



ASSOCIATION OF MEIBOMIAN GLAND DYSFUNCTION WITH DYSLIPIDEMIA

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ABSTRACT

Aim: To determine association of meibomian gland dysfunction with serum lipid levels and to correlate the severity of meibomian gland dysfunction with serum lipoprotein levels. **Material and Method:** This was a prospective observational case control study comprised of 120 patients attending the outpatient Department of Ophthalmology at Subharti Medical College, Meerut. This study was conducted over a period of 12 months from March 2021-March 2022. All cases underwent a detailed evaluation including ocular, systemic history and anterior segment slit lamp examination of lid margins, tear meniscus, conjunctiva, cornea and tear film. The study was done in two groups i.e Group A included 60 patients/cases more than 20 years age with moderate to severe MGD and Group B included 60 age matched controls from general population. All patients underwent complete ophthalmic examination and the signs and symptom scores were recorded. A fasting lipid profile was done for both these groups. **Results:** In this prospective observational study, there was statistically significant difference was observed in serum triglycerides level ($p=0.041$), serum LDL level ($p<0.01$) and serum HDL level ($p=0.007$) between cases and control groups. There was very statistically significant association of serum LDL level ($p<0.01$), serum triglycerides level ($p=0.0038$) and serum HDL level ($p=0.009$) with severity of meibomian gland dysfunction was observed. However, there was no statistically significant difference in serum total cholesterol (TC) between cases and control groups ($p=0.27$) and no statistically significant association of serum total cholesterol level with severity of MGD ($p=0.21$). **Conclusion:** This prospective observational study shows association of meibomian gland dysfunction with dyslipidaemia. It also reveals association of TG, LDL and HDL level with severity of meibomian gland dysfunction.

KEYWORDS :**INTRODUCTION**

Meibomian glands are also called tarsal glands, palpebral glands and tarsoconjunctival glands. These glands were mentioned by Galen in 200 AD¹ and were described by Heinrich Meibom (1638-1700), a German physician in his work *De Vasis Palpebrarum Novis Epistola* in 1666. Meibomian glands are modified holocrine sebaceous structures which secrete meibum, a lipid substance that forms the superficial layer of tear film and prevents evaporation of underlying aqueous layers and further development of dry eye.² Meibomian glands are present inside the tarsal plate along the rims of the eyelid. These glands are 25-40 in number in the upper eyelids and 20-30 in number in the lower eyelids.^{3,4} Each meibomian gland comprises of multiple acini-containing meibocytes, lateral ductules, a central duct, and an excretory duct that opens at the posterior lid margin.⁵

The secretion of meibomian gland is lipid in nature referred as meibum which reduces evaporation of aqueous phase. It is carried within the gland by the force of secretory process from continuous secretion and by actions of the orbicularis and iris muscles during blinking.⁶

Meibomian gland dysfunction, a term coined by Korn and Henriques in 1980 and is one of the major causes for ocular surface disorders and dry eye disease.⁷

Meibomian gland dysfunction is caused by terminal duct obstruction with thickened opaque meibum containing keratinized cell material and altered composition of meibum.⁵ The common symptoms of MGD are itching, dryness, foreign body sensation, watering, eyelid swelling, soreness of eyes and difficulty in using contact lenses. The common signs present in MGD are thickening of expressed meibum, pouting

or plugging of meibomian gland orifices, increased thickness and vascularity of eyelid margin. Diagnosis of asymptomatic MGD is done by clinical examination of gland expression with application of modest pressure over the lower eyelid while diagnosis of symptomatic MGD patients is done by examination of lid morphology, meibomian gland mass, meibum expressibility from the gland openings, Tear film breakup time (TBUT), Schirmer's test, conjunctival and corneal staining.⁸

The chemical analysis of lipids secreted from healthy meibomian glands shows the mixture of polar lipids (phospholipids and glycolipids) and non-polar lipids (wax esters, cholesterol and cholesterol esters).⁶

Dyslipidemia is defined as abnormal levels of lipids in the blood such as increased levels of total blood cholesterol (TC), Triglycerides (TG), Low density lipoproteins (LDL) and reduction in high density lipoproteins (HDL).⁹ The present study has been undertaken to assess meibomian gland dysfunction with dyslipidemia and to correlate the severity of meibomian gland with serum lipoprotein levels.

