Original Article

Correlation of meiboscale symptom score and sign score for primary meibomian gland dysfunction in Indian eyes – A cross-sectional study

Prateek Nishant, Achala Ramawat, Shrinkhal N, Neeti Gupta, Sanjeev K Mittal

Purpose: To evaluate the correlation of Meiboscale with symptom score (Ocular Surface Disease Index [OSDI]) and meibomian gland dysfunction (MGD) sign score. **Methods:** We performed a cross-sectional hospital-based study of 53 patients of primary MGD who filled the OSDI questionnaire form and underwent complete ocular examination. The MGD sign score was calculated in both eyes using the sum of six grading systems proposed by Arita *et al. i*n 2016. The participants underwent imaging of the upper and lower eyelids of both eyes (212 eyelids) by specular microscope. The area of meibomian gland loss (MGL) was visually assessed and scored using the Meiboscale photographic card. Correlation between these three values – OSDI score, sign score, and MGL score based on Meiboscale - was calculated using Spearman's correlation analysis and Jonckheere–Terpstra (J–T) test. Correlation coefficient $r_s > 0.5$ was considered clinically significant. **Results:** Associations between MGL score and OSDI score, as well as between OSDI and sign score were statistically significant, but not clinically significant ($r_s = 0.3684$, $P < 0.001$ and $r_s = 0.41179$, $P < 0.001$, respectively). The association between MGL score and MGD sign score was statistically as well as clinically significant ($r_s = 0.8392$, $P < 0.001$). J–T test revealed large effect size ($P < 0.001$, r-effect = 0.93). **Conclusion:** The Meiboscale card had not been tested for utility in the Indian outpatient setting yet. Meiboscale can be used for reliable assessment and grading of MGD, and has clinical utility similar to the sum of six MGD sign scores. Additionally, assessment of symptoms using OSDI or a similar questionnaire is also recommended.

Key words: Dry Eye, eyelid disease, meibomian gland dysfunction, Ocular Surface Disease Index, tarsal gland pathology

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Meibomian gland disease or meibomian gland dysfunction (MGD) is a chronic, diffuse abnormality of the meibomian glands characterized by terminal duct obstruction and changes in the glandular secretion. It is the most common cause of dry eye disease, associated in up to 86% of patients, but often asymptomatic and unrecognized.[1-3] Asymptomatic patients need early recognition, so that they can be managed at an early stage. Risk factors include aging, deficiency of sex hormones, notably androgens, other systemic conditions such as Sjogren's syndrome (SS), Stevens–Johnson syndrome (SJS), psoriasis, atopy, polycystic ovarian syndrome (PCOS), and hypertension. MGD results in stasis of meibum inside the glands, dilation of the ductal system, and loss of glandular tissue (gland dropout).[1-4]

There are various parameters in use for diagnosis of MGD in various studies, for example, plugging of meibomian glands, telangiectasia, collarettes, meibum secretion, and gland dropouts used alone or in combination.[1,4-6] There are many grading scales available for MGD, but they are very cumbersome. In addition, there is significant interobserver variability, leading to greater variation in the severity assessment. The Ocular Surface Disease Index (OSDI) evaluation (symptom score), the six MGD sign scores, and improved Meiboscale are means of assessment of MGD.[5,7,8] Although the three systems can help in grading of MGD, extensive literature review did not reveal evidence on whether a correlation exists between them.

Hence, this study was conducted to evaluate the correlation between the OSDI score, a composite MGD sign score, and Meiboscale and to analyze whether the improved Meiboscale used alone can determine the severity of MGD or a combination of grading systems is needed. To the best of the authors' knowledge, such a study to correlate meibomian gland loss (MGL) scores as per the improved Meiboscale with existing symptom and sign scores has never been conducted.

Methods

This was a hospital-based, cross-sectional study conducted on patients with MGD reporting to the outpatient clinic of the Department of Ophthalmology of a tertiary care university teaching hospital in Uttarakhand, India, from October 2019 to May 2020. The study protocol conformed to the Declaration of Helsinki and was approved by the institutional ethics committee. Patients with primary MGD willing to participate in the study and who gave written informed consent were

