Original Article

Association of Severity of Meibomian Gland Dysfunction in Diabetic Patients with and without Dyslipidemia

P. Priyadarshini[1], M. Loganathan[2]

[1]Senior Resident Ophthalmology, Indira Gandhi Medical College and Research Institute, Puducherry, India. [2]Professor & HOD, Department of Ophthalmology, Sri Venkateshwaraa Medical College Hospital and Research Centre, Puducherry, India

Abstract

Background: Meibomian Gland Dysfunction defined as "a chronic and diffuse anomaly of Meibomian glands, commonly characterized by obstruction of the terminal duct and /or qualitative or quantitative changes in glandular secretion". According to DEWS II workshop, diabetes is one of the risk factor for dry eye and the symptoms are more in diabetic than in non-diabetic population. The aim is to determine the association between the different levels of dyslipidemia and severity of Meibomian gland dysfunction in diabetic patients. **Material and Methods:** This is a cross-sectional analytical study from November 2019 to May 2021 comprising of 84 individuals with diabetes who have dysfunctional meibomian glands. Fasting serum lipid profile was done. **Results:** Total number of patients who belonged to stage 1 MGD was 24, stage 2 was 29, stage 3 was 16 and stage 4 was 15. Stage 2 had the greatest number of patients (n=29, 34.5%), whereas stage 3 had the fewest patients (n=15, 17.9%). Maximum number of patients with LDL cholesterol >130 mg/dL belonged to stage 3. Maximum number of patients with HDL cholesterol 40 mg/dL or less belonged to stage 4. Maximum number of patients with Triglyceride levels > 150mg/dl belonged to stage 4. The largest group of patients in our study (n = 29) were in stage 2, whereas the smallest group (n = 15) were in stage 4. Given the significance of the P value, there is a correlation between rising MGD stage and rising lipid profile component values. **Conclusion:** There is a strong association between severity of MGD and the level of dyslipidemia in the blood. As the lipid levels increases in the body, the severity of MGD increases.

Keywords: Meibomian gland dysfunction, dyslipidemia, dry eyes.

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Introduction

Meibomian Gland Dysfunction defined as "a chronic and diffuse anomaly of Meibomian glands, commonly characterized by obstruction of the terminal duct and /or qualitative or quantitative changes in glandular secretion.[1] According to DEWS II workshop indicated that diabetes is one of the risk factor for dry eye and the symptoms are more in diabetic than in non-diabetic population.[2] MGD is categorised as either high delivery (hypersecretory and seborrhoeic) or low delivery (hyposecretory) based on the reduced outflow (obstructive). Both Hyposecretory and Hypersecretory MGDs are influenced by endogenous factors like age, sex, hormonal disturbances and exogenous factors such as topical medications.[3] Given that meibomian gland secretion is lipid-based, it seems sense to look for any potential connections between meibomian lipids and abnormalities in systemic lipid levels.[4]

Considering all these factors, this study was planned to determine the association between Dyslipidemia and MGD among diabetic population. and also to assess the association between the severities of MGD with severity of Diabetic Retinopathy (as per ETDRS classification) in type 2 diabetic patients.

Materials and Methods

A cross-sectional analytical study done in department of Ophthalmology, Sri Venkateshwaraa Medical College Hospital and Research Centre involving the OPD patients from November 2019 to May 2021 comprising of 84 diabetic patients with meibomian gland dysfunction. Patients less than 18 years and recent ocular surgery or are on topical medications and ocular surface disorders were excluded from the study. The sample size has been calculated by assuming the prevalence of 15% of MGD (Grade 2 to 4) among the diabetics as reported in a study by Shamsheer et al,[5] with95% confidence level and corresponding Z score = 1.96 and at 5% significance level and the calculated sample size was 84.

After getting consent from the study participants, Meibomian gland status was assessed by Meibum quality (assessed in each of eight glands of central third of the lower eyelid on a 0–3 scale), Meibum expressibility (measured on a scale of 1 to 3) from the

Address for correspondence: Dr. P. Priyadarshini, Senior Resident Ophthalmology, Indira Gandhi Medical College and Research Institute, Puducherry, India.
E-mail: priyavanasi@gmail.com

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five glands in the central third of the lower eyelid, and fluorescein staining of the exposed cornea and conjunctiva, liid margin features were assessed. Ocular surface disease index questionnaire along with blink rate per minute, tear film break up time, lower tear meniscus height, Schirmer's test were used to assess the dry eye status. Fasting serum lipid profile was done.

