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Dyslipidemia and meibomian gland dysfunction

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Abstract
Background: Meibomitis or Meibomian Gland Dysfunction (MGD) is a common etiological factor for dry eye and the commonest cause for ocular irritation. Patients with abnormal lipid profile and high blood sugar levels (uncontrolled Diabetes), do often present with severe grade of MGD.
Purpose: To determine whether meibomian gland disease is associated with dyslipidemia.
Methods: A correlation between serum fasting lipids and MGD severity was performed, in 60 people.
Results: Dyslipidemia was significantly higher in those with MGD compared to those without. Factors such as age, total cholesterol, LDL, HDL, and triglycerides demonstrated a significant association.
Conclusions: Although the presence of MGD does not have any correlation with dyslipidemia, the prevalence of high triglyceride and low-density lipoprotein levels increases with the increasing severity of MGD. This might highlight the significance of monitoring fasting serum lipids due to its association with the potential correlation with the progression of MGD.

Keywords: Meibomian gland dysfunction, dyslipidemia

Introduction
Meibomitis or Meibomian Gland Dysfunction (MGD) is a common etiological factor for dry eye and the commonest cause for ocular irritation. MGD is one of the most under recognized, underappreciated, and undertreated disease in ophthalmic practice. MGD is a chronic diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/quantitative changes in glandular secretion. It may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation, and ocular surface disease. Patients may present with dry eye, redness, irritation, itching, burning sensation, unstable fluctuating vision, and occasionally blurred vision with visual tasks. Recent studies showed that the prevalence of MGD in general population varies between 30.5 and 54.1%.
MGD is classified into low delivery forms (hyposecretory and obstructive) and high delivery forms (Hypersecretory/Seborrheic). Obstructive MGD is thought to be the most common variety. Both hyposecretory and hypersecretory MGD are influenced by endogenous factors, such as age, sex, hormonal disturbances, as well as by exogenous factors such as topical medications. The obstructive process, however, causes stagnation of meibum in the ductules, which can then undergo mechanical and chemical changes. Studies have shown that meibomian gland secretion in patients with MGD has an increased melting point and hence altered viscosity. As meibomian gland secretion is lipid in nature, it is only logical to search for a possible link between systemic lipid level abnormalities and meibomian lipids.
Various etiological factors like exposure to dust & heat, uncontrolled Diabetes, abnormal lipid profile is contributing to chronic meibomitis. Among these factors, dyslipidemia is a major etiological cause which is always underdiagnosed in managing such cases. So, in the present paper, we would like to bring to notice that dyslipidemia and its management is one factor which needs to be concentrated on, while treating a patient with chronic meibomitis.

Materials and Methods
A total of 60 patients in the age group 30 - 80years, presenting with MGD were included. This study was done in Basweshwara Teaching and General hospital, Kalburgi over duration of 3 years.
The only two inclusion criteria were patients aged 18–54 years, and those diagnosed with MGD based on the signs and symptoms. Patients with age <18 and >54 years were excluded.
Exclusion criteria included patients with infectious keratoconjunctivitis or inflammatory ocular surface disorder, alterations of lacrimal drainage system, topical medications specially for glaucoma, topical steroids, Sjogren syndrome, Rosacea, Parkinson's disease.

Once patients were selected, baseline assessment included: Symptoms scaled according to Ocular Surface Disease Index questionnaire (mild/moderate/severe), Assessment of tear film breakup time (cut-off: 10 seconds), Schirmer's test (cut-off: 10 cm), Lacrimal drainage system was assessed (presence of DCR scar, soft/hard blocks, ectropion/ectropion).

Clinical staging of MGD

According to International Workshop on Meibomian Gland Dysfunction and Management in 2011, MGD is divided into four stages, taking both the symptoms and clinical signs into consideration.