MATERIAL AND METHOD

This was a prospective observational case control study comprised of 120 patients attending the outpatient Department of Ophthalmology at Subharti Medical College, Meerut. This study was conducted over a period of 12 months from March 2021-March 2022. All cases underwent a detailed evaluation including ocular, systemic history and anterior segment slit lamp examination of lid margins, tear meniscus, conjunctiva, cornea and tear film. An informed consent was taken from all the patients in the study. The study was done in two groups i.e

GROUP A included 60 patients/cases more than 20 years age with moderate to severe MGD

GROUP B included 60 age matched controls from general population

Patients were included in the study according to the following inclusion and exclusion criteria. Patients more than 20 years age or older diagnosed with moderate to severe MGD were included in the study. Patients with infectious keratoconjunctivitis or inflammatory ocular surface disorder unrelated to MGD, recent ocular surgeries, alterations of lacrimal drainage system, topical ophthalmic steroids taken during 4 weeks before study, pregnancy, previously taking statins or omega 3 fatty acid supplements that are known to alter lipid levels, presence of Sjogren syndrome, rosacea, parkinson's disease, History of hypercholesterolemia /intake of lipid lowering drugs, Diabetes mellitus, cholestatic liver disease or any other systemic, neurologic disorder, rheumatological or dermatologic disorder affecting health of ocular surface were excluded in the study. Diagnosis of meibomian gland dysfunction was made on the basis of complete ocular and systemic history and clinical examination based on glandular obstruction and meibum quality. Severity of five main symptoms was measured on a 4-point categorical scale (0–3) according to mild, moderate and severe. Slit lamp examination was performed to assess and record the severity of seven signs on a 4-point categorical scale.

Clinical Staging Of MGD

According to the report submitted by the International Workshop on Meibomian gland dysfunction and management in 2011, MGD was divided into 4 stages [14]:

1. STAGE 1 :

- a) No symptoms of ocular discomfort, itching.
- b) Expressibility of meibum – 1

2. STAGE 2

- a) Minimal to mild symptoms of ocular discomfort and itching
- b) Expressibility of meibum -1

3. STAGE 3

- a) Moderate symptoms of ocular discomfort and itching with limitation of activities
- b) Expressibility of meibum -2

4. STAGE 4

- a) Marked symptoms of ocular discomfort and itching with definite limitation of activities
- b) Expressibility of meibum -3

Serum Lipid Profile

This study included serum total cholesterol, serum HDL cholesterol, serum triglycerides and serum LDL levels.

Normal value of total cholesterol is <200mg/dl, serum triglycerides <150mg/dl, serum LDL is <100 mg/dl, serum HDL is >60 mg/dl.

Lipid Profile: Done after overnight fasting. 2ml blood sample was withdrawn in plain vile

Following Parameters were measured:

- 1. Triglycerides (TG): **Hypertriglyceridemia** > 150 mg/dl
- 2. Total cholesterol (TC): **Hypercholesterolemia** > 200mg/dl
- 3. Low density lipoprotein (LDL) cholesterol (LDL-C): **High LDL** > 100 mg/dl
- 4. High density lipoprotein (HDL)cholesterol (HDL-C): **LOW HDL** < 40mg/dl

Statistical Analysis

Data so collected was tabulated in an excel sheet, under the

guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). Difference between two groups was determined using student t-test as well as chi square test and the level of significance was set at $p < 0.05$.

RESULTS

Patients above 20 years age group were included in the study and divided into 2 groups:

GROUP A included 60 patients (cases) with moderate to severe MGD.

GROUP B included 60 age matched controls from general population.

As in Table 1, Out of the total 120 subjects included in the study, Group A included 26 (43.33%) male subjects and 34 (56.67%) female subjects and Group B included 23 (38.33%) males and 37 (61.67%) female subjects. There was no significant difference between the groups in terms of gender ($p=0.63$).

Table 1: Gender distribution among the study groups

Gender	Group A		Group B		p value
	N	%	N	%	
Male	26	43.33	23	38.33	0.63
Female	34	56.67	37	61.67	
Total	60	100	60	100	

As in Table 2, The study subjects were divided into three age groups, i.e., 20-40 years, 41-60 years and >60 years. In age group ranging from 20-40 years, Group A included 8 (13.33%) subjects and Group B included 11 (18.33%) subjects. In 41-60 years, age range, Group A included 33 (55%) subjects and Group B included 29 (48.33%) subjects. In age group >60 years, Group A included 19 (31.67%) subjects and Group B included 20 (33.33%) subjects. There was no significant difference between the groups in terms of age ($p=0.58$).