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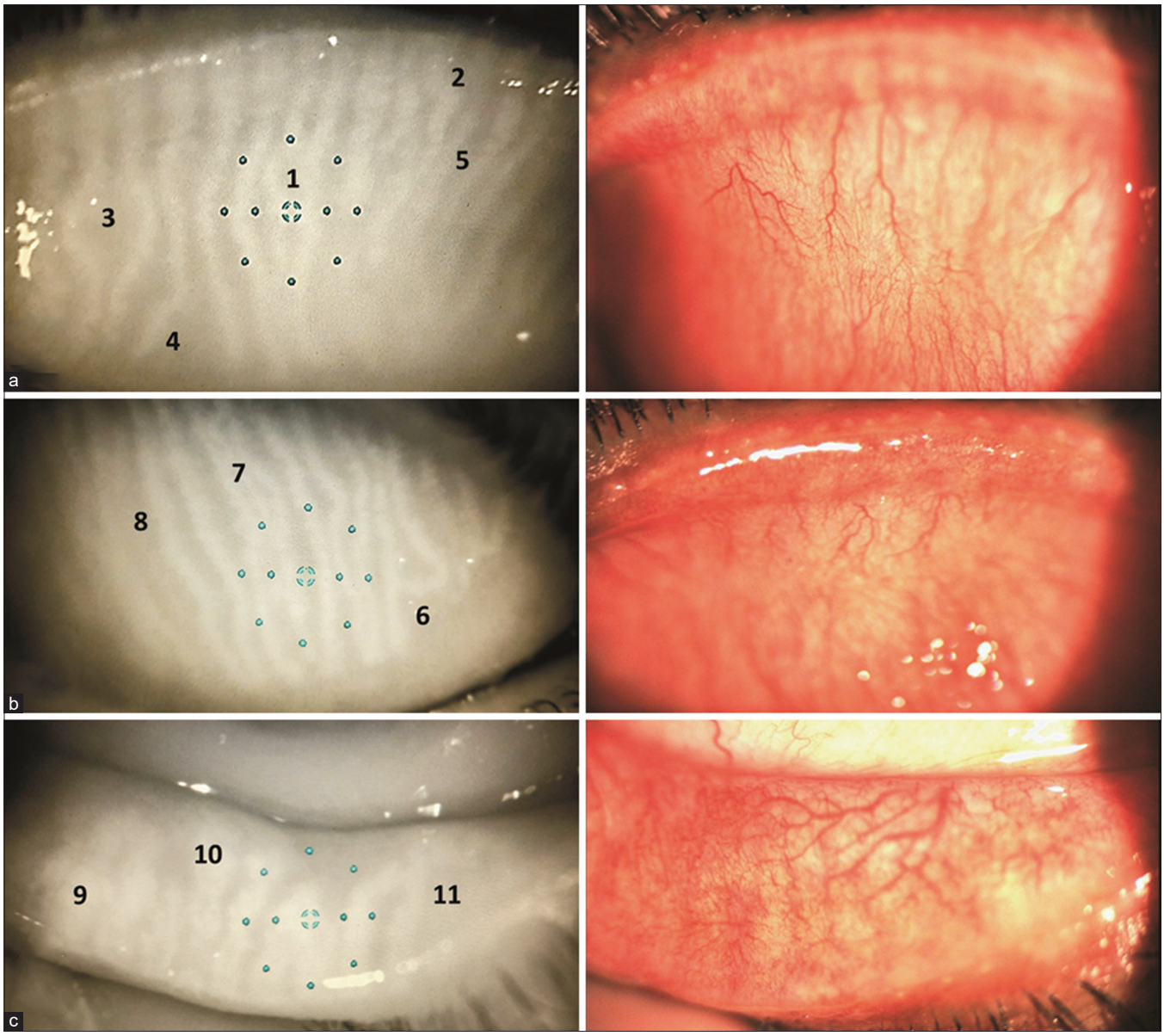

Figure 1: Patterns of meibomian gland loss identified by infrared meiboscopy on a specular microscope: (a) 1. distorted gland, 2. tortuous gland, 3. abnormal gap, 4. tadpoling. 5. thinned glands; (b) 6. hooked gland, 7. overlapping glands, 8. ghost glands; (c) 9. thickened glands, 10. no extension to lid margin, 11. gland dropout. Eyelid in image "A" was assigned meiboscore of 7 and Meiboscale score of 1, in image "B" 10 and 2, respectively, and in image "C" 14 and 3, respectively. Terminologies are as per Daniel *et al.*

included. Patients with history or findings suggestive of any accompanying ocular disease, any topical medications or contact lens usage, any ocular surgery within 6 months, or aqueous deficiency dry eye were excluded.

