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Original Research Article

Study of Association Between Lipid Parameters With Asymptomatic and Symptomatic Meibomian Gland Dysfunction and its Severity

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ABSTRACT:

Purpose: This study aimed to determine association between lipid parameters and asymptomatic and symptomatic meibomian gland dysfunction (MGD) and its severity.

Materials and methods: This hospital based cross-sectional study was conducted in the ophthalmology department of a tertiary hospital consisting of 190 patients (95 patients with MGD and 95 controls without MGD). Patients undergone comprehensive ocular examination including visual acuity, slit lamp examination, intraocular pressure. We performed slit lamp examination to look for lid margin signs. Meibomian gland functionality was assessed by fluorescein staining. We assessed the disease severity according to International Workshop on Meibomian Gland Dysfunction and management 2011. MGD was divided into four stages taking both symptoms and signs into consideration and eye with more severity of MGD was included in study. Controls were age and sex matched patients without MGD but who visited OPD for refractive error. Abnormal lipid parameters were defined by TC ≥200 mg/dl, TGs ≥150 mg/dl, LDL-C ≥130 mg/dl and/or HDL-C <40 mg/dl. Lipid parameters were assessed for both cases and controls. Data analysis was done by SPSS version 17.0. Unpaired t test, Mann-Whitney U test, Chi-square test, Fisher's exact test and logistic regression model were used appropriately.

Results: Patients with MGD showed higher mean OSDI, TGs, TC, LDL-C, HDL-C as compared to controls. WE found that higher lipid parameters were associated with increasing severity of disease. Increased OSDI, LDL-C ≥130 mg/dl and HDL-C <40 mg/dl were significantly correlated with MGD in logistic regression model. Conclusion: Our study showed that symptomatic MGD patients were significantly associated with deranged lipid profile.

Keywords: Symptomatic MGD, OSDI, Lipid parameters.

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1. INTRODUCTION

Meibomian gland dysfunction (MGD) is defined as chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and /or qualitative/quantitative changes in glandular secretion.[1] Major cause of evaporative dry eye was recognized as MGD.[2]

The main source of lipids for the human tear film are the meibomian glands. The meibomian gland secretions consist of a complex mixture of various polar and non-polar lipids containing cholesterol and wax esters, diesters, triacylglycerol, free cholesterol, free fatty acids and phospholipids.[3] Considering that meibum is primarily composed of lipid, disorders of lipid metabolism or production may also lead to MGD. Meibum of MGD patients has different components and proportions of cholesterol compared to the meibum of controls.[4]

Deranged lipid parameters has been linked to the development of MGD, but direct evidence supporting this relationship is lacking.[5-8] Meibomian gland was affetcted by plasma lipids as well, but the evidence is largely circumstantial. Moreover there were reports stating that there is no relationship between the status of plasma lipids and MG lipid composition.[9,10] Whether pathologic levels of systemic lipids contribute to MGD remains speculative.[11] It is thus important to determine if any correlation exists between deranged lipid parameters and MGD and its severity. Hence, to screen cardiovascular disease at an iceberg level, it is important to determine whether MGD either asymptomatic or symptomatic can be the presentation of deranged lipid profile.

2. MATERIALS AND METHODS

This was a hospital-based cross-sectional study conducted from October 2019 to April 2020 at a tertiary care centre. Ninety five meibomian gland dysfunction (MGD) patients and ninety five controls visiting the ophthalmology outpatient department (OPD) with refractive error were assessed and those fulfilling the inclusion and exclusion criteria were included in the study.

INCLUSION CRITERIA FOR CASES

Patient aged from 18-60 years with MGD were included in the study. Diagnostic criteria for MGD was taken as MGD was clinically defined as meibomian gland obstruction (meibomian gland orifice plugging) and/or gland dropout and abnormal gland secretions.[8]

INCLUSION CRITERIA FOR CONTROLS

The control group included age and sex matched patients who did not have meibomian gland dysfunction and visited the eye OPD refractive error.

EXCLUSION CRITERIA FOR BOTH CASES AND CONTROLS

Patients with infectious keratoconjunctivitis, inflammatory ocular surface disorders unrelated to MGD, recent ocular surgery, concomitant topical medications for glaucoma, topical ophthalmic steroids taken four weeks before study, treatment with drugs affecting tearing or lipid levels (antihypertensives/cholinergics/OCPs/isotretinion/statins), history of pregnancy, presence of Sjögren's syndrome, rosacea, Parkinson's disease.