Table 2: Age distribution among the study groups

Age Group (in years)	Group A		Group B		p value
	N	%	N	%	
20-40	8	13.33	11	18.33	0.58
41-60	33	55.00	29	48.33	
>60	19	31.67	20	33.33	
Total	60	100	60	100	

As in Table 3, Out of the total 60 subjects in case group, majority of subjects 43 (71.67%) had moderate meibomian gland dysfunction and 17 (28.33%) had severe meibomian gland dysfunction

Table 3 : Meibomian gland dysfunction among the case group

Dysfunction	N=60	%
Moderate	43	71.67
Severe	17	28.33

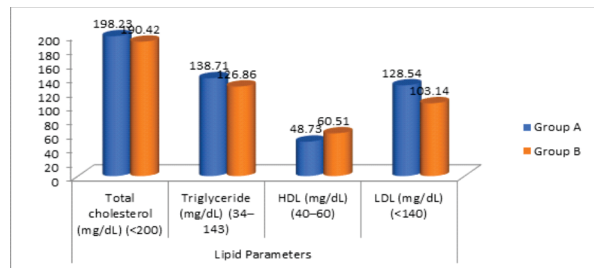
As in Table 4, Mean Total cholesterol (TC) score was 198.23 ± 34.79 and 190.42 ± 36.18 , in Group A and Group B respectively. There was no statistically significant difference in TC between cases and control groups ($p=0.27$). Mean score of Triglyceride (TG) was 138.71 ± 18.37 and 126.86 ± 16.04 , in Group A and Group B respectively. There was statistically significant difference in TG between cases and control groups ($p=0.041$). Mean score of High-density lipoproteins (HDL) was 48.73 ± 13.84 and 60.51 ± 11.38 in Group A and Group B respectively. There was a statistically highly significant difference in HDL between cases and control groups ($p=0.007$). Mean score of Low-density lipoproteins (LDL) was 128.54 ± 20.05 and 103.14 ± 24.96 in Group A and Group B respectively. There was a statistically highly significant

difference in LDL between cases and control groups ($p < 0.01$).

Table 4: Comparison of lipid profile among the study groups

Lipid Parameters	Group A		Group B		P value
	Mean	SD	Mean	SD	
Total cholesterol (mg/dL) (<200)	198.23	±34.79	190.42	±36.18	0.27
Triglyceride (mg/dL) (34–143)	138.71	±18.37	126.86	±16.04	0.041 *
HDL (mg/dL) (40–60)	48.73	±13.84	60.51	±11.38	0.007**
LDL (mg/dL) (<140)	128.54	±20.05	103.14	±24.96	<0.01**

*: statistically significant, **: highly significant



As shown in Table 5, 43 subjects had moderate meibomian Gland Dysfunction and 17 subjects had severe meibomian gland dysfunction.

Out of 43 subjects with moderate meibomian gland dysfunction, 31 subjects (72.09%) had desirable total cholesterol level, 11 (25.58%) had borderline total cholesterol level and 1 subject (2.33%) had severe total cholesterol level. Out of 17 subjects with severe meibomian gland dysfunction, 10 subjects (58.82%) had desirable total cholesterol level, 6 (35.29%) had borderline total cholesterol level and 1 (5.88%) had severe total cholesterol level. **This shows that there was no statistically significant association of total cholesterol level with severity of MGD ($p=0.21$).** Out of 43 subjects with moderate meibomian gland dysfunction, 29 subjects (67.44%) had desirable TG level, 13 (30.23%) had borderline TG level and 1 (2.33%) had high TG level. Out of 17 subjects with severe meibomian gland dysfunction, 5 subjects (29.41%) subjects had desirable TG level, 11 (64.71%) had borderline TG level and 1 (11.76%) had severe TG level. **This shows that there was statistically significant association of TG level with severity of MGD ($p=0.038$).** Out of 43 subjects with moderate meibomian gland dysfunction, 20 subjects (46.51%) had desirable HDL level and 23 (53.49%) had borderline HDL level. Out of 17 subjects with severe meibomian gland dysfunction, 2 subjects (11.76%) had desirable HDL level, 12 (70.59%) had borderline HDL level and 3 (17.65%) had severe HDL level. **This shows that there was statistically highly significant association of HDL level with severity of MGD ($p=0.009$).** Out of 43 subjects with moderate meibomian gland dysfunction, 26 subjects (60.47%) had desirable LDL level and 17 (39.53%) had borderline LDL level. Out of 17 subjects with severe meibomian gland dysfunction, 2 subjects (11.76%) had desirable LDL level, 13 (76.47%) had borderline LDL level and 2 (11.76%) had severe LDL level. **This shows that there was statistically highly significant association of LDL level with severity of MGD ($p < 0.01$).**