The data were entered in MS Excel program, SPSS software version 23.0 used for analysis. Numerical data was expressed as median (IQR) and Percentages. IndependentT-test was used to determine the association between the lipid levels and severity of MGD in diabetic patients with dyslipidemia and without dyslipidemia. Chi square tests was used to assess the association between the presence and severity of MGD with severity of Diabetic retinopathy. Statistical significance was defined as a P value of less than 0.05.

Results

Demographic and Clinical Characteristics: A total of 84 diabetic patients with meibomian gland dysfunction (MGD) were included in the study. The majority of participants were between 60–69 years of age (32.1%), while only 3.6% were younger than 40 years (Table 1). Females constituted 56.0% of the study population, with a mean age of 56.4 ± 10.7 years, while males represented 44.0%, with a mean age of 55.4 ± 10.2 years [Table 1].

Regarding disease severity, Stage 2 MGD was the most prevalent (34.5%), followed by Stage 1 (28.6%), Stage 3 (19.0%), and Stage 4 (17.9%) [Table 1]. Symptom severity, as assessed by the Ocular Surface Disease Index (OSDI), increased progressively with advancing MGD stage. The mean OSDI scores were 10.97 ± 3.97 in Stage 2, 24.06 ± 3.23 in Stage 3, and 37.93 ± 2.19 in Stage 4, with an overall mean score of 15.14 ± 13.77 [Table 1]. No statistically significant association was observed between OSDI scores and meibomian gland expressibility status across stages.

A statistically significant difference in mean age was observed between Stage 2 and Stage 3 patients (p = 0.004), with Stage 3 patients being older by a mean difference of 9.8 years. No significant age differences were identified between other stage comparisons.

Table 1: Demographic Characteristics, Distribution of MGD Stages, and OSDI Scores (N = 84)

Variable	Category	n (%)	Mean ± SD
Age Group (years)	<40	3 (3.6)	—
	40–49	22 (26.2)	—
	50–59	23 (27.4)	—
	60–69	27 (32.1)	—
	≥70	9 (10.7)	—
Gender	Female	47 (56.0)	56.4 ± 10.7 years
	Male	37 (44.0)	55.4 ± 10.2 years
MGD Stage	Stage 1	24 (28.6)	—
	Stage 2	29 (34.5)	10.97 ± 3.97
	Stage 3	16 (19.0)	24.06 ± 3.23
	Stage 4	15 (17.9)	37.93 ± 2.19
Overall OSDI Score	—	—	15.14 ± 13.77

Table 2: Association of Various Components of lipid parameters across different stages of MGD

Variables (in mg/dL)		Stage 1 MGD (n=24)		Stage 2 MGD (n=29)		Stage 3 MGD (n=16)		Stage 4 MGD(n=15)		Total (n=84)	
		N	%	N	%	N	%	N	%	N	%
Total Cholesterol**	<200	18	75.0	20	69.0	5	31.3	3	20.0	46	54.8
	>200	6	25.0	9	31.0	11	68.8	12	80.0	38	45.2
HDL*	<40	5	20.8	12	41.4	6	37.5	8	53.3	31	36.9
	>40	19	79.2	17	58.6	10	62.5	7	46.7	53	63.1
LDL**	<130	19	79.2	19	65.5	7	43.8	7	46.7	52	61.9
	>130	5	20.8	10	34.5	9	56.3	8	53.3	32	38.1
Triglycerides*	<150	19	79.2	19	65.5	6	37.5	1	6.7	45	53.6
	>150	5	20.8	10	34.5	10	62.5	14	93.3	39	46.4

Table 3: Difference of mean of total cholesterol across various stages of severity of MGD

