_____

Correlation between serum lipid profile with severity of meibomian gland dysfunction

Poluri Swarna latha[1], Sravani Lakshmi Kota[2], Ch Mohanrao[3]

[1,2] Assistant Professor, Department of Ophthalmology, Katuri Medical College & Hospital, Chinakondrupadu, Guntur, Andhra Pradesh, India
[3]Professor, Department of Ophthalmology, Katuri Medical College & Hospital, Chinakondrupadu, Guntur, Andhra Pradesh, India

Abstract

Meibomian Gland Dysfunction (MGD) is a chronic diffuse abnormality of themeibomian glands, commonly characterized by terminal duct obstruction andcauses qualitative or quantitative changes in glandular secretion. Both forms of MGD are influenced by endogenous factors like age, sex, hormonal disturbances, lipid profile of the patient and exogenous factors like topical medications. Hence, we have conducted this prospective trial to study the correlation between serum lipid profile with severity of meibomian gland dysfunction at Katuri Medical college. Out of 100 patients we recruited, major of them were 40-50 years of age with female predominance (p<0.03). And most of them 40.5% had belonged to grade 2. The severity had positive association with age >50 had grade 3 and 4 more. 70/100 had triglyceride (TG)level >150 mg/dl. 86.66% among them had 4 severity(p 0.03). 60/100 had > 200mg/dl of the cholesterol (CH) level 80% of them had Grade 4 MSD followed by 74.07% of grade 3 (p 0.02). Among the patients with <40 mg/dl of the HDL level, about 93.33% of them had the grade 4 severity. By these finding we would like to conclude that, severity of MGD has strong positive corelation with age, female gender, high TG and CH levels.
Keywords: Meibomian Gland Dysfunction (MGD), Cholesterol, Triglycerides, Hrmonal Distrubance.

Introduction

Meibomian Gland Dysfunction (MGD) is a chronic diffuse abnormality of themeibomian glands, commonly characterized by terminal duct obstruction andcauses qualitative or 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.[1] Patients may present with dry eye, redness, irritation, itching, burning sensation, and occasionally blurred vision.[2]Meibomian glands contribute to the lipid component of the tear film, and their normal secretion prevents premature evaporation of tears from the ocular surface.[3]Their secretions consist of a complex mixture of various polar and nonpolar lipids containing cholesterol and wax esters, diesters, triacyl glycerides, free cholesterol, free fatty acids, and phospholipids.[4]Meibomian Gland Dysfunction is classified into low delivery forms like hyposecretory or obstructive variety, and high delivery forms like hypersecretory or seborrheic variety. Obstructive type of Meibomian Gland Dysfunction is thought to be the most common variety . [5]

Both hyposecretory and hypersecretory forms of Meibomian Gland Dysfunction are influenced by endogenous factors like age, sex, hormonal disturbances , and exogenous factors like topical medications.Prevalence of MGD in general population varies between 30.5% and 54.1%.[6]

Objective of the study: To study the correlation between serum lipid profile with severity of meibomian gland dysfunction.

Materials and Methodology

After taken clearance from Institutional Ethics committee, A prospective, observational case control study was conducted at Katuri medical college among patients attending tertiary care centre between august 2019 to march 2020.

*Correspondence
Dr. Sravani Lakshmi Kota
Assistant Professor, Department of Ophthalmology, Katuri Medical College & Hospital, Chinakondrupadu, Guntur, AP, India.
E-mail: kotasravani1@gmail.com

Sample size was calculated to be 100 based on the sample of convenience. Patients who were aged 20years and above and were willing to give valid written informed consent were included in the study. Whereas, Patients below the age of 20 years of either sex, patients who had undergone any ocular surgery in past, the patients with abnormality in the drainage system of the lacrimal apparatus, those suffering with keratoconjunctivitis infection, rosacea, Sjogren's syndrome, and cholestatic liver disease and the female patients on oral contraceptive pills were excluded from the study.

100 patients were enrolled based the above-mentioned inclusion criteria. Epidemiological details of the patients were noted. Based on meibomian gland status which was evaluated by meibum quality, express ability and numerical scoring, they were categorised under 4 grades.