All participants filled the OSDI form, which measured severity of discomfort due to MGD.[7] As part of routine workup, they underwent complete ocular examination including anterior and posterior segment examination to assess eligibility. Eyelid margin examination was done using a slit-lamp biomicroscope by which MGD sign score was calculated using the sum of six grading systems.[5] The participants also underwent infrared imaging of the upper and lower eyelids of both eyes by a specular microscope (Nidek CEM-530; Nidek Co., Tokyo, Japan). The areas of MGL were visually assessed and score was assigned based on improved Meiboscale photographic card.[8] All tests for a particular patient were done on the same day by different examiners with each blinded to the findings of the others.

Scoring systems

OSDI was calculated as (sum of scores × 25) ÷ number of questions.[7] A score of ≥13 was considered to be symptomatic MGD, whereas a score of <13 was considered to be asymptomatic MGD.[9]

"MGD sign score" was calculated as per the new grading system proposed by Arita *et al*.[5] This is the sum of the following six grades assigned on slit-lamp examination and infrared meibography, that is, abnormal lid margin findings of vascularity (0–3), plugging of gland orifices (0–3), lid margin

Table 1: Descriptive statistics on the age, OSDI, MGD sign scores, and MGL scores of the subjects included

Parameter	Age of subjects in years (*n*=53)	OSDI (*n*=53)*	MGD sign scores (*n*=212)	Meiboscale MGL score (*n*=212)
Mean	57.04	40.62	7.79	1.73
Standard deviation	12.63	20.18	4.02	1.02
Median	60	41	7	1
Range	28-79	6-90	0-15	0-4

MGD=meibomian gland dysfunction, MGL=meibomian gland loss, OSDI=Ocular Surface Disease Index. Age and OSDI calculated per subject; MGD sign score and MGL score calculated per eyelid. *Kolmogorov-Smirnov test D=0.1133, *P*=0.0079

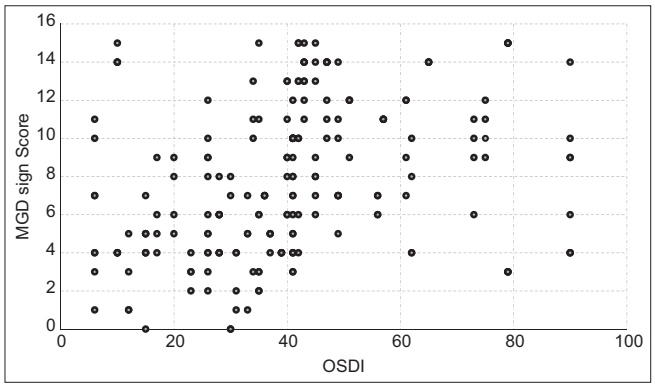

Figure 2: Scatter diagram showing comparison of OSDI with MGD sign score (*N* = 212). MGD = meibomian gland disease, OSDI = Ocular Surface Disease Index

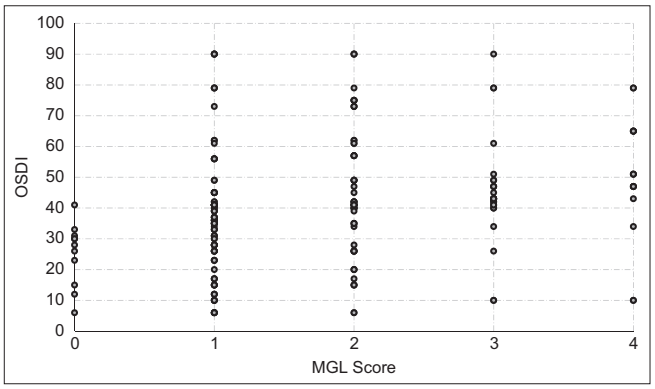

Figure 3: Scatter diagram showing comparison of MGL score with OSDI (*N* = 212). MGL = meibomian gland loss, OSDI = Ocular Surface Disease Index

irregularity (0–2), lid margin thickening (0–2), partial glands (0–3), and gland dropout (0–2).

"MGL score" was assigned by assessing MGL areas by infrared meibography [Fig. 1] and comparing them with standard photographs of the improved Meiboscale as revised by Pult in 2016.[8,10]

Sample size calculation

Based on the findings from a pilot study conducted for a similar objective, a minimum sample size of 124 eyelids was calculated at a level of significance of 0.05, power of 80%, and for an expected correlation coefficient of 0.250. This corresponds to 31 patients.