MGD STAGE		Mean Difference	P value	95% Confidence Interval	
				Lower bound	Upper bound
Stage 1 MGD	Stage2 MGD	-4.95833	0.997	-33.4875	23.5709
	Stage3 MGD	-32.02083**	0.045	-63.5420	-.4997
	Stage4 MGD	-47.82500**	0.048	-95.6032	-.0468
Stage2 MGD	Stage1 MGD	4.95833	0.997	-23.5709	33.4875
	Stage3 MGD	-27.06250**	0.028	-52.0597	-2.0653
	Stage4 MGD	-42.86667	0.063	-87.4904	1.7571
Stage 3 MGD	Stage1 MGD	32.02083**	0.045	.4997	63.5420
	Stage2 MGD	27.06250**	0.028	2.0653	52.0597
	Stage4 MGD	-15.80417	0.896	-61.9421	30.3338
Stage4 MGD	Stage1 MGD	47.82500**	0.048	.0468	95.6032
	Stage2 MGD	42.86667	0.063	-1.7571	87.4904
	Stage3 MGD	15.80417	0.896	-30.3338	61.9421

*p>0.05 non-significant **p<0.05 significant

Association Between Lipid Profile Parameters and MGD Severity

A significant association was observed between total cholesterol levels and MGD severity ($p < 0.05$) [Table 2]. The proportion of patients with total cholesterol >200 mg/dL increased progressively from Stage 1 (25.0%) and Stage 2 (31.0%) to Stage 3 (68.8%) and Stage 4 (80.0%). This increasing trend across stages is illustrated in [Figure 1].

Pairwise comparisons demonstrated significant mean differences in total cholesterol between Stage 1 and Stage 3 (mean difference: 32.0 mg/dL; $p = 0.045$), and between Stage 1 and Stage 4 (mean difference: 47.8 mg/dL; $p = 0.048$) [Table 3, Figure 2]. Additionally, a significant difference was observed between Stage 2 and Stage 3 (mean difference: 27.1 mg/dL; $p = 0.028$). Confidence intervals for these comparisons did not cross zero, confirming statistical significance [Figure 2]. No significant differences were observed between Stage 3 and Stage 4.

Low-density lipoprotein (LDL) cholesterol levels >130 mg/dL were also significantly associated with higher stages of MGD ($p < 0.05$) [Table 2]. Elevated LDL was present in 56.3% of Stage 3 and 53.3% of Stage 4 patients, compared with 20.8% in Stage 1.

Similarly, triglyceride levels >150 mg/dL demonstrated a significant association with MGD severity ($p < 0.05$) [Table 2]. Elevated triglycerides were observed in 62.5% of Stage 3 and 93.3% of Stage 4 patients. Mean triglyceride levels were significantly higher in Stage 4 compared to Stage 1 (mean difference: 130 mg/dL; $p = 0.002$) and Stage 2 (mean difference: 122 mg/dL; $p = 0.003$). While Stage 4 patients had a greater percentage of HDL cholesterol levels below 40 mg/dL (53.3%), the association was less pronounced compared to other lipid parameters [Table 2].

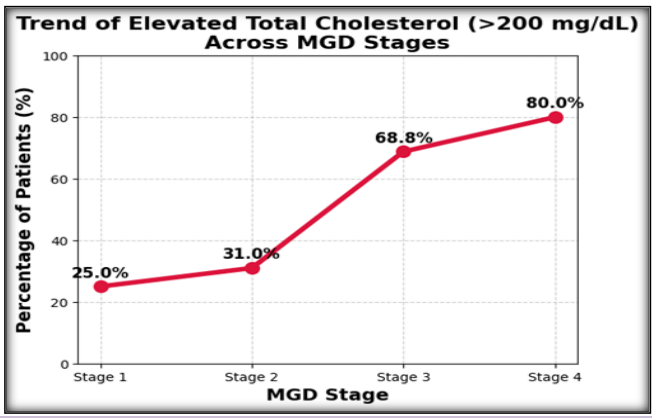

Figure 1: Trend of elevated total cholesterol (>200 mg/dL) across stages of Meibomian Gland Dysfunction (MGD).

