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Serum Lipid Profile in Meibomian Gland Dysfunction

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Abstract: *This study was conducted to determine the association between the serum lipid profile and meibomian gland dysfunction (MGD). The study was carried out on patients attending Outpatient Department Of Ophthalmology at M.L.B Medical College, Jhansi. 100 patients with dry eye symptoms, satisfying the inclusion criteria were selected . After complete ocular examination , Tear film tests and lid margin examination to detect MGD were done and allotted two groups as: patients with meibomian gland dysfunction(MGD) [cases] and without MGD [control] ,with no history of dyslipidemia. Both the groups were investigated and compared for Serum Fasting Lipid Profile .Unpaired t test was used to calculate the p- value. There was statistically significant difference in the levels of TCH , TGs , LDL between MGD (CASES) and NonMGD (CONTROLS) with p-value 0.012 , 0.014 , 0.015 respectively . Levels of VLDL and HDL in both groups were insignificant. It may be summarized that patients with MGD with no history of dyslipidemia may have undiscovered abnormal serum cholesterol levels compared to controls without MGD and may become a sign of undiagnosed dyslipidemia and ophthalmologists will have a role in early detection of an important risk factor for cardiovascular disease.*

Keywords: *holesterol ,Dyslipidemia ,Dry Eye,Gland Dysfunction ,Lipid Profile, Meibomian.*

I. Introduction

The meibomian glands (or tarsal glands) are a special kind of sebaceous gland at the rim of the eyelids inside the tarsal plate(Fig 1,2), responsible for the supply of meibum, an oily substance that prevents evaporation of the eye's tear film**[1]**.

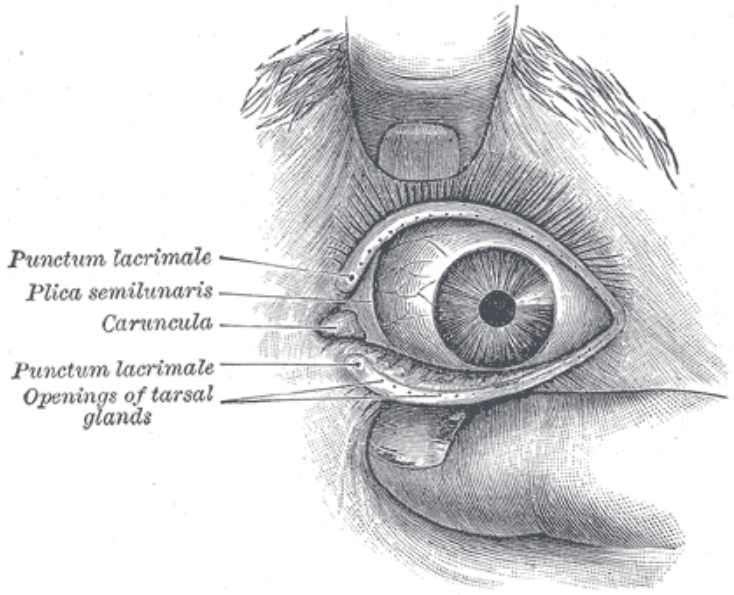

Figure 1 . Meibomian gland[2]

Dysfunctional meibomian glands often cause dry eyes, one of the more common eye conditions. They may also contribute to blepharitis. Inflammation of the meibomian glands (also known as *meibomitis*, *meibomian gland dysfunction*, or *posterior blepharitis*) causes the glands to be obstructed by thick waxy secretions. Besides leading to dry eyes, the obstructions can be degraded by bacterial lipases, resulting in the formation of free fatty acids, which irritate the eyes and sometimes cause punctate keratopathy**[3]**.