Table 5: Association of lipid profile with severity of MGD among cases

Lipid Profile	N=60	Meibomian Gland Dysfunction				p value
		Moderate		Severe		
		N=43	%	N=17	%	
Serum Cholesterol (mg/dl)						
Desirable (<200)	41	31	72.09	10	58.82	0.21

Borderline (200-239)	17	11	25.58	6	35.29	
High (>239)	2	1	2.33	1	5.88	
Serum TG (mg/dl)						
Desirable (<150)	34	29	67.44	5	29.41	0.038*
Borderline (150-199)	24	13	30.23	11	64.71	
High (>199)	2	1	2.33	1	11.76	
Serum HDL (mg/dl)						
Desirable (<40)	22	20	46.51	2	11.76	0.009*
Borderline (40-60)	35	23	53.49	12	70.59	*
High (>60)	3	0	0.00	3	17.65	
Serum LDL (mg/dl)						
Desirable (<100)	28	26	60.47	2	11.76	<0.01
Borderline (100-129)	30	17	39.53	13	76.47	**
High (>129)	2	0	0.00	2	11.76	

DISCUSSION

Meibomian gland dysfunction is a common chronic condition affecting millions worldwide.

Meibum with higher concentration of cholesterol is more viscous at physiological temperature that leads to obstruction of meibomian glands.¹¹ Obstruction of meibomian glands impedes secretion of meibum onto the tear film causes tear film instability. As a result, patient with MGD presents with eye irritation and dry eye.

The present study was conducted with the aim to determine the association of meibomian gland dysfunction with serum lipid levels and to correlate the severity of meibomian gland dysfunction with serum lipoprotein levels.

In our study, females were slightly more as compared to males. There were 56.67% females in group A and 61.67% in group B in comparison to 43.33% males in group A and 38.33% in group B. When gender distribution was compared between group A and B, it was found to be statistically insignificant ($p=0.63$). These findings were in the accordance with the study conducted by **Kashkoui MB et al¹⁰, Guliani BP et al¹¹, Bukhari et al¹², Kumar J et al¹³ and RN Kothari et al¹⁴.**

In our study, subjects were divided into three groups i.e 20-40 years, 41-60 years and > 60 years. The maximum number of subjects were found in age group from 41-60 years i.e 33 subjects (55%) in group A and 29 subjects (48.33%) in group B. There were 19 subjects (55%) in group A and 20 subjects (33.33%) in group B in age group >60 years. The least number of subjects were found in age group from 20-40 years i.e 8 subjects (13.33%) in group A and 11 subjects (18.33%) in group B. When age distribution was compared statistically between group A and group B, it was found to be statistically insignificant ($p=0.58$). These findings were in consistency with the study conducted by **Badian R A et al¹⁵ and Kaur P et al¹⁶**

In our study, there were 43 subjects (71.67 %) with moderate meibomian gland dysfunction and 17 (28.33%) subjects with severe meibomian gland dysfunction. The findings of our study were consistent with the study conducted by **Hiremath CH et al¹⁷, Mobin M et al¹⁸ and Singh J et al¹⁹**

In our study, It was observed that the mean score of total cholesterol level was not statistically significant between cases and control groups ($p=0.27$) i.e 198.23 ± 34.79 in group A and 190.42 ± 36.18 in group B respectively. These findings were in consistent with the study conducted by **Sen F et al²⁰** reported that there was no statistically significant difference in serum total cholesterol (TC) between cases and control groups ($p=0.047$).