Table 1: Meibomian gland disease staging

Stage	Mgd Grade	Symptoms	Corneal Staining
1	Minimally Altered Expressibility And Secreation Quality	None	None
2	Mildly Altered Expressibility And Secreation Quality	Minimal To Mild	None To Limited
3	Moderately Altered Expressibility And Secreation Quality	Moderate	Mild To Moderate Mainly Peripheral
4	Severely Altered Expressibility And Secreation	Marked	Marked Central & Peripheral

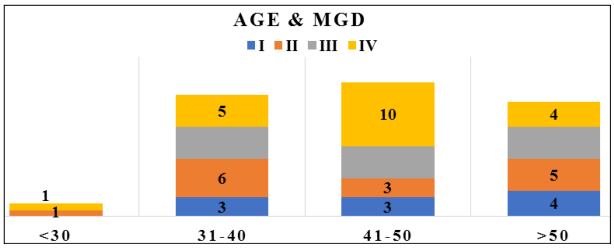

Fig 1: Age & MGD

Lipid profile was done after overnight fasting of 8hrs. 2 mL blood was drawn in plain vial. Lipid profile was done on fully automated analyzer at Department of Biochemistry. Parameters measured were triglycerides (TG), total cholesterol (TC), Low density lipoproteins (LDL), High density lipoprotein (HDL). Dyslipidemia was considered when:

- TG >150 mg/dL (Hypertriglyceridemia)
- TC >200 mg/dL (Hypercholesterolemia)
- LDL >130 mg/dL (High LDL)
- HDL <40 mg/dL (Low HDL)

Statistics and Results

Descriptive and inferential statistical analysis has been carried out in the present study. The results were analyzed by using SPSS version 18 (IBM Corporation, SPSS Inc., Chicago, IL, USA). Results on categorical measurements were presented as frequency (%). Significance was assessed at 5% level of significance. Inferential statistics like Fischer exact test was used.

Age-wise distribution of study subjects

The number of patients in the age groups <30, 31–40, 41–50, >50 were 2, 19, 21 and 18 respectively. Maximum number of patients belonged to stage 3, whereas stage 1 had the least number of patients. Similarly, maximum number of patients in our study were 41-50years of age, while lesser patients belonged to the <30 age group.

Table 2: Age distribution in different stages of MGD

Age	MGD Stage				Total
	One	Two	Three	Four	
<30	0	1	0	1	2
31-40	3	6	5	5	19
41-50	3	3	5	10	21
>50	4	5	5	4	18
Total	10	15	20	15	60

Sex ratio

Out of the 60 patients in the study, 27 were male and 33 were female. Out of which maximum number of female patients in our study belonged to stage 3, while maximum number of male patients belonged to stage 4.

Table 3: Sex & MGD

Sex	MGD Stage				Total
	One	Two	Three	Four	
Female	6	7	14	6	33
Male	4	8	6	9	27
Total	10	15	20	15	60

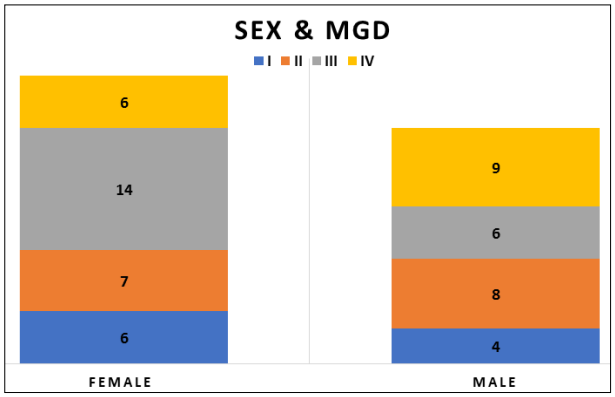

Fig 2: Sex & MGD

Total cholesterol and mgd

The number of MGD patients with TC <200 mg/dL and >200 mg/dL were 17 and 43, respectively. Maximum number of patients with TC <200 mg/dL in our study belonged to stage 2, while maximum number of patients with TC >200 mg/dL belonged to stage 3.

Table 4: Total cholesterol & MGD

Total Cholesterol	MGD Stage				Total
	One	Two	Three	Four	
<200	2	13	1	1	17
>200	2	7	20	14	43
TOTAL	4	20	21	15	60

Triglyceride and mgd

The number of patients with TGs <150 mg/dL and >150 mg/dL were 2 and 58, maximum number of patients belonged to stage 2, whereas stage1 had the least number of patients. Maximum number of patients with TGs >150 mg/dL belonged to stage 2 & 3.