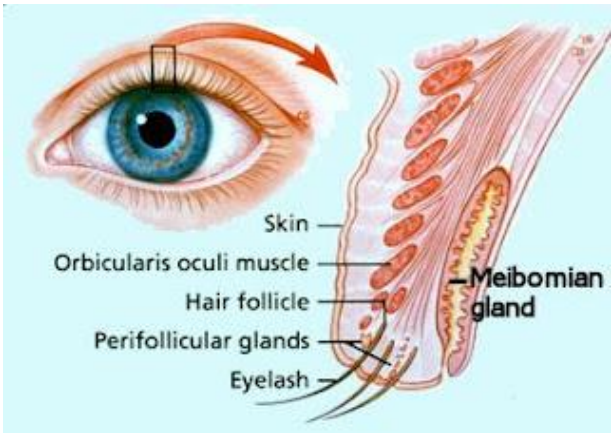

Figure 2 : Anatomy of upper Eye Lid

Meibomian gland dysfunction is more often seen in women and is regarded as the main cause of dry eye disease**[4]**. Factors that contribute to meibomian gland dysfunction can include things such as a person's age and/or hormones**[5]**. Treatment can include warm compresses or expression of the gland by a professional. In some cases antibiotics or steroids are prescribed.

One can have MGD without frank inflammation of the posterior lid margin. In its early phase, MGD could be demonstrated simply by an alteration of the meibomian gland secretions with abnormal quality of the expressant or by decreased or absent expressibility. As the dysfunction progresses, inflammation may indeed occur with related changes such as vascularization of the posterior lid margin.

The Classification of meibomian gland dysfunction based on pathophysiology is also described with two main subcategories: Low delivery and high delivery. Low delivery can occur as a result of hyposecretion or obstruction of the glands. Obstructive MGD, as a result of terminal gland obstruction or altered secretions, is thought to be the "most common form of MGD."

With a number of changes in lifestyle involving dietary preferences, work habits and the advent of computer usage in all spheres of life, the incidence and prevalence of dry eye has increased dramatically in the general population. Meibomian gland dysfunction (MGD) is a major cause of dry eye, but is often overlooked in busy out-patient settings. Meibomian glands contribute to the lipid component of the tear film, and their normal secretion prevents premature evaporation of tears from the ocular surface.

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. Indeed, as the pathogenic mechanism of MGD is being understood, studies have been designed in various parts of the world to detect any correlation between blood lipids and MGD.

At present, there are only a limited number of studies investigating a link between MGD and blood lipids. If a positive correlation can be obtained, this can contribute to early detection and treatment of Dyslipidemia in patients with dry eye due to MGD and vice-versa.**[6]**

II. Materials And Method

A Prospective study was conducted at the OPD of Department Of Ophthalmology at *M.L.B* Medical College, Jhansi. A total number of 100 patients were selected from the routine OPD who presented with dry eye symptoms over a period of 14 months from February 2015 to March 2016 and were categorized based on eligibility/inclusion criteria . A written informed consent was taken from all participants selected for the study.

Inclusion Criteria
Patients with dry eye symptoms :
Cases: those patients with clinical features of MGD [GROUP A]
Controls: those patients without clinical features of MGD [GROUP B]

Exclusion Criteria
1) Patients presently on any regular topical medication, including dry eye treatment.
2) Patients with previous history of any ocular surgery including refractive surgery and eyelid surgeries.
3) Patients already on regular anti-hyperlipidemia drugs.
4) History of dyslipidemia.

Consecutive patients presenting with symptoms suggestive of dry eye were evaluated. A detailed history using a Symptom Assessment in Dry Eye (SANDE) questionnaires was taken. Thorough clinical examination using Slit Lamp was performed to confirm the diagnosis of dry eye and for the probable etiology.

For this, standard tests like Tear Film break-up time [TFBUT], Schirmer's test, Phenol Red Thread test were employed.

Patients found to have dry eye were evaluated further by slit-lamp biomicroscopy of the lid margins for posterior blepharitis and the degree of meibomian gland dysfunction, if any, was graded. After a complete ocular examination, they were allotted into the groups.

Laboratory investigation that was performed in each patient included **Serum Fasting Lipid Profile**.