Age and sex were the basic demographic features of cases and controls which were noted. Baseline assessment was done and symptoms were assessed on the basis of Ocular Surface

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disease Index (OSDI) questionarrie.[12] OSDI questionarrie was explained to all the patients in local language. All the patients underwent fasting blood lipid profile levels estimation.

OPHTHALMOLOGICAL EXAMINATION

All patients underwent comprehensive ocular examination including visual acuity, slit lamp examination, intraocular pressure. Slit lamp examination was performed to look for lid margin signs for posterior lid margin erythema/hyperemia, lid margin thickening/irregularity, meibomian gland orifice plugging, turbidity of meibomian gland secretions, lid margin telangiectasia, and meibomian gland plugging. Meibomian gland functionality was assessed by the expressibility and secretion quality which was determined by giving moderate digital pressure over the central (±nasal) third of the lower/upper lids and was used to express the meibum. For meibum quality it was assessed in each of eight glands of the central third of the lower eyelid, graded as 0 to 3 for each gland in which 0= clear meibum,1= cloudy meibum, 2= cloudy with debris,3= thick like toothpaste. Range = 0-24.

In the central third of the lower eyelid expressibility was assessed on a scale of 0 to 3 in five glands, according to the number of glands expressible: 0= all glands expressible 1= 3-4 glands expressible 2= 1-2 glands expressible 3= no glands expressible. The surface damage to the exposed eye was assessed by fluorescein staining. Staining was represented by punctate dots on a series of panels. After instillation of the dye, the eye was examined with the slit-lamp biomicroscope using ×16 magnification with ×10 oculars using the Haag-Streit slit-lamp in cobalt blue exciter filter with a complementary yellow barrier filter. Staining scores were obtained by summing the scores of the exposed cornea and conjunctiva (OXFORD SCHEME GRADING).[13] The disease severity was assessed 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. The eye with more grading of MGD was included in the study. Institutional ethical clearance was taken for the study. Written informed consent was taken from all the patients included in the study and during study period and we adhered to the tenets of the Declaration of Helsinki.

STATISTICAL ANALYSIS

Statistical analysis was performed by the Statistical Package for Social Sciences (SPSS) program for Windows, version 17.0 (SPSS, Chicago, Illinois). Continuous variables were presented as mean ± SD, and categorical variables were presented as absolute numbers and percentage. Data was checked for normality before statistical analysis. Normally distributed continuous variables were compared using the unpaired t test, whereas the Mann-Whitney U test was used for those variables that were not normally distributed. The categorical variables were analyzed using either chi square test or Fisher's exact test. To identify potential factors associated with dyslipidemia univariate analyses was performed. To identify independent risk factors for cases and dyslipidemia multivariate logistic regression model was used. A stepwise approach was used to enter new terms into the model, with a limit of $p<0.05$ to enter the terms.

3. RESULTS

Ninety five MGD patients and ninety five controls without MGD were taken for the study from the ophthalmology OPD of a tertiary hospital.

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COMPARISON BETWEEN CASES AND CONTROLS

The demography and lipid parameters results are shown and compared in table 1. Both the cases and controls were matched for age, sex (p=0.767 and p=0.559). The mean OSDI (p <0.001), mean TG (p<0.005), mean LDL-C (p<0.005), mean HDL-C (p<0.005), and mean TC (p=0.027) was significantly higher in the cases as compared to controls.

FACTORS SIGNIFICANTLY ASSOCIATED WITH MGD AS A DEPENDENT VARIABLE

Taking MGD as a dependent variable, in the logistic regression model, the Odds Ratio and 95% CI calculated for the factors associated with cases with model Nagelkerke R^2=0.817.As shown in the model greater OSDI had thirty one times the odds of having MGD than those with lesser OSDI (p <0.001).

Compared to cases with LDL-C <130 mg/dl, the cases with LDL-C ≥130 mg/dl had 0.05 times greater odds of having MGD (p=0.025) whereas the cases with HDL-C <40 mg/dl had about seven times greater odds of having MGD compared with cases with HDL-C ≥40 mg/dl (p=0.010). The model did not show significant association between raised TGs, TC and MGD. This is shown in table 2.