In our study, It was also observed that the mean score of triglycerides level was statistically significant between cases and control groups i.e. 138.71 ± 18.37 and 126.86 ± 16.04 in

group A and group B ($p=0.041$) respectively. These findings were consistent with that of Braich PS et al²¹ who observed that mean score of TG had statistically significant association ($p < 0.05$) i.e. 98.5 ± 42.1 in cases and 82.3 ± 36.5 in control groups respectively. The findings were consistent with the study conducted by Dao et al² reported statistically significant association of triglyceride level between cases and control groups ($p=0.0049$)

The study conducted by Pinna et al²² reported mean LDL, and HDL score were 127.6 ± 3.9 , and 61.6 ± 1.8 mg/dl in cases and 94.2 ± 2.6 , and 52.5 ± 1.3 mg/dl in controls respectively. All these differences were statistically significant ($P \leq 0.0001$). In our study, the mean score of high-density lipoproteins and low-density lipoproteins i.e., 48.73 ± 13.84 , 128.54 ± 20.05 in cases and 60.51 ± 11.38 , 103.14 ± 24 in controls was statistically significant ($p=0.007$).

These findings are consistent with the studies conducted by Kumar J et al¹³ who reported statistically significant association of LDL level ($p=0.015$) and HDL level ($p < 0.05$) between cases and control groups. Another study conducted by Braich PS et al⁽²³⁾ reported that mean levels of LDL and HDL were 126.1 ± 10.2 , 53.3 ± 4.2 mg/dL in cases and 92.2 ± 12.4 , 45.8 ± 2.6 mg/dL in controls respectively. All differences were statistically significant ($P < 0.001$).

It was observed in our study that out of total 43 subjects with the moderate meibomian gland dysfunction, majority of subjects 31 (73.09%) had desirable total cholesterol level and only 1 subject (2.33%) had high serum total cholesterol level. Similarly, the study also showed that majority of subjects 29 (67.44%) had desirable serum triglyceride level and only 1 subject (2.33%) had high triglyceride level. However, it was seen that majority number of subjects 23 (53.49%) had borderline serum HDL level and 20 subjects (46.51%) had desirable serum HDL level while majority number of subjects 26 (60.47%) had desirable serum LDL level and 17 (39.53%) had borderline serum LDL level.

The study also demonstrated that out of total 17 subjects with severe meibomian gland dysfunction, majority of subjects 10 (58.82%) had desirable serum cholesterol level and only 1 subject (5.88%) had high serum total cholesterol level. Also, our study revealed that majority of subjects 11 (64.71%) had borderline serum triglyceride level and only 1 subject (11.76%) had high serum triglyceride level. Similarly, majority of subjects had borderline serum HDL level i.e., 12 subjects (70.59%) as well as serum LDL level i.e., 13 subjects (76.47%) while only 3 subjects (17.65%) had high serum HDL level and 2 subjects (11.76%) had high serum LDL level.

Thus, our study showed that there was statistically significant association of Triglyceride ($p=0.038$), HDL ($p=0.009$) and LDL ($p < 0.01$) with severity of MGD. However, the study showed no statistically significant association of total cholesterol with MGD severity ($p=0.21$). The findings in our study were consistent with that of Guliani BP et al¹¹ who reported that there was a very strong association between increased LDL (levels > 130 mg/dL) and MGD severity ($p < 0.0001$). The study also showed that there was a statistically significant association between serum HDL level ($p=0.012$) and serum TGs level ($p=0.006$) with severity of MGD. Similar to our study, Irfan KSA et al²⁴ reported that there was a significant association between the severity of MGD and elevated triglyceride levels ($p=0.0001$) and a significant association between the severity of MGD and elevated LDL levels ($p=0.015$)

Our findings were also in accordance with the study conducted by Mobin M et al¹⁸ who reported that there was statistically significant association ($p=0.0001$) between TG

level and severity of meibomitis. The study showed that there was significant association of serum LDL level and severity of meibomitis ($p=0.008$).

Study Limitations

- This Observational prospective study had some limitations hence cannot prove a cause-and-effect association.
- The unknown etiology of MGD and may be multifactorial.
- The Sample size was smaller obviating the need for larger studies to further strengthen this observation.
- The study's generalizability was restricted by the fact that all of the subjects were Indians.

CONCLUSION

In conclusion, this prospective observational study shows association of meibomian gland dysfunction with dyslipidaemia. It also reveals association of TG, LDL and HDL level with severity of meibomian gland dysfunction. Due to the probable association between serum fasting lipid levels and the development of MGD, the current study emphasises the importance of monitoring these levels. Regardless of the type of cholesterol involved whether "good" or "bad," MGD may be a probable sign of hypercholesterolemia, that has not yet been recognised. Additionally, clinicians may use oral cholesterol lowering drugs for the treatment of MGD if prospective studies demonstrate a causal link between dyslipidaemia and MGD.

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