Original Article

Association of Meibomian Gland Dysfunction and Serum Lipid Profile in Adults: A Hospital Based Cross Sectional Study

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Abstract

Background: The aim is to study the possible association between meibomian gland dysfunction and serum lipid profile in adults. **Material and Methods:** This cross-sectional study examined 380 patients (male = 49.73%, female=50.26%) with a mean age of 40.29 years (SD=11.48) for males and 41.10 years (SD=13.67) for females. MGD Patients were clinically classified based upon ocular surface staining, meibomian gland expressibility and meibum quality. Results of lipid profile were recorded and analysed with MGD severity with the help of ANOVA. Mann-Whitney and Spearman rho statistical test were used to find MGD association with age and sex respectively. **Results:** No significant difference in MGD grades distributions were noted among the two sex (P=0.107). Significant correlation was observed in MGD severity grade with age (P=0.003) and TG, TC and LDL (P<0.00). **Conclusion:** Increasing age is associated with disease severity. No effect of sex with MGD grades could be established paving the way for future research. The present study has found a significant association of MGD grades with lipid profile, particularly with TG, TC, and LDL, reinforcing the role of systemic dyslipidemia in MGD severity.

Keywords: dyslipidemia, meibomian gland dysfunction, age, sex, lipid profile.

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Introduction

Dry eye disease is a complex condition affecting the ocular surface. It involves multiple contributing factors that disrupt the tear film balance due to elevated tear solute levels, inflammation, injury to the eye surface, and surface neurotrophoic factors. It is manifested as discomfort and irritation in the eye.[1]

The ocular surface comprises of corneal/conjunctival cells, accessory lacrimal glands, and orifices of meibomian glands (MGs). Meibomian glands are located in the tarsal plates of the eyelids. They stabilise the tear film by producing lipids that form meibum and thus play a pivotal role in maintaining the health of the ocular surface. The dysfunction of the meibomian glands is a prevalent ocular disorder characterized.[2]

The analysis of recent studies reveals a global prevalence of Meibomian Gland Dysfunction (MGD) ranging from 21.2% to 71.0% across different ethnic groups.[3] Studies have underscored the multifactorial etiology of MGD, which includes age-related changes, hormonal influences, systemic diseases, and environmental factors.[4] Among these, dyslipidemia, a known risk factor for cardiovascular diseases, has been increasingly recognized as potentially influencing the pathophysiology of MGD.[5] On reviewing the literature, components of serum lipid profile (S. triglyceride, S. total cholesterol, S. LDL and S. HDL) have shown a variable association with severity of MGD.[6]

The present study was carried out to study the possible association between meibomian gland dysfunction and serum lipid profile in adults of North- West region of Haryana, India.

Materials and Methods

Present cross-sectional study was carried out in the OPD of Ophthalmology, at a tertiary care center between Jan 2024 to Dec 2024 after taking permission from IEC. Sample size was calculated based on the prevalence of MGD which according to a study conducted by Chatterji et al is 65%.7 The calculation was done assuming a statistically significant difference at a 95% confidence interval and absolute error of 5%. Adult patients (>18 years) with MGD were enrolled sequentially in the study. Individuals with history of topical steroid administration for 1 month preceding the study, and/or on treatment with systemic drugs affecting the tear film were excluded. Pregnant patients, those suffering from infectious keratoconjunctivitis or inflammatory ocular surface diseases unrelated to MGD, patients having history of recent ocular surgery and alterations of the

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lacrimal drainage system, were also excluded from the study. Patients on lipid lowering drugs, or with any other systemic diseases like neurological, rheumatological, or dermatological disorder affecting the health of the ocular surface were also excluded from the study.

Examination: Diagnosis of dry eye disease was made according to the guidelines of Dry Eye Workshop II (DEWS II).[4] Symptoms were scored according to Ocular Surface Disease Index Questionnaire (OSDI Score). Lid margin was evaluated for plugging [Figure 1A], rounding, vascularity and frothy discharge [Figure 1B]. Tear film break up time (TBUT) [Figure 1C], Schirmer's strip wetting [Figure 1D], Tear meniscus height Marx Line Score were measured. Grading of corneal and conjunctival staining was done based on Oxford and DEWS scale.

The MGD grade was determined on the basis of meibum quality, expressibility of meibum, corneal and conjunctival staining.

