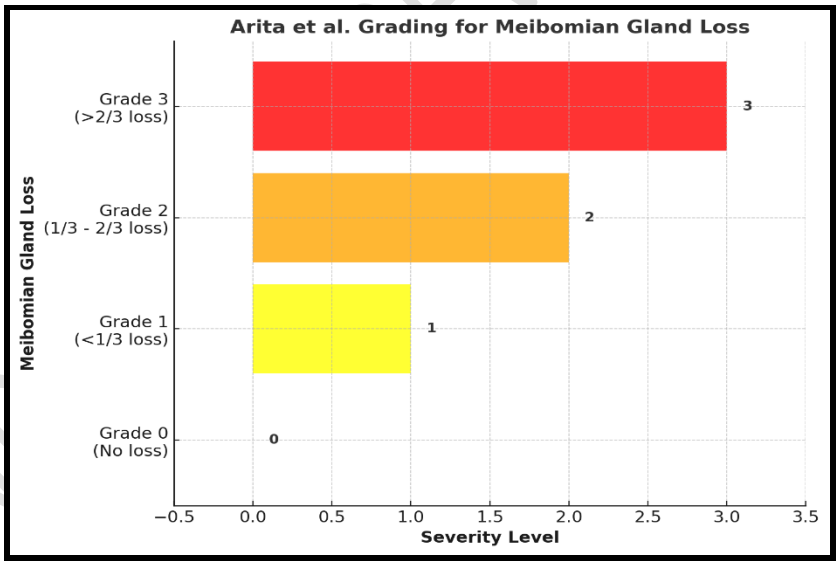
SCH I (mm)	Severity of Dry Eye
11-15 mm	Mild
6-10 mm	Moderate
≤5 mm	Severe



The **Arita et al. grading system** categorizes **meibomian gland loss** into four grades based on the **extent of gland atrophy**. **Grade 0** represents no loss, while **Grade 3** indicates severe atrophy, with loss exceeding **two-thirds of the total gland area**. This classification plays a crucial role in assessing the **severity of meibomian gland dysfunction (MGD)** and its impact on dry eye disease, as shown in **Table 7**.

Table 7: Arita et al. [5] Grading for Meibomian Gland Loss

Grade	Area of Gland Loss
0	No loss of meibomian glands
1	Loss of less than one-third of the total MG area
2	Loss between one-third and two-thirds of the total MG area
3	Loss of more than two-thirds of the total MG area



The correlation analysis revealed a negative association between TBUT and SCH I with both age and meibomian gland loss, indicating that tear film stability and aqueous secretion decline as age and gland atrophy increase. Conversely, gland loss exhibited a positive correlation with age, suggesting that meibomian gland dysfunction progresses with aging, ultimately contributing to more severe dry eye disease, as shown in Table 8.

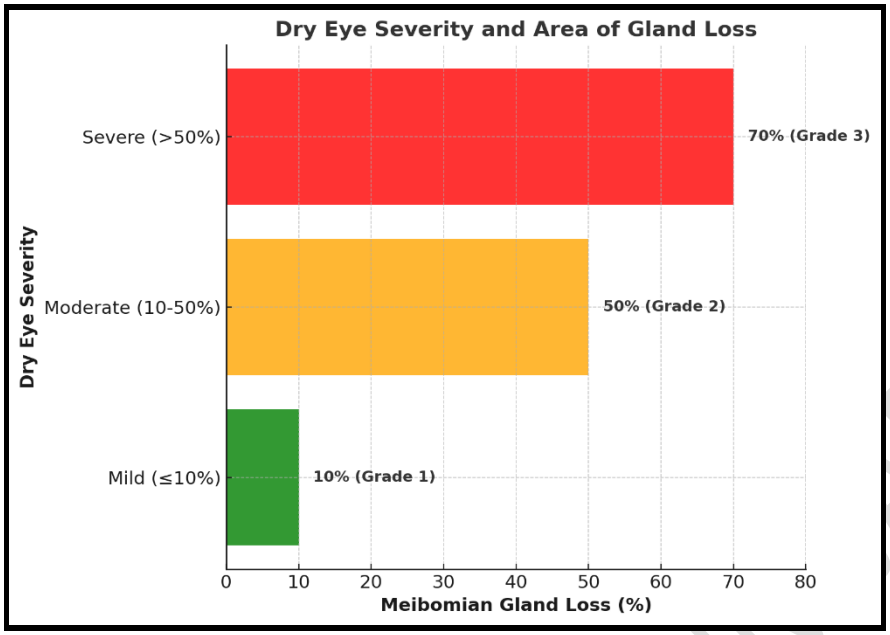
Table 8: Correlation Between Age, Gland Loss, and Dry Eye Severity

Variable	Correlation with Age	Correlation with Area of Gland Loss
TBUT	Negative	Negative
SCH I	Negative	Negative
Area of Gland Loss	Positive	Positive

The severity of dry eye disease is strongly correlated with meibomian gland loss, as graded by Arita et al. Mild dry eye is associated with ≤10% gland loss (Grade 0/1), whereas moderate cases exhibit 10–50% loss (Grade 1/2). Severe dry eye corresponds to more than 50% gland atrophy (Grade 2/3), highlighting the progressive nature of meibomian gland dysfunction (MGD) and its impact on tear film stability, as shown in Table 9.