Table 5: Triglycerides & MGD

Triglyceride	MGD Stage				Total
	One	Two	Three	Four	
<150	0	1	0	1	2
>150	9	20	20	9	58
Total	9	21	20	10	60

LDL cholesterol and MGD

The number of MGD patients with LDL <130 mg/Dl and >130 mg/dL were 13 and 47, respectively. Maximum number of patients with LDL cholesterol <130 mg/dL in our study belonged to Stage 2, while maximum number of patients with LDL cholesterol >130 mg/dL belonged to stage 3.

Table 6: LDL & MGD

LDL	MGD Stage				Total
	One	Two	Three	Four	
<130	0	12	0	1	13
>130	8	9	22	8	47
Total	8	21	22	9	60

HDL cholesterol and MGD

The number of patients with HDL <40 mg/dL and >40 mg/dL were 45 and 15. Maximum number of patients with HDL cholesterol <40 mg/dL belonged to stage 3. While maximum number of patients with HDL cholesterol >40 mg/dL belonged to stage 1.

Table 7: HDL & MGD

HDL	MGD Stage				Total
	One	Two	Three	Four	
<40	5	8	17	15	45
>40	6	4	1	4	15
TOTAL	11	12	18	19	60

Discussion

MGD can cause chronic ocular irritation and is seldom reported accurately. Studies postulate an MGD prevalence of up to 70%. The cause of MGD is incompletely understood, but changes in meibum composition and/or obstruction of the meibomian glands is thought to be central to the process.

Studies show that meibum of MGD patients has different components and proportions of cholesterol compared to the meibum of controls. Specifically, cholesterol esters were always present in the glands of patients with MGD but not necessarily in normal controls. Recent study postulates that increased cholesterol in meibum may play a role in the pathology of MGD. Organic substances with a greater number of saturated bonds or larger side chains have higher melting points. This concept can explain why the melting point of normal meibomian secretions ranges from 30 to 34 °C, while cholesterol, with its numerous structural differences, has a typical melting point of 148 °C. Theoretically, meibum with higher concentrations of cholesterol would be more viscous at physiological temperatures, thus clogging the meibomian glands.

Many studies have been done in the past to find association between MGD and a deranged lipid profile. Dyslipidemia is a term that represents an abnormal value in one or more of the lipid profiles. Certain types of dyslipidemia, i.e., low levels of HDL, high levels of LDL, and high levels of TC, have been shown to be independent risk factors for vascular pathological events.

In our study, we found a strong association between increasing age and severity of MGD. This is in accordance with a study by Villani *et al*., which evaluated age-related changes of the meibomian gland using *in vivo* laser scanning confocal microscopy. Their work demonstrated that meibomian gland density and diameter significantly decreased with age.

This observation was similar with the results obtained by Bukhari *et al*. and Punit Briach *et al*.

The prevalence of dyslipidemia in the general population is well described by current literature, which extrapolated data from the National Health and Nutrition Examination Survey. The prevalence of TC >200 mg/dL is 45.1% and TC >240 mg/dL is 15.7%. The prevalence of LDL >130 mg/dL is 32.8%, HDL <40 mg/dL is 15.5%, and TGs >150 mg/dL is 33.1%. Our study has found out that patients with higher stages of MGD more often had serum TGs >150 mg/dL, TC >200 mg/dL, an LDL >130 mg/dL, and serum HDL <40 mg/dL, and there exists an association between increasing stage of MGD, and age, female sex, and increasing values of all the lipid profile components. However a larger prospective study is required to show that abnormal serum cholesterol levels can cause MGD. Secondly, the etiology of MGD is unknown and may be multifactorial. Thirdly, the sample size was small, obviating the need for larger studies to further strengthen this observation and finally the study only includes Indian population. MGD may be a possible marker of yet undiagnosed hypercholesterolemia, regardless the type of cholesterol involved, Moreover, if a causal relationship between dyslipidemia and MGD is proved by prospective studies, and oral lipid-lowering medications may be tried by clinicians for the treatment of MGD. Further studies are needed to evaluate the effect of controlling serum triglyceride and LDL levels on controlling MGD.

Conclusion

A very strong association exists between increasing age and increasing severity of stage of MGD. A positive association exists between female sex and increasing severity of stage of MGD. A positive association exists between increasing severity of MGD and derangement in all the components of lipid profile namely LDL, HDL, Total cholesterol and Triglycerides.

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