All the participants were tested for serum lipid profile levels after overnight fasting to evaluate the status of triglycerides, total cholesterol, high-density lipoprotein levels and low-density lipoprotein levels. And the reference normal values considered were as follows;

1) Triglycerides (TGs): Hypertriglyceridemia >150 mg/dl.
2) Total cholesterol (TC): Hypercholesterolemia >200 mg/dl.
3) Low-density lipoprotein (LDL)-cholesterol (LDL-C): High LDL >130 mg/dl.
4) High-density lipoprotein (HDL)-cholesterol (HDL-C): High HDL >40 mg/dl.

Complete ophthalmic examination, assessment of the patient was done for lacrimal system for abnormality. Assessment of meibomian glandwas done by putting pressure at the middle one-third of both upper and lower eyelids while observing under the slit lamp. The diagnosis of MGD was done by

Diagnosis of MGD by criteria based on the international workshop of MGD considering following indices [7]

Meibum quality

Which was assessed in each of the eight glands of the central third of the lower eyelid on a 0–3 scale for each gland:

0	Clear meibum
1	Cloudy meibum
2	Cloudy with debris
3	Thick toothpaste (range 0–24)

_____

Expressibility of meibum
Assessed from the five glands of the central third of the lower eyelid on a scale of 1- 3: 1 being 3–4 glands expressible, 2 with 1–2 expressible glands and 3 having no expressible glands.
Numerical staining
Scores refer to a summed score of staining of the exposed cornea and conjunctiva. For staining Fluorescein stains were used. And according to Oxford scale it has a range of 0–15.
Clinical staging of meibomian gland dysfunction
MGD is divided into four stages, taking both the symptoms and clinical signs into consideration.
Stage 1: No symptoms of ocular discomfort, itching, or photophobia.Minimally altered secretions: ≥ grade 2 to < grade 4 and with Expressibility 1 and having no ocular surface stinging.
Stage 2: Minimal to mild symptoms of ocular discomfort like itching, or photophobia. Minimal to mild MGD clinical signs with Scattered lid margin features having Mildly altered secretions grading ≥ 4 and < 8, Expressibility 1and having None to limited ocular surface staining.

Stage 3: Moderate symptoms of ocular discomfort, itching, or photophobia with limitations of activities. Moderate MGD clinical signs with Increased lid margin features: plugging, vascularity, Moderate altered secretions of grade ≥ 8 to < 13, Expressibility 2 and having Mild-to-moderate conjunctival and peripheral corneal staining, often inferior.
Stage 4: Marked symptoms of ocular discomfort, itching, or photophobia with definite limitations of activities Severe MGD clinical signs of iincreased lid margin features like dropout, displacement with Severely altered secretions grading ≥13, Expressibility 3 and having, increased conjunctival and corneal staining, including central staining.
Statistical Analysis
Epidemiological feature, clinical, laboratory, grading of MGD assessment from all the participants are noted and has been analysed by using the descriptive statistics by calculating the mean, average and percentage. Results have been tabulated, expressed as bar and pie charts and Chi square test had been done to look for the intra group difference. Pearson's correlation test had been applied after that to obtain the degree of correlation.

Results:

Table 1: Distribution of age among the clinical classification of MGD Grade

All the data collected from the patients had been subjected to the descriptive analysis and the results are as follows.

AGE	GRADE-1	GRADE-2	GRADE-3	GRADE-4
20-30 years (N=19)	4 (21.05%)	9 (47.36%)	5 (26.31%)	1 (5.26%)
30-40 years (N=37)	7 (18.91%)	15 (40.5%)	11 (29.72%)	4 (21.055%)
40-50 years (N= 31)	7 (22.58%)	11 (35.48%)	9 (29.03%)	4 (12.90%)
>50 years (N=13)	0	3 (23.07%)	3 (23.07%)	7 (53.84%)

Distribution of the age with respect to the clinical classification had been tabulated in Table1. In our study, major portion of the study participants had belonged to the age between 30 to 40 years. Out of which most of them, about 15 patients accounted for 40.5% had grade 2 severity according to the clinical classification of MGD. 7 had grade 1, 11 (29.72%) – Grade 3 and only 4 them i.e, 21.05% had Grade 4 severity.Then the another most prevalent age group was between 40 to 50 years with the greatest severity among them being Grade 2 accounting for 35.48% and 22.58% had grade 1, 29.03% and 12.9% were having grade 3 and grade 4 severity respectively. 19 patients were between the age 20 to 30 years. Out which the 47.36% had Grade 2 severity. 21.05%, 26.31% and hardly 5.26% had Grade 1, 3 and grade 4 severity respectively.