Table 9: Dry Eye Severity and Area of Gland Loss

Severity of Dry Eye	Area of Gland Loss (%)	Area of Gland Loss Classification (Arita et al.)
Mild	≤10%	Grade 0/1
Moderate	10-50%	Grade 1/2
Severe	>50%	Grade 2/3



DISCUSSION

This cross-sectional study aimed to assess meibomian gland structure and function in dry eye disease (DED) using an innovative meibography approach. We analyzed 130 dry eyes from the study group and 130 control eyes, evaluating parameters such as TBUT, Schirmer's Test I, and gland morphology grading.

Age and Gender Distribution

In our study, the majority of participants were aged 41–60 years, with 26.15% in the 41–50 age group and 30.77% in the 51–60 age group. The prevalence of dry eye was significantly higher in individuals above 40 years, consistent with studies by Moss et al., who reported a 13% incidence of DED in individuals aged 48–91 years [12]. Similarly, Rege et al. found a 37.6% increase in dry eye prevalence in elderly populations [11]. These findings confirm that gland loss and dysfunction become more pronounced with aging, as also suggested by Arita et al. [5].

In terms of gender distribution, females constituted 66.9% of the study group and 66.2% of the control group. This aligns with prior research, including a retrospective study at the Miami and Broward Veterans Affairs eye clinics, which reported a 22% prevalence of DED in females compared to 12% in males [13]. However, in our study, the gender difference was not statistically significant (P =

0.01), suggesting that while females are more commonly affected, additional factors contribute to DED pathophysiology.

Types of Dry Eye and Meibomian Gland Dysfunction

Evaporative dry eye was the most prevalent form, observed in 68.46% of the study group and 86.92% of the control group. This finding is consistent with Rege et al., who also reported evaporative dry eye as the most common type of DED [11]. Meibomian gland dysfunction (MGD) was strongly associated with dry eye severity, with a statistically significant correlation (P = 0.000), aligning with previous findings that reported a 95% prevalence of dry eye in patients with blocked meibomian glands [14]. Additionally, Cuevas et al. identified MGD as the leading cause of mild to moderate evaporative dry eye, which further supports our findings [6].

Correlation Between Gland Loss, Age, and Dry Eye Severity

Meibography findings revealed a strong correlation between age and meibomian gland loss (P = 0.000), with older individuals showing greater gland atrophy. This aligns with the findings of Arita et al., who demonstrated that gland atrophy is progressive with age [5]. TBUT and Schirmer's Test I (SCH I) were negatively correlated with both age and gland loss, confirming that as gland dysfunction progresses, tear film stability and production decline.

Based on Arita et al.'s [5] grading, 55.2% of eyes with grade 3 gland loss exhibited severe dry eye symptoms, while 44.8% had moderate dry eye [5]. These findings indicate a direct relationship between meibomian gland atrophy and DED severity. In the control group, even among eyes without dry eye symptoms, 17.02% exhibited gland loss, reinforcing the concept that gland loss may precede clinical symptoms.

Our study demonstrates the importance of incorporating meibography in DED assessment, as gland loss strongly correlates with disease severity. This aligns with previous findings by Messmer et al., who emphasized that clinical signs do not always correlate with symptoms, making objective testing crucial for accurate diagnosis [10]. The ability to visually assess gland morphology and correlate it with dry eye severity provides valuable insights into disease progression. Our

results support the growing evidence that MGD is a key driver of DED, and objective evaluation methods such as TBUT, Schirmer's Test I, and meibography are essential for early diagnosis and management.

CONCLUSION

We concluded that meibography is a valuable diagnostic tool for assessing meibomian gland structure and function in dry eye disease (DED). Our findings demonstrated a strong correlation between meibomian gland loss, age, and dry eye severity, with evaporative dry eye being the most prevalent type. Meibomian gland dysfunction (MGD) was significantly associated with DED, and tear film instability was evident through reduced TBUT and Schirmer's Test I scores. These results emphasize the importance of early detection and targeted interventions to prevent disease progression and improve clinical

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