Dyslipidemia was defined as any of the following :

Hypercholesterolemia – Total Cholesterol >200 Mg/Dl Hypertriglyceridemia – Triglyceride >150mg/Dl
High Levels Of Ldl – > 100 Mg/Dl
High Level Of Vldl – > 33 Mg/Dl
Low Levels Of Hdl – < 40 Mg/Dl

III. Results

The age of the patients included in the study ranged from 20 to >70 years and were divided into 3 groups. Majority of the patients were in the age group of 41-70 years of age (59%). The study included 49 males (49 %) and 51females (51 %) i.e slightly higher female preponderance of simple dry eye itself. Among MGD patients , 26 were females(50.98%) and 24 were males(48.91%) depicting slightly higher female preponderance.

Most of the patients in our study were of rural origin (65%) and rest were urban . Among rural patients, 33 had MGD(50.77%) and rest 32 were NonMGD(49.23%) showing almost equal distribution. Among urban population , 17 patients were of MGD and 18 were of NonMGD. 50.77% in rural population had MGD and only 48.57% of urban population had MGD. Among MGD patients ,maximum were in farmer/ agriculture group(57.89%) second were in household group(55.88%), least were students(10%).

Patients with altered LDL were 60% ;TGs 57% ; TCH and VLDL 55%; HDL 50% (Table 1/Fig 2)

Table 1 : Altered Lab Test/Serum Lipid Profile

S.No.	Lab Test/Serum Lipid Profile	Total Patients
1	TCH	55
2	TG	57
3	LDL	60
4	VLDL	55
5	HDL	50

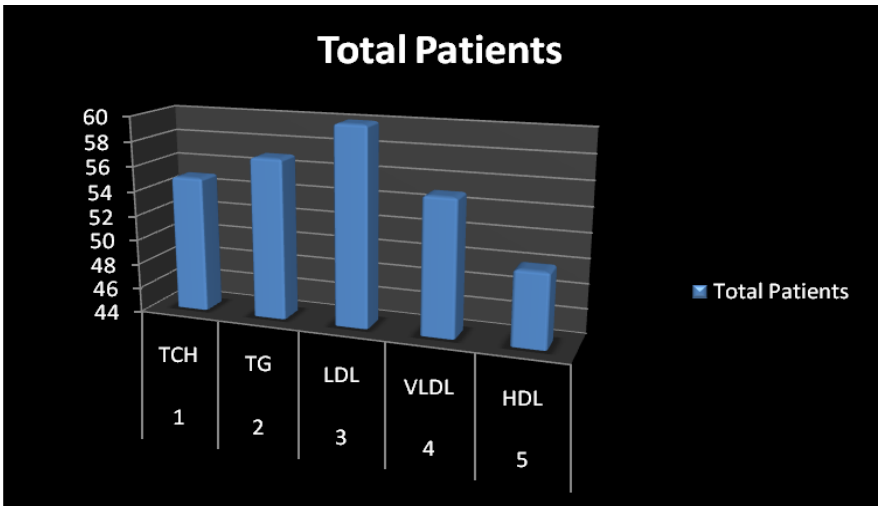

Figure 2: Altered Lab Test/Serum Lipid Profile

Among MGD patients ,94% patients had altered TCH,TGs and 92% had altered LDL(Table 2/Fig 3).

Table 2: Altered Lab Test/Serum Lipid Profile In Mgd Cases And Non Mgd Control

S.No.	Lab Test/Serum Lipid Profile	MGD (Cases)	Percentage	Non MGD (Control)	Percentage
1	TCH	47	94%	8	16%
2	TG	47	94%	10	20%
3	LDL	46	92%	14	28%
4	VLDL	11	22%	44	88%
5	HDL	06	12%	44	88%