Apart from this, none in the age group >50 had grade 1 severity. Whereas equal portion of them with 23.07% had Grade 2 and grade 3 severity. But the prevalence of grade 4 among them was highest being 53.84% of distribution. Hence the increased age had manifested the positive associate with P value of <0.05
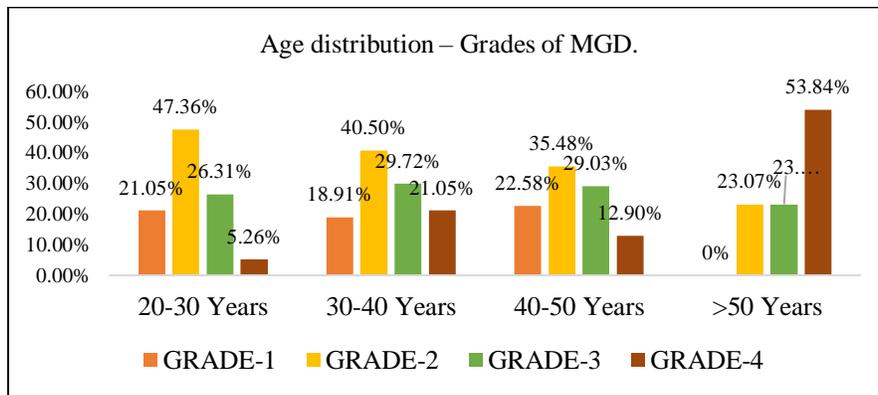

Fig. 1: Representation of distribution of age with respect to the clinical grading of MGD

The above findings tabulated and discussed have been illustrated as the bar graph in figure1

Out of 100 study participants, major of them were females with the prevalence of 67% whereas 33% were male patients. We can see the strong association with female gender and the prevalence of the disease with P value 0.03
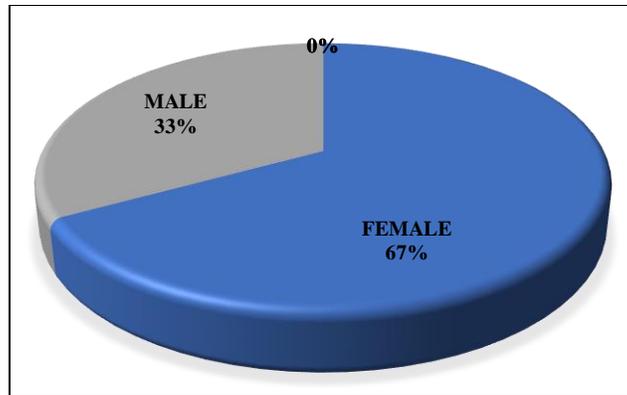
Fig. 2: Distribution of gender among the recruited study participants.

Table 2: Distribution of clinical grading of MGD among either gender

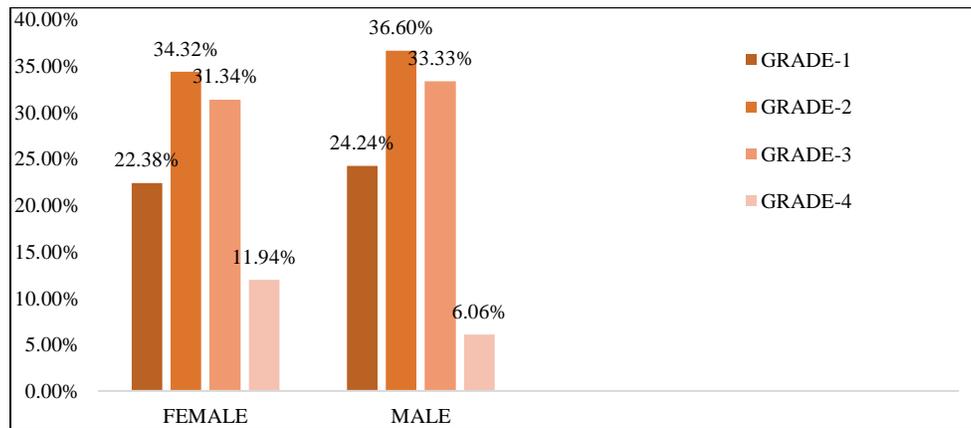| GENDER	GRADE -1	GRADE - 2	GRADE -3	GRADE -4
FEMALES	15(22.38%)	23 (34.32%)	21 (31.34%)	8(11.94%)
MALES	8(24.2%)	12 (36.3%)	11 (33.3%)	2 (6.06%)