Statistical analysis

Descriptive statistics were calculated for the age of the subjects, including mean, standard deviation, median, and range. Data on the OSDI were analyzed using the Kolmogorov–Smirnov test for normality and nonparametric tests were chosen accordingly. Scatter diagrams were constructed to visualize the ordinal data. Spearman's correlation coefficient was used to determine the correlation between the symptom score, sign score, and Meiboscale. A *P* value <0.05 was considered statistically significant, and r_s > 0.5 as clinically significant.[11] There were no missing data. All tests were conducted on the software Statistical Package for the Social Sciences (SPSS, 22.0; IBM Corporation, New York, USA). The Jonckheere–Terpstra (J–T) test was applied to evaluate the distribution of OSDI in patients with varying ordinal MGD scores and MGL scores. The *r*-effect from the J–T test was used to evaluate the effect size from the analysis. Sensitivity analysis and subgroup analysis between symptomatic and asymptomatic MGD was beyond the scope of this study.

Results

Sixty-eight Indian subjects were screened during the study period, of which 53 fulfilled the eligibility criteria, amounting to 212 eyelids. Mean age of the subjects was 57 years [Table 1]. There were 29 males (54.7%) and 24 females.

Median OSDI score was 41 and did not follow a normal distribution (*P* = 0.008) with a skewness of 0.54 [Table 1]. MGL scores ranged from 0 to 4. Median MGL score was 1. Majority (46%) of the subjects had a score of 1, whereas only 5% had a score of 4. Median MGD sign score was 7 (range 0–15). Only five patients had asymptomatic MGD and the rest had symptomatic MGD.

Comparison of OSDI with MGD sign score showed a weak correlation, which was statistically significant (Spearman's correlation coefficient r_s = 0.41179, *P* < 0.000001) [Fig. 2]. Comparison between MGL scores and OSDI again showed a weak correlation that was statistically significant (r_s = 0.3684, *P* < 0.000001) [Fig. 3]. The J–T test applied to evaluate the distribution of OSDI in patients with varying MGL scores was statistically significant (J–T statistic = 10,339, *P* < 0.000001). The *r*-effect from the J–T test was calculated to be 0.37.

Comparison of MGL score with MGD sign score showed a strong correlation, which was statistically significant (r_s = 0.8392, *P* < 0.000001) [Fig. 4]. Furthermore, the J–T test applied to evaluate the distribution of MGD sign scores in patients with varying MGL scores was found statistically significant (J–T statistic = 14,233, *P* < 0.000001). The *r*-effect from the J–T test was calculated to be 0.93.

Discussion

Our study evaluated a validated symptom score (based on OSDI questionnaire), a validated sign score

Table 2: Correlation analysis for comparison of OSDI, sign score, and MGL score

Comparison		Spearman's rho	95% Confidence interval	*P* (two tailed)	Interpretation
MGL score (Meiboscale)	MGD sign score	0.84	0.79-0.88	<0.000001	Strong correlation, clinically significant
	OSDI	0.37	0.24-0.48	<0.000001	Weak correlation, clinically not significant
OSDI	MGD sign score	0.41	0.29-0.52	<0.000001	Weak correlation, clinically not significant

MGD=meibomian gland dysfunction, MGL=meibomian gland loss, OSDI=Ocular Surface Disease Index

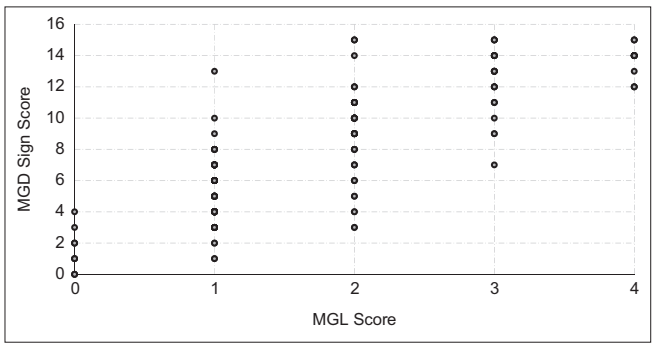

Figure 4: Scatter diagram showing comparison of MGL score with MGD sign score (*N* = 212). MGL = meibomian gland loss, MGD = meibomian gland disease

(sum of six grading systems), and the improved Meiboscale to demonstrate the extent of association and correlation between them in a sample of 53 patients (212 eyelids, exceeding the calculated sample size).[5,7,8] The nonavailability of a validated MGD grading scale suited for the Indian outpatient setting is a gap in present knowledge, which had motivated the investigators to propose the present project. There are few comparable studies conducted in the past which have evaluated the clinical utility of photographically aided scales such as the Meiboscale in comparison with existing symptom scores or sign scores.