STUDY OF MGD SEVERITY WITH LIPID PARAMETERS

It was observed that as the stage of MGD increased the number of patient with TG ≥150 mg/dl increased. The frequency of TG ≥ 150 mg/dl in stage 1 was 3 (9.1%), in stage 2 was 7 (21.2%), and in stage 3 and 4 was 11 (33.4%) and 12 (36.4%) respectively. The maximum number of patients with raised TG were in stage 4 MGD and the p value was <0.001 which was significant and hence, there was direct association of increasing severity of MGD and raised TGs.

The frequency of cases with TC ≥200 mg/dl in stage 1 was 2 (6.1%), in stage 2 was 6 (18.2%), and in stage 3 and 4 was 14 (42.4%) and 11 (33.3%) respectively. The maximum frequency of raised TC was in stage 3 MGD. As the p value was found to be significant i.e. p <0.001, there was direct association of increasing severity of MGD and abnormal TC.

The frequency of cases with LDL-C ≥130 mg/dl in stage 1 was 2 (5.2%), in stage 2 was 7 (18.4%), and in stage 3 and 4 was 17 (44.7%) and 12 (31.6%) respectively. The maximum frequency of raised LDL-C was in stage 3 MGD. As the p value was found to be significant i.e. p <0.001, there was direct association of increasing severity of MGD and abnormal LDL-C.

The frequency of cases with HDL-C ≥40 mg/dl in stage 1 was 24 (55.8%), in stage 2 was 18 (41.9%), and in stage 3 and 4 was 1 (2.3%) and 0 respectively. The maximum frequency of HDL-C ≥40 mg/dl was in stage 3 MGD. The HDL-C ≥40 mg/dl level showed a direct association with staging of MGD as the severity of MGD increased , number of patients with HDL ≥40 mg/dl also increased and number of patients with HDL-C <40 mg/dl reduced as the severity of MGD increased. The distribution is shown in table 3

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Table 1: Demography, lipid parameters and p value in cases and controls

S No	PARAMETERS	CASES (mean± standard deviation)	CONTROLS (mean± standard deviation)	P VALUE
1	Age (years)	34.54±9.16	35.07±9.56	0.767
2	Gender – M/F	46/49	42/53	0.559
3	OSDI	28.91±23.66	10.57±0.38	<0.001
4	Triglycerides (mg/dL)	131.03±54.94	110.51±40.83	0.003
5	LDL-C (mg/dL)	129.22±45.81	110.55±40.83	0.003
6	HDL-C (mg/dL)	42.86±8.29	40.37±6.80	0.003
7	TC (mg/dL)	171.76±58.78	155.31±39.07	0.027

Table 2: Table showing factors associated significantly with MGD as a dependent variable

PARAMETERS	**B**	**S.E.**	**Wald**	**Df**	**p value**	**Odds Ratio**	**95.0% C.I.**	
							Lower	**Upper**
OSDI	3.425	0.645	28.233	1	<0.001	31.714	8.684	108.634
TG≥150	-0.418	1.308	0.102	1	0.749	0.658	0.051	8.555
LDL≥130	-3.068	1.369	6.019	1	0.025	0.047	0.003	0.681
HDL<40	1.742	0.678	7.593	1	0.010	6.709	2.51	22.58
TC≥200	-0.057	1.717	0.001	1	0.973	0.945	0.033	28.334
Constant	-38.787	7.108	30.777	1	<0.001	0		

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Table 3: Distribution of MGD severity and lipid parameters