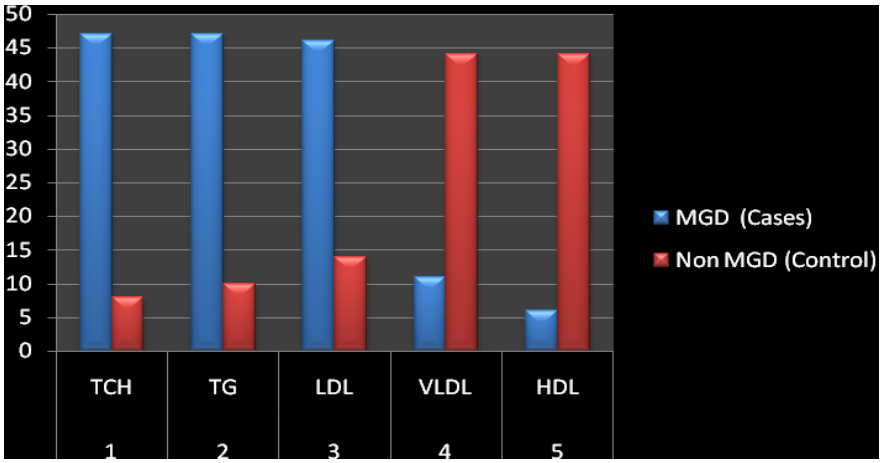

Figure 3: Altered Lab Test/Serum Lipid Profile In Mgd Cases And Non Mgd Control**.**

Table 3: Fasting Lipid Profile Components In Cases Vs Controls

IV. Discussion

Meibomian gland dysfunction (MGD) is a common chronic condition, affecting millions worldwide, and is one of the most frequent pathologies observed on a daily basis by eye specialists throughout the world. In the last decade ,Nichols et al 2011**[7]** stated that MGD has become recognised as the major cause of evaporative dry eye. The scientific literature reports wide variations in the prevalence of MGD, with published rates ranging from as low as 3.5% to close to 70% in clinical and population-based studies [Jie et al.2009;Schein et al .1997] [8]. Although differences in the diagnostic criteria used to define MGD account for much of this variation, and consequently preclude direct comparison between studies, the published results to date present a compelling case to suggest that MGD is markedly more prevalent in Asian populations [schaumberg et al 2011**]** [9]
Our study was conducted at MLB Medical College in the year 2015-2016 which included 100 patients who fulfilled the inclusion criteria.

Age And Sex Distribution

This study included 49 males and 51 females . Majority were in the age group of 41-70 yrs of age (59 %). Patients suffering from MGD in this age group were 35 (59.32%) , more than age group of 20-40 yrs where only 34.21% had MGD. Number of patients in age group >71 yrs were only 3 , out of which 2 had MGD (66.66 %).Our study was consistent with the studies which supports higher prevalence of MGD with ageing i.e of Den et al**[10]** who reported about the possible effects of aging in cross-sectional study in which evaluation of lid margin anatomy, meibomian gland, ocular surface epithelium, and tear function was conducted in 354 eyes of 177 subjects. These authors observed that whereas only a few patients aged 50 years and younger showed notable abnormalities in the lid margin or meibomian glands, the frequency of such abnormalities increased dramatically in those older than 50 years.

Hykin and Bron**[11]**have reported in a cross-sectional study with 80 subjects between 5 and 87 years old that an increase in eyelid margin vascularity, keratinization, telangiectasia, and opacity of meibomian gland secretions was observed with aging.

Sullivan et al**[12]** also showed significant alterations in older versus younger individuals' polar and neutral lipid profiles derived from meibomian gland secretions by high-performance liquid chromatography or mass spectrometry. Such findings appear to coincide with a documented increase in the incidence and prevalence of dry eye disease with aging as stated by Subcommittee of the International Dry Eye WorkShop. (2007). **[13]** In our study 51% were females , out of which 50.98% had MGD which was only slightly higher than that of males i.e 48.91% with MGD .

Conner and colleagues**[14]** pointed out that women who were taking oral contraceptives had significantly higher goblet cell density than those who were not taking oral contraceptives. Statistically significant difference in goblet-cell count between men and women over the 30-day test period. The mean goblet-cell count measured for men was 3.75% +/- 1.04%, while the mean count for women was 2.545% +/- 0.8%. A significant difference in goblet-cell count was also noted when subjects using oral contraceptives (3.065% +/- 0.98%) are compared with those not using oral contraceptives (2.28% +/- 0.92%).