Signs of MGD include abnormal lid margin findings of vascularity, plugging of gland orifices, lid margin irregularity, lid margin thickening, partial glands, and meibomian gland dropout. Arita *et al*.[5] have assigned scores to each of these six parameters, the sum of which forms the existing basis of diagnosis of MGD and the assessment of its severity. In their article, they have defined the clinical parameters based on slit-lamp biomicroscopy and meibography and have provided representative images for the grading of MGD. Though useful for the assessment of MGD in clinical settings, the combination of six different parameters may be cumbersome and time-consuming. In comparison, the visual scale known as Meiboscale[8] comprises a picture card of clinical images of meibomian gland area loss of increasing severity, which allows the observer to assign a score to the patient depending upon the image to which his condition corresponds. This revised Meiboscale is an improvement over the initial work of the same author[12] and includes grading of both eyelids separately. Combining MGL of both lids by linear regression analysis results in the best predictive ability of OSDI;[13] however, this is impractical in the outpatient setting. Hence, we have correlated the MGL score of each eyelid separately to the OSDI of the subject. Weng *et al*.[14] have used the sum of scores of both eyelids to report a score of 0–8 for each eye with MGD. However, they have not correlated MGL with OSDI, but with the SPEED questionnaire. We chose to analyze the MGL score for each eyelid separately for comparing to the sign scores that were calculated for each eyelid.

Meibography is a method to assess the structure of meibomian glands, including the ducts and acinar distribution. Apart from meibomian gland analyzers, meibography can also be performed using instruments commonly available in outpatient clinics, such as autorefractometers and specular microscopes, whose infrared camera is effective for visualizing the meibomian glands in everted eyelids.[15-18] We used a specular microscope in our study.

Pult reported that among subjects with dry eye disease, the OSDI was correlated with MGL area observed on meibography as a percentage of the total area calculated by computer software (correlation coefficient 0.52).[19] Guarnieri *et al*. quantified MGL area using ImageJ software.[20] However, the availability of such computer software in the outpatient setting is limited.

Robin *et al*.[21] reported the mean age of subjects with MGD to be 56.32 years, which is comparable to the present study. They found that in 91 MGD subjects, the mean OSDI was 55.37 ± 22.05 and the mean MGL score was 1.5 ± 1.13. However, they did not correlate the two parameters among MGD patients. Brooks and Gupta[22] showed that the mean Meiboscale score was 0.89 for subjects <35 years of age going for refractive surgery and 1.38 for those >35 years. However, they have not provided details about those with preexisting MGD.

In the present study, the association between OSDI and sign score was statistically significant, but not clinically significant (r_s = 0.41179, P < 0.000001). Similarly, the association between Meiboscale and OSDI score was statistically significant, but not clinically significant (r_s = 0.3684, P < 0.000001). The *r*-effect from the J–T test was 0.37, which amounts to relatively moderate effect size. However, the association between Meiboscale and MGD sign score was statistically as well as clinically significant (r_s = 0.8392, P < 0.000001, Table 2). The *r*-effect from the J–T test in this case (0.93) amounts to a large effect size.

Our findings, therefore, indicate that Meiboscale alone can be used for reliable assessment and grading of MGD and has clinical utility similar to the sum of the six sign scores. Given the large sample size, results of this study are generalizable and will enable examiners to visually assess, diagnose, and grade patients with MGD efficiently in Indian outpatient settings. However, we still recommend independent symptom assessment through OSDI or similar questionnaire for dry eye in all patients, as the Meiboscale alone has poor clinical utility in predicting symptoms.

Limitations of this study include our inability to examine the association between the parameters considered and Schirmer's test values, tear film breakup time, lipid layer thickness, or tear meniscus height, as well as the concentrations of various

maternal hormones, gestational age, and tear film function in pregnancy, which may have affected our findings in a minority of patients. The effect of recall bias on OSDI scores may have been insignificant, but cannot be ignored, given that our analysis also included geriatric patients. A further extended multicentric, multiethnic study is desirable to firmly establish our findings and to evaluate the effect of other confounders not addressed in our exclusion criteria.

Conclusion

Meiboscale alone can be used for reliable assessment and grading of primary MGD, as the score so obtained has clinical utility similar to the sum of six sign scores. The authors still recommend independent symptom assessment through OSDI or a similar questionnaire for dry eye in all patients, as the Meiboscale has poor clinical utility in predicting symptoms.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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