The line graph shows a progressive increase in the proportion of patients with elevated total cholesterol from Stage 1 (25.0%) to Stage 4 (80.0%), indicating a positive association between increasing MGD severity and higher total cholesterol levels.

Summary of Key Findings: Advancing MGD severity was associated with progressively higher levels of total cholesterol, LDL cholesterol, and triglycerides. A clear increasing trend in the proportion of patients with elevated total cholesterol across stages was demonstrated [Figure 1], and statistically significant mean differences in total cholesterol between early and advanced stages were confirmed through pairwise analysis [Table 3, Figure 2]. Symptom severity, as measured by OSDI, also increased with stage progression [Table 1]. These findings indicate a significant association between dyslipidemia and the severity of MGD in diabetic patients.

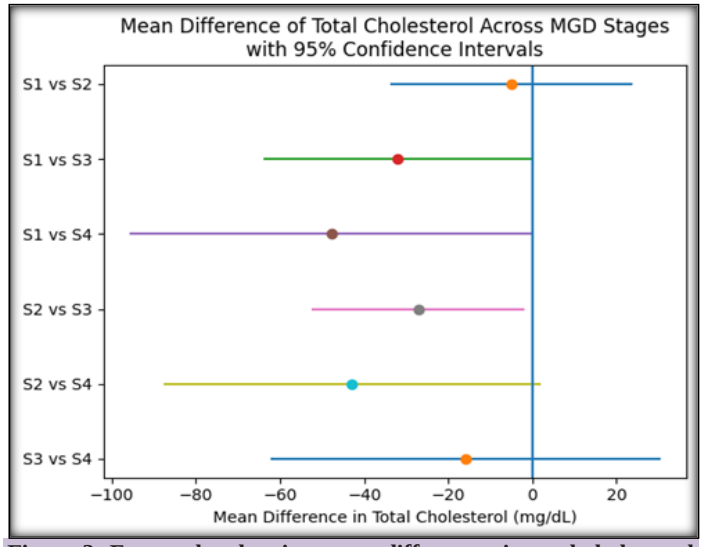

Figure 2: Forest plot showing mean differences in total cholesterol levels (mg/dL) between stages of Meibomian Gland Dysfunction (MGD) with 95% confidence intervals.

The vertical reference line at 0 indicates no difference between stages. Comparisons whose confidence intervals do not cross 0 represent statistically significant differences ($p < 0.05$), demonstrating higher total cholesterol levels in advanced stages compared to earlier stages.

Discussion

The Meibomian Gland Dysfunction (MGD) is one of the common causes for ocular irritation with minimal accuracy while reporting. Current evidences in clinical settings, report the prevalence of MGD up to 70%.[6,7] However, recently, few comparative studies have reported and found out that patients of MGD have had derangement of cholesterol composition,[8,9] to the extent that cholesterol in meibum was found to be the precursor for MGD pathology by making its function hampered.[10]

Total number of participants in our study was 84. The number of patients with stage 1 MGD was 24, stage 2 MGD was 29, stage 3 was 16 and stage 4 MGD was 15. In contrast to Stage 4, which had the fewest patients (n=15, 17.9%), Stage 2 had the most patients (n=29, 34.5%). In a similar vein, the study's minimum number of patients were under 40 years old, while its maximum number of patients were between 60 and 69.

The current study reported that the prevalence of MGD was more common among female population (56%) when compared to males (44%). This is in consistent with the majority of the

previous studies by Justin timothy et al,[11] which shows strong association between female sex and severity of MGD. We discovered that there is little correlation between growing older and the severity of MGD. In contrast, Villani et al,[12] work used in vivo laser scanning confocal microscopy to assess age-related alterations in the meibomian gland. Villani et al.'s study also showed that meibomian gland diameter and density dramatically declined with age. The findings of the current investigation and those of the studies by Bukhari et al,[13] and Puneet Briach et al,[8] are also in agreement with this observation.

There was no association between increase in duration of diabetes mellitus and dyslipidemia. This is in contrast to the findings of study by Sandra Johanna et al in her study which showed as the duration of diabetes mellitus increases, the severity of dyslipidaemia also increases.[12] One another study by Manjula et al showed the increase in prevalence of MGD with increase in duration of diabetes.[16] This difference between other studies and our study may be attributed to the uneven distribution of the participants with regards to the duration of diabetes in each category.