Krenzer and colleagues**[15]** reported that chronic androgen deficiency is associated with meibomian gland dysfunction. Schaumberg and colleagues and Uncu and colleagues**[16]** reported that postmenopausal women who use hormonal replacement therapy (HRT) have a higher prevalence of DED compared with those who have never used HRT. In total also, in our study patients with dry eye itself were higher in 41-70 yrs age group, both in males and females,(24 and 35 respectively).

Residential Status And Occupation

In our study 65% of the patients were of rural origin and 35% were urban.

Out of them 50.77% in rural population had MGD and only 48.57% of urban population had MGD , which is slightly higher than urban population.

However, according to one of the the metaanalysis by Ning-ning Liu, Lei Liu, Jun Li and Yi-zhou Sun **[17]** No significant difference was found in dry eye prevalence rate between urban China and rural China (15.3% and 21.3%, resp., OR: 1.06, 95% CI: 0.97–1.17, and $P = 0.205$).

Lipid Profile In Mgd And Non Mgd (Table 3)

A. In our study, out of 50 MGD cases ,47 patients had altered total cholesterol (**TCH**) as compared to 8 patients in Non MGD controls. This difference was statistically significant with P- value 0.012. 95% CI (confidence interval) = 3.89 to 31.18 SE (std. error) difference = 6.87 .

Our study was consistent with the study of Pinna A, Blasetti F, Zinellu A, Carru C, Solinas G.**[18]**According to them , Hypercholesterolemia was found in 35 cases (58.3%) and 4 controls (6.3%), a statistically significant difference ($P < 0.0001$). Mean total Cholesterol was 210.8 ± 4.4 in cases and 162.9 ±

4.1 In Controls.

Another study by Braich PS , Howard MK , Singh JS**[20]** showed consistent results and defined Dyslipidemiaas , by either a fasting total cholesterol level of **≥** 200 mg/dL, was detected in 70 cases (64 %) and 21 controls (18 %), $P < 0.001$. Mean levels total cholesterol, 203.1 ± 13.2, in cases and 156.6 ± 14.5 , in controls. All differences were statistically significant ($P < 0.05$). MGD was significantly associated , total cholesterol **≥**200 mg/dL (OR 14.3; 95 % CI 8.220.7,$P < 0.01$).

Another study by Dao AH , Spindle JD, Harp BA, Jacob A, Chuang AZ, Yee RW **[19]** showed Patients with moderate to severe MGD had a higher incidence of dyslipidemia with respect to elevated total cholesterol (>200 mg/dL), 67.4% to 45.1% ($P = .0012$) when compared to population controls.

B. Out of MGD cases and Non MGD controls , 47 patients had altered triglycerides (**TGs**) as compared to 10 in Non MGD controls.

This difference was statistically significant with P-value 0.014. 95% CI (confidence interval) = 3.44 to 31.07 SE (std. error) difference = 6.96 Result was consistent with the study of by Braich PS , Howard MK , Singh JS**[20]**who defined Dyslipidemiaas , by either a fasting total triglycerides **≥**150 mg/dL, was detected in 70 cases (64 %) and 21 controls (18 %), $P < 0.001$. Mean levels of triglycerides 98.5 ± 42.1, in cases and 82.3 ± 36.5, in controls. All differences were statistically significant ($P < 0.05$). MGD was significantly associated , serum triglyceride concentration **≥**150 mg/dL (OR 3.2; 95 % CI 1.94.4; P= 0.03)

Another study by Dao AH , Spindle JD, Harp BA, Jacob A, Chuang AZ, Yee RW**[19]** showed statistically smaller number of MGD patients with high triglycerides (TG > 150 mg/dL), 15.2%, when compared to controls, 33.1% (P= .0049).