Fig. 2: Distribution of Distribution of clinical grading of MGD among either gender as bar graph. P value <0.003

The above table 2 and figure 2 represents the distribution of clinical classification of MGD among the participated male and female patients. Out of 67 female patients, major of them had grade 2 severity, accounted for 34.32% and among rest others, 31.34% and 22.38% had grade 3 and grade 1 followed by 11.94% of the grade 4 severity.

Whereas, among 33 men 36.6%, 33.33%, 24.24% were having grade 2, grade 3 and grade 1 severity respectively. Hardly 6.06% of the men had grade 4 severity of the MGD, which is almost half of the prevalence of grade 4 among female patients.

Table 3: Correlation between the Triglyceride level and grades of MGD

TRIGLYCERIDES	GRADE -1 MGD	GRADE -2 MGD	GRADE -3 MGD	GRADE-4 MGD
< 150 mg/dl	13 (61.90%)	10 (27.02%)	5 (18.51%)	2 (13.33%)
> 150 mg/dl	8 (38.09%)	27(72.97%)	22 (81.48%)	13 (86.66%)

The correlation between the level of serum triglycerides and clinical grades of MGD have been tabulated above, according to which we can see that, major portion of the patients; 70/100 had the S.triglyceride level >150 mg/dl out of which, most of them had grade 4 severity with the statistical prevalence of 86.66% which is very high and the mist significant finding. It was followed by, 82.48%, 72.97% and 38.09% having grade 3, grade 2 and grade 1 respectively. 30 out of 100 participants had the S.triglyceride level of < 150mg/dl, among these low risk profile too had 61.9% of the grade 1 prevalence. Whereas the severity of grade 2,3 and 4 was distributed with 27.02%, 18.51% and 13.33% respectively. Which indicated the increased MGD severity among the patients with high triglyceride level. The same has been illustrated as the bar diagram in figure 3 below.
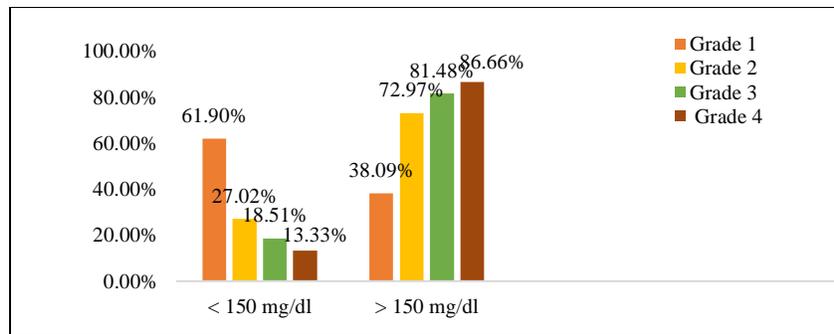
Kota *et al*   International Journal of Health and Clinical Research, 2021; 4(21):173-178
www.ijhcr.com
175

Fig. 3: Distribution of clinical MGD grading among the patients with < 150 and >150mg/dl of the Serum triglyceride level. P value <0.002

Table 4: Association between the total cholesterol and clinical grading of the MGD

TOTAL CHOLESTEROL	Grades 1	Grade 2	Grade 3	Grade 4
<200 Mg/dl	15 (71.42%)	15 (40.54%)	7 (25.92%)	3 (20%)
> 200 Mg/dl	6 (28.57%)	22 (59.45%)	20 (74.07%)	12(80%)