Clinical staging of MGD

According to the report submitted by the International Workshop on Meibomian Gland Dysfunction and Management in 2011, taking both the symptoms and clinical signs into consideration, MGD has been divided into four stages [Table 1].[8]

Table 1: Staging of meibomian gland dysfunction according to the international workshop on meibomian gland dysfunction8

Stage	MGD Grade	Symptoms	Corneal Staining
1	+ (Minimally altered expressibility and secretion quality)	None	None
2	++ (Mildly altered expressibility and secretion quality)	Minimal to mild	None to limited
3	+++ (Moderately altered expressibility and secretion quality)	Moderate	Mild to moderate
4	++++ (Severely altered expressibility and secretion quality)	Marked	Marked
MGD: Meibomian gland dysfunction;			
Grade +,++, +++ and ++++:			

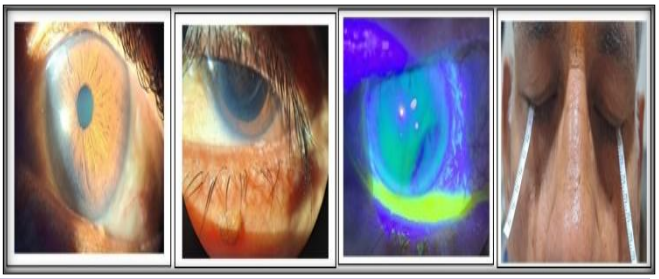

Figure 1: Clinical photos of signs of Meibomian Gland Dysfunction; 1A: Mucus plugging, 1B: Frothy discharge, 1C: Break up of tear film during TBUT and increased tear meniscus height, 1D: Reduced wetting of the Schirmer's Strip

Data Collection and Statistical Analysis: A Microsoft Excel spreadsheet was used to code and enter the data. SPSS version 23 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) for Windows was used to analyse the findings. Quantitative data were expressed as mean (SD). Nonparametric test (Spearman's rho and Mann–Whitney U test) was applied to observe the relationship between two independent groups namely age and sex. Assuming no difference in mean values of lipid profile across the MGD grades, One-way ANOVA was performed to test the hypothesis. The level of significance was set at P≤0.05.

A total of 191 females (50.3%) and 189 males (49.7%) participated in the study. Mean age of participants was 41.10 years (SD=13.67) for females and 40.29 years (SD=11.48) for males. Six age groups (groups 1 to 6) were created.

Results

The maximum number of study participants [90 (23.7%)] belonged to the age group of 50–59 years (group 5) while only 11 participants were younger than 20 years of age (group 1), representing 2.9% of the sample [Figure 2].

Females with MGD grade 1 and 2 outnumbered males. Whereas Grade 3 MGD was more common in males (8.43%) compared to females (2.89%) [Figure 3].