Stage of MGD	Triglyceride				Total cholesterol				LDL cholesterol				HDL cholesterol			
	TG <150	**TG ≥150**	**TOTAL**	**p value**	**TC <200**	**TC ≥200**	**TOTAL**	**p value**	**LDL-C <130**	**LDL-C ≥130**	**TOTAL**	**p valve**	**HDL ≥40**	**HDL<40**	**TOTAL**	**p value**
STAGE 1	**30** (48.4%)	**3** (9.1%)	**33** (34.7%)	<0.001	**30** (49.2%)	**3** (8.8%)	**33** (34.73%)	<0.001	**31** (54.4%)	**2** (5.2%)	**33** (34.7%)	<0.001	**9** (17.3%)	**24** (55.8%)	**33** (34.7%)	<0.001
STAGE 2	**26** (41.9%)	**7** (21.2%)	**33** (34.7%)		**27** (44.3%)	**6** (17.64%)	**33** (34.73%)		**26** (45.6%)	**7** (18.4%)	**33** (34.7%)		**15** (28.8%)	**18** (41..9%)	**33** (34.7%)	
STAGE 3	**6** (9.7%)	**11** (33.4%)	**17** (17.9%)		**3** (4.9%)	**14** (41.17%)	**17** (17.9%)		**0**	**17** (44.7%)	**17** (17.9%)		**16** (30.8%)	**1** (2.3%)	**17** (17.9%)	
STAGE 4	**0**	**12** (36.4)	**12** (12.6%)		**1** (1.6%)	**11** (32.4%)	**12** (12.6%)		**0**	**12** (31.6%)	**12** (12.6%)		**12** (23.1%)	**0**	**12** (12.6%)	

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4. DISCUSSION

This study was conducted to study the correlation between lipid parameters with meibomian gland dysfunction and its severity. The OSDI questionnaire was a subjective measurement tool used for assessing the symptoms of MGD. In the present study, mean OSDI was significantly greater in MGD patients as compared with the mean OSDI in controls without MGD in which OSDI was normal (p <0.001). Study done by Guilani *et al.*[9] had also used OSDI score as the baseline assessment of MGD symptoms.

It was found in our study that patients with MGD had significantly higher mean values for TGs, TC, LDL-C and HDL-C versus individuals of similar age and gender without MGD (p <0.05). There was greatest variation in mean values of TGs and LDL-C levels where the absolute differences in the mean values were 21 and 19 mg/dl, respectively. This is consistent with previous study by Pinna *et al.*[10] and Braich *et al.*[5] who found significantly higher mean values for TGs, TC, LDL-C and HDL -C. The greatest variation in mean values was observed in LDL-C and TC levels in study by Braich *et al.*[5]

In our study patients with MGD more often had serum TGs ≥150 mg/dl, TC ≥200 mg/dl, and LDL-C ≥130 mg/dl. However when considering patients with serum HDL-C <40 mg/dl there was no significant difference between those with 'or' without MGD.Study done by Dao *et al*[7] which showed that MGD was associated with raised TG, hypercholesterolemia, raised HDL-C. A study by Pinna *et al.*[6] showed that MGD was associated with hypercholestereolemia, high HDL-C, high LDL-C and the study by Braich *et al.*[5] which showed that MGD was associated with high TG, high LDL-C, high TC. A study by Banait *et al.*[14] showed positive correlation between MGD and increased LDL-C, TGs and TC.

The number of MGD patients with raised lipid parameters belonged to higher stage of MGD whereas lower lipid parametrs belonged to lower stages of MGD. This is consistent with the studies done by Bukhari *et al.*[6], Dao *et al.*[7] and Guilani *et al.*[9]

In the logistic regression model (table 2), the model revealed that greater OSDI had thirty one times the odds of having MGD than those with lesser OSDI (p <0.001). As compared to cases with LDL-C <130 mg/dl, the cases with LDL-C ≥130 mg/dl had 0.05 times greater odds of having MGD (p=0.025) whereas the cases with HDL-C <40 mg/dl had about seven times greater odds of having MGD compared with cases with HDL-C ≥40 mg/dl (p=0.010). The model did not show significant association between raised TGs, TC and MGD. This is not consistent with the previous study by Braich *et al.*[9], in which there was age >65, abnormally high LDL-C, TC and TGs which showed raised odds of having MGD.

There are few limitations of our study like it was a cross-sectional study and hence cause and effect could not be established between MGD and deranged lipid parameters. Whether treatment of deranged lipid profile has any effect on MGD was not studied by us due to time constraint.

5. CONCLUSION

We found a strong association of abnormal lipid components with MGD. We found a strong association of severity of MGD with deranged lipid parameters. Hence, MGD patients should be routinely evaluated for lipid parameters. MGD is associated with elevated levels of LDL-C, TGs, TC, which are known risk factors for cardiovascular events. Hence all MGD patients should be screened for cardiovascular diseases.

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