60 out 100 patients had > 200mg/dl of the cholesterol level falling the high risk category to develop different comorbid condition. Among these 60 patients, major of them had grade 4 MSD with prevalence of 80% followed by 74.07% of grade 3, 59.45% of grade 2 and 28.57% with grade 1 MSD. Whereas the patients with <200mg/dl of the total cholesterol level, major portion of them, about 71.42% had grade 1 MSD only. And 40.54%, 25.92% and 20% of them had grade 2, grade 3 and grade 4 respectively.
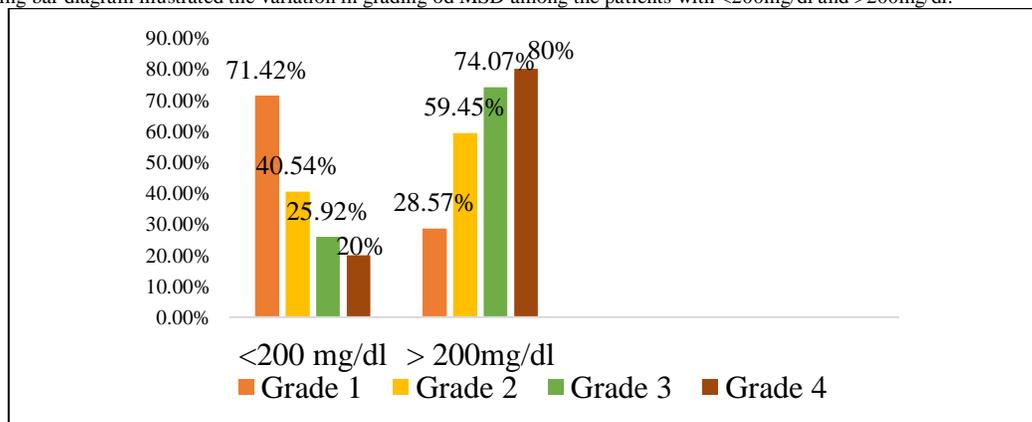The following bar diagram illustrated the variation in grading od MSD among the patients with <200mg/dl and >200mg/dl.

Fig. 4: Correlation between total cholesterol and Grades of MGD.

Table 5: Correlation between LDL cholesterol and grades of MGD

LDL-C	GRADE -1	GRADE - 2	GRADE - 3	GRADE- 4
< 130mg/dl	13 (61.90)	17 (45.94%)	8 (29.62%)	2 (13.33%)
> 130 mg/dl	8(38.09%)	20 (54.05%)	19 (70.37%)	13 (86.66%)

Out of 100 study participants, 60 patients had their LDL cholesterol level the reference range. Among these 60 patients with >130mg/dl of LDL cholesterol, major portion of them had grade 4 MSD with the percentage of 86.66% which was followed by the grade 3 in 70.375 of the patients and 54.05% and 38.09% with grade 2 and grade 1 severity of MSD. Among the another 40 study participants with <200mg/dl of the LDL cholesterol level, major of them had Grade 1 followed by grade 2, grade 3 and grade 4 MSD. The below bar graph shows the variation of MSD clinical score with respect to the LDL cholesterol level.
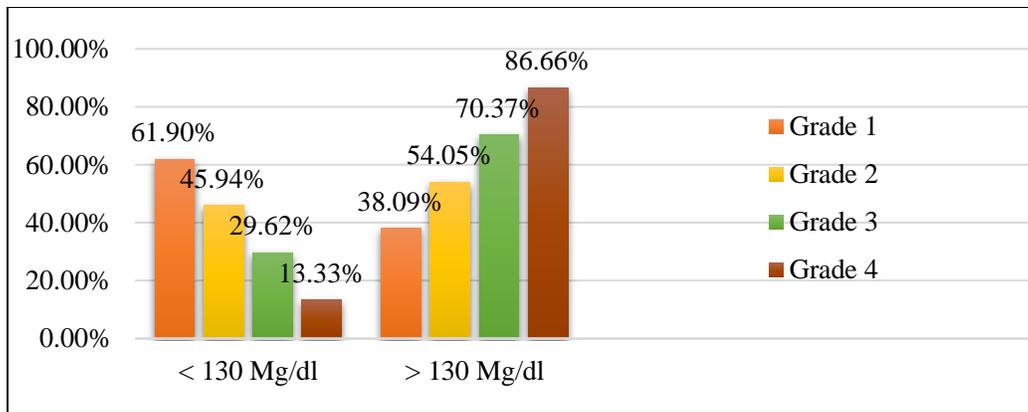
Fig. 5: Correlation between LDL-C and Grades of MGD
Table 6: Correlation between HDL cholesterol and grades of MGD

HDL-C	GRADE-1	GRADE-2	GRADE-3	GRADE-4
<40 mg/dl	11 (52.38%)	25 (67.56%)	17(62.96%)	14 (93.33%)
> 40 mg/dl	10 (47.61%)	12 (32.43%)	10 (37.03%)	1 (6.66%)