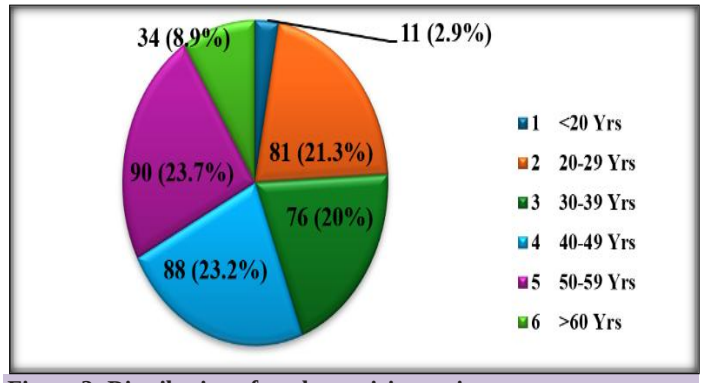

Figure 2: Distribution of study participants into age groups

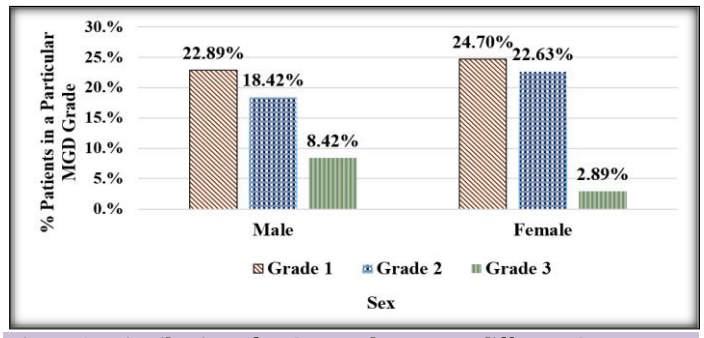

Figure 3: Distribution of MGD grades among different Sex

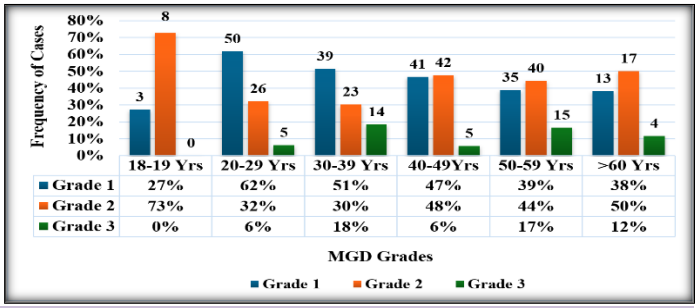

Figure 4: Distribution of MGD grades among Age Groups

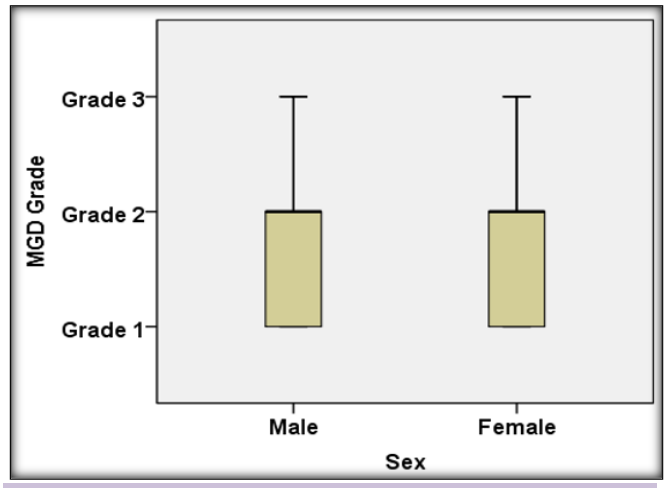

Figure 5: Box plot: Distribution of MGD grades in each sex

Frequency of MGD grade was calculated in each age group [Figure 4]. MGD grade 1 was more common in the age groups 2 and 3. MGD grade 2 was more in age groups 1 and 4 to 6. The highest number of cases of MGD grade 3 (18%) was seen in age group 3 (30-39 Years).

Distribution of MGD grades in both the sexes showed no significant difference (P=0.107) by Mann-Whitney test. A box plot is drawn to visualize the distribution of different MGD grades in each sex [Figure 5].

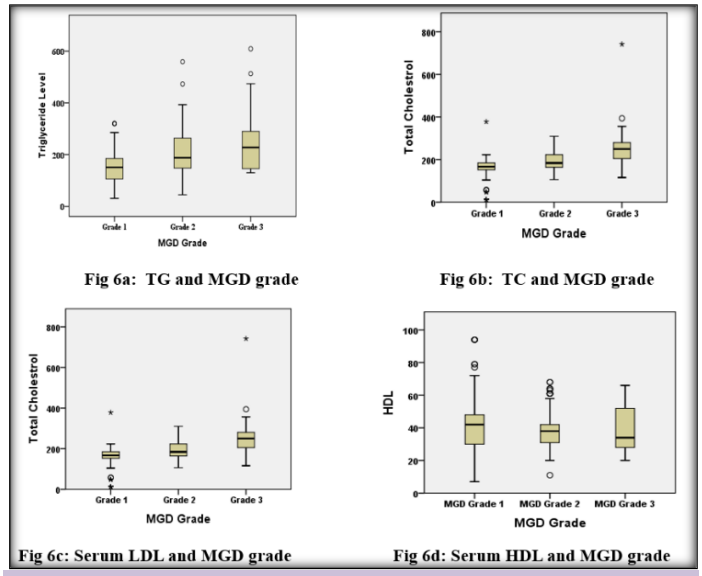

Fig 6a: TG and MGD grade

Fig 6b: TC and MGD grade

Fig 6c: Serum LDL and MGD grade

Fig 6d: Serum HDL and MGD grade

Fig.(6a-6d) Whisker Box Plot: Distribution of MGD grades with lipid profiles (TG= Triglyceride, TC= Total Cholesterol, LDL= Low Density Lipid, HDL= High Density Lipid).

Table 2: Nonparametric Correlation of MGD grades with Age

			MGD Grade	Age
Descriptive Study Mean (SD)			**1.64 (0.67)**	**40.70 (12.67)**
Spearman's rho	MGD Grade	Correlation Coefficient	1.000	.154**
		Sig. (2-tailed)		.003
		N	380	380
**. Correlation is significant at the 0.01 level (2-tailed).				

Relationship between MGD Grades and age was assessed with nonparametric correlation (Spearman's rho) and showed significant association (P=0.003) [Table 2].