C. In our study , out of 50 MGD cases ,46 patients had altered low density lipoproteins (**LDL**) as compared to 14 patients in Non MGD controls. This difference was statistically significant with P-value 0.015. 95% CI (confidence interval) = 3.86 to 35.69 SE (std. error) difference = 8.02

It was consistent with the study of Pinna A, Blasetti F, Zinellu A, Carru C, Solinas G.**[18]** According to them , MGD was found to be significantly associated with increased blood levels of LDL (OR,1.07; 95% CI, 1.04-1.09; $P < 0.001$) with values 127.6 ± 3.9,in cases and 94.2 ± 2.6 in controls.

In a study by Braich PS , Howard MK , Singh JS**[20],** and defined Dyslipidemiaas , by either a fasting LDL **≥**130 mg/dL, was detected in 70 cases (64 %) and 21 controls (18 %), $P < 0.001$.

Mean levels of LDL was 126.1 ± 10.2, in cases and 92.2 ± 12.4, in controls. All differences were statistically significant (P < 0.05). MGD was significantly associated LDL ≥130 mg/dL (OR 9.1; 95 % CI 6.613.2, P < 0.01).

D. In our study , out of 50 MGD cases ,11patients had altered very low density lipoproteins (VLDL) as compared to 44 patients in Non MGD controls. This difference was not statistically significant with P-value 0.254 95% CI (confidence interval) = 2.735 to 10.215 SE (std. error) difference = 3.26

E. In our study , out of 50 MGD cases ,06 patients had altered high density lipoproteins (HDL) as compared to 44 patients in Non MGD controls.

This difference was not statistically significant with P-value 0.347 95% CI (confidence interval) = -5.89 to 10.215 SE (std. error) difference = 3.26 However, this result was inconsistent with the study of Pinna A, Blasetti F, Zinellu A, Carru C, Solinas G**[18]**which showed MGD to be significantly associated with increased blood levels of HDL i.e Mean total HDL to be 61.6 ± 1.8 mg/dl , in cases and 52.5 ± 1.3 mg/dl, in controls with (OR, 1.11; 95% CI, 1.06-1.17; P <0.001). In another study Braich PS , Howard MK , Singh JS **[20].** Dyslipidemia, defined by either a fasting total HDL ≤40 mg/dL, was detected in 70 cases (64 %) and 21 controls (18 %), P < 0.001. Mean levels of HDL was 53.3 ± 4.2 mg/dL in cases and 45.8 ± 2.6 mg/dL, in controls. All differences were statistically significant (P < 0.05).

V. Conclusion

Meibomian gland dysfunction is the most common ocular sign encountered in patients and cause of evaporative dry eye. In our study ; we also found that Patients with MGD with no history of dyslipidemia may have undiscovered abnormal serum cholesterol , triglycerides and LDL levels compared to controls without MGD that were statistically significant .

Changes in serum VLDL and HDL levels were not significant. Since, Hyperlipidemia is a health problem of enormous magnitude that affects many patients.The recently updated guidelines by the National Cholesterol Education Program (NCEP III) emphasize this and address related issues, such as primary prevention of coronary artery disease (CAD) by lowering low-density lipoprotein (LDL) levels and correcting modifiable risk factors of patients with elevated lipid levels**[21]** The diagnosis of hyperlipidemia is primarily made by using laboratory methods to analyze blood samples for their levels of various lipids.

MGD may be associated with hyperlipidemia and an elevated risk of CAD primarily in young men and may be a normal part of aging in some individuals. Perhaps the most clinically relevant conclusion that can be drawn from the above discussion is that any patient with either sign should be screened for hyperlipidemia and CAD, given the possibility that an increased risk does exist.

It may be summarized, on the basis of the findings in this study, that hyperlipidemia is at least one of the major causes for MGD. Ophthalmologists can be alert to suspect hyperlipidemia in MGD patients. MGD may become a sign of undiagnosed dyslipidemia and ophthalmologists will have a role in early detection of an important risk factor for cardiovascular disease.

This might highlight the significance of monitoring fasting serum lipids due to its association with the potential correlation with the progression of MGD.

The presence of MGD might have any correlation with dyslipidemia and the prevalence of high total cholesterol, 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. Treatment aimed at correcting hyperlipidemia may also improve the clinical features of MGD.

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