There was no significant association between the fundus findings for diabetic retinopathy and stages of MGD. However the severity of diabetic retinopathy depends on various factors such as age of onset of diabetes and glycemic control of diabetes mellitus which is not taken into account in this study.

In this study, 45.1% of people had TC >200 mg/dL, while 15.7% have TC >240 mg/dL. 32.8% of people had LDL >130 mg/dL, and 33.1% have HDL <40 mg/dL.[7] The number of MGD patients with TC <200 mg/dL in our study were 46 (54.8%) and >200 mg/dL is 38 (42.8%), respectively. Stage 4 included the greatest number of patients with TC >200 mg/dL. The degree of TC and the severity of MGD are positively correlated, as indicated by the substantial P value. This is in line with the results of the research done by Bukhari et al. and Dao et al.[13,17] Of the MGD patients, 32 (38.1%) had LDL cholesterol levels greater than 130 mg/dL, and 52 (61.9%) had LDL cholesterol levels below 130 mg/dL. Stage 2 had the greatest number of patients, while Stage 4 had the fewest cases. Stage 3 included the greatest number of individuals with LDL cholesterol levels more than 130 mg/dL. There was a positive correlation between the stages of MGD and level of LDL cholesterol as the P value was significant. This observation aligns with the results of every study that was previously mentioned.[7,12-14,17,18]

In the present study, stage 2 had the greatest number of patients (n = 29), whereas stage 4 had the fewest patients (n = 15). However, stage 4 included the greatest number of patients with HDL cholesterol levels of 40 mg/dL or below. Because of the significant P value and the correlation between rising MGD stage, age, female sex, and rising values of all lipid profile components. A "cause and effect" relationship, however, cannot be established by a prospective observational study, such as the one being conducted now. To demonstrate that aberrant serum cholesterol levels can result in MGD, a bigger prospective investigation is needed. Second, MGD's aetiology is unclear and could involve multiple factors. Thirdly, because of the small sample size, further extensive research is required to confirm this finding. Fourth, our study's generalisability was limited because all of the subjects were Indian. Regardless of whether "bad" or "good" cholesterol is implicated, MGD may be a sign of undetected hypercholesterolaemia.

We recommend that diabetic patients with MGD should undergo a fasting lipid profile test to identify the dyslipidemia and prevent the ocular and systemic complications associated with dyslipidemia. Good control over dyslipidemia may be included as a part of treatment protocol in the management of meibomian gland dysfunction.

Conclusion

In this cross-sectional analytical study of 84 diabetic patients with meibomian gland dysfunction (MGD), Elevated levels of serum lipid markers, including total cholesterol, low-density lipoprotein (LDL), and triglycerides, were substantially linked to increasing MGD severity. A progressive increase in the proportion of patients with total cholesterol >200 mg/dL was observed from early to advanced stages, and significant mean differences in total cholesterol were demonstrated between Stage 1 and Stages 3 and 4. Elevated triglyceride levels showed a particularly strong association with advanced MGD. Symptom severity, as measured by the Ocular Surface Disease Index (OSDI), also increased with advancing stage of disease.

These findings suggest that dyslipidemia is significantly associated with the severity of MGD in diabetic patients. While causality cannot be established due to the cross-sectional design, the results highlight the importance of systemic metabolic evaluation in patients presenting with moderate to severe MGD. Screening for lipid abnormalities may be clinically relevant in this population.

Limitations: Several limitations should be considered when interpreting the findings of this study. First, the cross-sectional design precludes establishing a temporal or causal relationship between dyslipidemia and MGD severity. Second, the sample size was relatively small (N = 84), which may limit statistical power and generalizability of the findings. Third, all participants were recruited from a single center and belonged to a relatively homogeneous population, potentially limiting external validity. Future large-scale, prospective, multicenter studies are warranted to further clarify the relationship between systemic lipid levels and the progression of MGD and to explore potential pathophysiological mechanisms.

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Conflicts of interest

There are no conflicts of interest.

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