Table 3: Descriptive Values of Serum Lipid Profile {Mean (SD)} in Different Grades of Meibomian Gland Dysfunction

Lipid profile	Meibomian Gland Dysfunction Grades		
	Grade 1 (n=181)	Grade 2 (n=156)	Grade 3 (n=43)
S. Triglyceride (mg/dl)	149.7 (59.5)	202.7 (75.4)	240.2 (111.8)
S. Total cholesterol mg/dl)	159.9 (46.5)	193.6 (47.4)	261.4 (93.2)
S. LDL (mg/dl)	144.3 (17.8)	199.6 (14.4)	232.1 (4.9)
S. HDL (mg/dl)	40.8 (15.2)	38.3 (11.3)	38.3 (12.4)

Serum lipid profile (mean, SD) in different MGD grades have been tabulated (Table 3) and distribution of cases has been represented as Box and Whisker plots (Fig 6a-6d). Serum Triglycerides ranged from 149.7 mg/dL (SD 59.5) in Grade 1 to 240.2 mg/dL (SD 111.8) in Grade 3. Increase in serum Total Cholesterol and serum LDL levels with increasing severity of MGD grades was noted. Whereas a slight decrease in serum HDL levels was observed with increasing MGD grades.

Table 4: One-way Analysis of Variance (ANOVA) to determine the variation in log {Mean (SD)} values of Serum Lipid Profiles across MGD grades.

Lipid profile	Meibomian Gland Dysfunction Grades			
	Grade 1 (n=181)	Grade 2 (n=156)	Grade 3 (n=43)	P- VALUE
log S. Triglyceride (mg/dl)	4.91 (0.46)	5.24(0.37)	5.39 (0.42)	0.000
log S. Total Cholesterol (mg/dl)	4.98 (0.55)	5.23 (0.24)	5.52 (0.28)	0.000
log S.LDL (mg/dl)	4.96 (0.12)	5.29 (0.07)	5.44 (0.02)	0.000
log S.HDL (mg/dl)	3.63 (0.42)	3.60 (0.30)	3.59 (0.32)	0.720

As there was a large variation in values of lipid profile (represented as outliers in Box and Whisker plot, [Figure 6], a

log transformation of data was done in SPSS 23 to reduce the impact of outliers. Oneway ANOVA was applied to observe the association between log of mean serum lipid profile variables and MGD grades. MGD grades were significantly (P=0.000) associated with the three serum lipid profile variables namely TG, TC and LDL levels. However, no significant association (P=0.718) was observed between serum HDL levels and severity of MGD grades [Table 4].

Discussion

In the present study significant association between age and MGD grades was observed. This observation is consistent with previous research of Tomioka et al and Guilani et al.[6,9] The similarity in findings can be attributed to the shared underlying biological mechanisms, where aging affects the ability of meibomian gland to secrete clear and stable lipids, leading to tear film instability and evaporative dry eye disease. According to a study by Nien et al, aging causes a reduction in the signalling of the peroxisome proliferator-activated receptor c, which decreases differentiation and cell cycling of meibocytes eventually resulting in acinar atrophy and MGD.[10]

According to our study, sex was not a significant predictor of MGD severity as Mann Whitney test failed to provide any significant association (P=0.107). Whereas, Huang et al who conducted a study on elderly population (>60 yrs) ,observed a significantly higher severity of MGD grade in males (Chi square test: X2 = 7.899, P = 0.048).[11] Similarly, Hashmi et al observed a significantly higher (p<0.001) prevalence of MGD in men in their simple logistic regression model.[12] On the other hand, Guillani et al found female predisposition of MGD grades, however their association was weak (P=0.023).9 Pinna et al have also reported a higher prevalence of MGD in women.[13]

According to a mini review by Noland et al, the sex-specific prevalence of MGD varied significantly among the population and hospital-based research. Most clinic-based research found no significant difference, whereas population-based studies showed that men were more affected. The discrepancy in findings highlights how age functions as a selection bias in epidemiological research. Other possible factors, as enumerated by the research team were, subjective variation in symptom intensity, use of medications and cosmetics.[14]

One of the risk factors for MGD is androgen insufficiency, and the meibomian gland is an androgen target organ. Men and women experience a varied rate of drop in androgen levels throughout the course of their lives. Despite the fact that men's androgen concentrations remain higher throughout life, as compared to women, Men lose more androgens than women do, both in absolute and relative terms, and at a younger age. Absolute serum concentration may not be as significant as relative variation in androgens. This could corroborate the findings that males are more vulnerable to the negative effects of ageing on the health of their meibomian glands because of a possibly larger protective effect of high androgen levels in youth, which is followed by a faster decline in androgen levels.[15] Estrogens appear to have antagonizing effects on the physiology of the meibomian gland compared to androgens. The loss of trophic support of androgens on the meibomian gland is more critical to the worsening of tear film instability and other DED signs in aged women than the reduced estrogen support explaining increased prevalence of DED in postmenopausal women.[16,17] In view of the above literature, further research involving a larger population which is age matched, is warranted to establish the association between MGD and sex.