67 participated patients had <40 mg/dl of the HDL level. Out of which, the highest percentage, about 93.33% of them had the grade 4 severityfollowed by the grade 2, grade 3 and grade 1 with the proportion of 67.56%, 62.96% and 52.38% respectively. And among the 33/100 patients who had the HDL level of >40mg/dl, most of them had the grade 1 MSD and 37.03% of them had Grade 3 and hardly 6.66% had the MSD of grade 4.
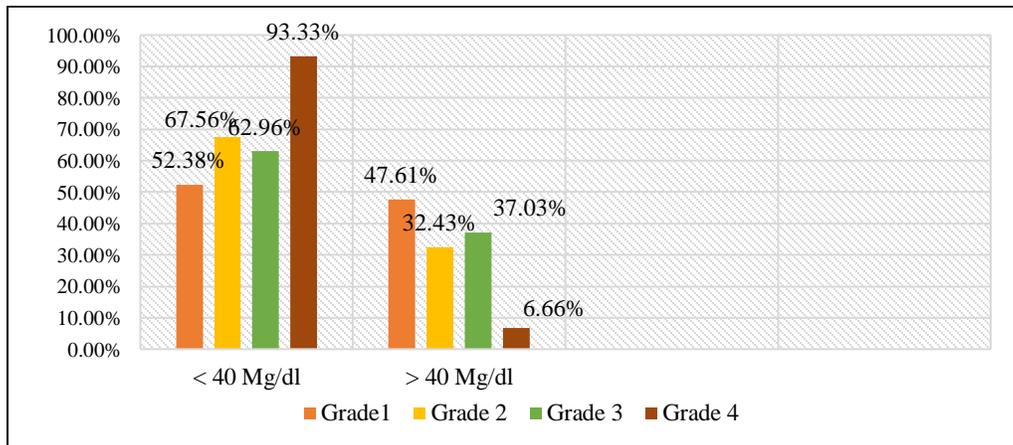

Fig 6: Correlation between HDL and grading of the MSD

The following table 6 and figure 6 represents the correlation between the HDL and the MSD grading.

Discussion

MGD can cause chronic ocular changes in meibum composition and/or obstruction of the meibomian glands is thought to be the main cause [8] [9] Meibum of MGD patients has different components and proportions of cholesterol compared to the meibum of controls[10] Specifically, cholesterol esters were always present in the glands of patients with MGD but not necessarily in normal controls[11] Increased cholesterol in meibum may play a role in the pathology of MGD [12.] Cholesterol esters may be a consequence of the dysfunction . meibum with higher concentrations of cholesterol would be more viscous at physiological temperatures, thus clogging the meibomian glands. The tear film's lipid layer may get altered as a result of this obstruction, increasing tear evaporation, and in turn leading to evaporative dry eye disease.

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. The number of patients in the age groups 20-30 ,30-40,40-50,>50 years were 19,37,31,13% respectively, Fig. 1 represents the age-wise distribution of patients as compared to the stage of MGD. Maximum number of patients belonged to stage 2, whereas stage 4 had the least number of patients. Which shows strong association with increasing age and increased severity of MGD. The finding was similar with Banait et al[13]in which the majority of cases were in Stage 2 (50%) and most of them (30%) were in the age group of 61–70 years. The age group of 51–60 years had 20% of these patients. The percentage of patients in Stage 3 was 26.6 of all cases, with majority in the age group of 61–70 years (20%).

_____

In this study of total 100 patients among them 67 were females and 33 males of which most of them belongs to grade 2 MGD. As p value is < 0.05 shows females gender have positive association with increased severity of meibomian gland dysfunction.

The number of MGD patients with TC < 200 mg/dL and > 200 mg/dL in our study were 40 and 60 respectively. Maximum number of patients with TC < 200 mg/dL belonged to grade 1 whereas maximum number of patients with TC>200 mg/dL belong to grade 4. Showed the strong association with P value <0.03 The number of MGD patients with TG < 150 mg/dL and > 150 mg/dL in our study were 40 and 60 respectively and maximum number of patients TC >150 mg/dL belong to grade 4. With P value is <0.002. Another study conducted by Irfan et al[14] had also observed that48.3% of the participants had serum total cholesterol levels ≥200 mg/dl, with a significant association between higher cholesterol levels and severity of MGD Whereas 66.4% had serum triglycerides levels of ≥150 mg/ dl, elevated LDL level With significant p value of 0.0001, p=0.015 respectively, showing the strong association severity of MGD