The association between MGD grades and lipid profile has been a focal point in ophthalmic research, as MGD is a primary contributor to evaporative dry eye disease.6 In the present study, as evidenced by one-way ANOVA outcomes, a significant association of raised TG, TC, and LDL levels with increasing MGD severity were observed [Table 3].

In a meta analysis of five studies, Tomioka et al observed a significant association (P < 0.001) of MGD severity with high TC (Odds ratio = 5.245; 95% CI: 1.582–17.389) and high TG (Odds ratio = 3.264; 95% CI: 1.047–10.181). However, no significant association of MGD severity with high LDL (Odds ratio = 3.429; 95% CI: 1.836–6.403; p = 0.106) or low HDL (Odd ratio = 1.018; 95% CI: 0.649–1.597; p = 0.459) was seen.[6]

Guilani et al (2018), also found that higher cholesterol and triglyceride levels correlated with severe glandular dysfunction.[9] Likewise, Jacob et al reported a significant association of increased LDL with MGD severity (P =0.0001).[18] Braich et al conducted a case-control study and found that MGD patients had significantly higher levels of TG (≥150 mg/dL), TC (≥200 mg/dL), and LDL (≥130 mg/dL) compared to controls (P < 0.05).[19] Based on above results it can be reiterated that the lipid profile components particularly TG and TC are critical biomarkers, as their dysregulation can promote inflammation and oxidative stress on the ocular surface, contributing to symptoms like dryness and irritation.[20]

However, discrepancies arise with LDL and HDL; while the present study showed significant LDL increase (e.g., 144.3 ± 17.8 mg/dL in Grade 1 to 232.1 ± 4.9 mg/dL in Grade 3), a Korean study in 2021, found no consistent LDL elevation across MGD subtypes, attributing this to ethnic and methodological differences.[21]

Interestingly, in the present study, HDL levels did not show a statistically significant correlation (P = 0.78) with MGD severity (Table 3). This contrasts with findings of Dao et al. (2010), who reported lower HDL levels in MGD patients compared to controls (P = 0.045).21 However, other researchers, such as Akowuah et al. (2023), found a weak association between HDL and MGD (OR: 1.15, 95% CI: 0.74–1.79), suggesting that while dyslipidemia plays a key role in MGD pathogenesis, not all lipid fractions are equally implicated.[22]

These inconsistencies may stem from variations in sample sizes, diagnostic tools (e.g., meibography vs. lipidomics), and population demographics. The emphasis on Indian cohorts in the present study adds context, as genetic factors may influence lipid responses, but limitation in generalizability arise from the lack of cross-ethnic validation. Overall, while agreements on triglycerides and cholesterol strengthen the evidence for a lipid-MGD link, the contradictions underscore the need for standardized grading and diverse studies on large groups, to resolve these gaps.

Limitation: The study was conducted at a single tertiary care center, which may limit the generalizability of the findings to the broader population. Regional and genetic variations in lipid metabolism and ocular surface disease susceptibility may influence the association between dyslipidemia and MGD. A multicentric approach with a larger and more diverse population would provide more robust conclusions. Another limitation was use of subjective assessment methods such as the Ocular Surface Disease Index (OSDI) score, while useful, have inherent biases. Future research employing objective tear film analysis like meibography through advanced imaging methodologies would enhance diagnostic accuracy.

Conclusion

In conclusion, increasing age is associated with disease severity. No effect of sex with MGD grades could be established. The present study's findings on the association between MGD grades and lipid profile, particularly with TG, TC, and LDL, substantiate the role of systemic dyslipidemia in MGD severity, while acknowledging discrepancies in HDL responses. The present study emphasizes the importance of integrating lipid profiling into MGD diagnostics, paving the way for personalized treatments that could improve patient outcomes. However, limitations in study design, including potential biases in grading and sampling, underscore the need for more standardized, large-scale investigations to enhance reliability and address gaps.

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Conflicts of interest

There are no conflicts of interest.

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