The number of MGD patients with LDL cholesterol > 130 mg/dl were more and maximum number of them belong to stage 4. as It had a strong association between increased LDL-C with increasing severity of stage of MGD. This finding is similar to the study conducted by Guliani et al[15] in which the patients with higher stages of MGD more often had the serum TGs >150 mg/dL, total cholesterol >200 mg/dL, an LDL >130 mg/dL, and serum HDL >40 mg/dL. Proving to be having the stronger positive association between increasing stage of MGD, and age, female sex, and increasing values of all the lipid profile components.The number of MGD patients with HDL cholesterol <40 mg/dL were more and most of them had stage 4 MSD whereas maximum number of patients with >40 mg/dl belong to stage 1. Which had a near association between increased HDL-C with increasing severity of stage of MGD. Chandrshekarayya et al have also observed that, more than half of their study patients with MSD had increased severity among the patients with high TC, LDL and no much difference among patients with less HDL[15].

Conclusion

By this observations of our study, we conclude that A very strong association exists between increasing age and increasing severity of stage of MGD. There is a positive association exists between female sex and increasing severity of stage of MGD and also increasing severity of MGD and increasing levels of the lipid profile namely LDL-C, Total cholesterol and Triglycerides and decreased levels of HDL-C has the positive correlation with severity of MGD.

References

1. Nelson JD, Shimazaki J, Benitez-del-Castillo JM, Craig JP, McCulley JP,DenS, etal. The international workshop on meibomian gland dysfunction: Report of the definition and classification subcommittee. Invest Ophthalmol Vis Sci 2011;52:1930-7.
2. Lemp MA, Nichols KK. Blepharitis in the United States 2009: A survey-based perspective on prevalence and treatment. Ocul Surf 2009;7:S1-S14.
3. Jacob JM, Pillai SS, Goudinho SJ. The association of meibomian gland dysfunction with dyslipidemia-A casecontrol study. World J Pharm Res 2016;5:13906.
4. Nichols KK, Foulks GN, Bron AJ, Glasgow BJ, Dogru M, Tsubota K, et al. The international workshop on meibomian gland dysfunction: Executive summary. Invest Ophthalmol Vis Sci 2011;52:1922-9
5. Zierhut M. Ocular surface and tear film and their dysfunction in dry eye. SurvOphthalmol 2001;45:S203-10.
6. Viso E, Gude F, Rodríguez-Ares MT. The association of meibomian gland dysfunction and other common ocular diseases with dry eye: A population based study in Spain. Cornea 2011;30:1-6.
7. Nichols KK, Foulks GN, BronAJ, Glasgow BJ, Dogru M, Tsubota K, et al. The international workshop on meibomian gland dysfunction: Executive summary. Invest Ophthalmol Vis Sci 2011;52:1917-2085.
8. Driver P, Lemp MA. Meibomian gland dysfunction. SurvOphthalmol1996;40:343-67.
9. Knop E, Knop N, Millar T, Obata H, Sullivan DA. The International Workshop on Meibomian Gland Dysfunction: Report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland. Investig Ophthalmol Vis Sci 2011;52:1938-78. 1
10. McCulley JP, Dougherty JM, Denau DG. Classification of chronic blepharitis. Ophthalmology 1982;89:1173-80.
11. Shine WE, McCulley JP. Role of wax ester fatty alcohols in chronic blepharitis. InvestigOphthalmol Vis Sci 1993;34: 3515-21.
12. Banait S. Association of meibomian gland dysfunction with dyslipidemia contributors. J Datta Meghe Inst Med Sci Univ2019;14:346-51.
13. Irfan, Khan, Anupam & Mittal, Sanjeev & Samanta, Ramanu Shrinkhal. Association of Lipid Profile with Severity of Meibomian Gland Dysfunction. Nepalese journal of ophthalmology . 2020;12. 216-225.
14. Guliani BP, Bhalla A, Naik MP. Association of the severity of meibomian gland dysfunction with dyslipidemia in Indian population. Indian J Ophthalmol. 2018 ;66(10):1411-1416..
15. Jiremat HC, Amin H, Study on meibomian gland dysfunction and serum lipid profile. Indian J app resea. Jan 2020; 10(1):5-6.