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A STUDY OF PREVALENCE OF DYSLIPIDAEMIA AMONG PATIENTS PRESENTING WITH DIFFERENT GRADES OF MEIBOMIAN GLAND DYSFUNCTION IN A TERTIARY CARE CENTRE OF PUNJAB.

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ABSTRACT - This is a prospective, cross-sectional study to assess association of meibomian gland dysfunction (MGD) with dyslipidaemia in patients attending the ophthalmology outpatient department at Government Medical College, Patiala. The study will include patients of Meibomian Gland Dysfunction (MGD) attending the ophthalmology outpatient department at Government Medical College, Patiala during the period from 1-2-2021 to 31-7-2022. The patients diagnosed with Meibomian gland dysfunction (MGD) and willing to participate in the study will be subjected to Schirmer's test, corneal and conjunctiva! fluorescein staining, tear film breakup time measurement; and blink rate, blink interval, meibum quality and meibum expressibility will be assessed. Then, Lipid profile testing [Triglycerides (TG), Total cholesterol (TC), Low-density lipoprotein (LDL) and High-density lipoprotein (HDL)] will be done after overnight fasting. Patient data will be collected according to the proforma. All observations will be entered in MS Excel spreadsheet and analysis done using Statistical Package for the Social Sciences (SPSS).

KEYWORDS – Meibomian Gland Dysfunction, Dyslipidaemia, Dry eyes, Lipid profile

ABBREVIATIONS- MGD - Meibomian Gland Dysfunction.

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INTRODUCTION - According to the International workshop on MGD and the TOFS DEWS II, both held in 2011, Meibomian gland dysfunction (MGD) is a chronic, diffuse abnormality of the meibomian glands, commonly characterized by obstruction of the terminal duct and/or quantitative/qualitative changes in the secretions of the meibomian glands. This may result in alteration of the tear film, clinically apparent inflammation, symptoms of eye irritation, and ocular surface disease.[1,2]

Multiple ophthalmic, systemic, and medication-related risk factors may coexist with, and may contribute to, the pathogenesis of MGD. Systemic factors that may promote MGD include androgen deficiency, menopause, dyslipidaemia, acne, atopy, rosacea, and benign prostatic hyperplasia (BPH).[6,7,8,9,3]

Lipids are key components of the tear film, which maintain a smooth corneal surface and prevent premature evaporation of tears from the ocular surface.[10] The lipids in the tear film are mainly released by the meibomian glands.[11] Chemical analysis of meibomian gland secretions showed that it consists of a mixture of non-polar lipids (77% wax and sterol esters), polar lipids (8% phospholipids and glycolipids) and 9% diglycerides and triglycerides (TG), and these are responsible for variations in melting temperature.[12] Emerging studies have showed association between increased cholesterol levels in meibomian secretions of patients with meibomian gland dysfunction (MGD).[13,14] Furthermore, patients with MGD may have higher total blood cholesterol levels as compared to the general population (Dao et al., 2010 and Bukhari et al., 2013). [8,16] Abnormal serum lipids have been established as a significant risk factors for cardiovascular disease and stroke (Shi et al., 2016).[17]

The primary purpose of this study was to determine if there was an association between dyslipidaemia and MGD. The secondary purpose of this study was to identify the factors, if any, that play a role in this association.

MATERIALS AND METHODS - It is a Cross-sectional, prospective, observational study that included patients diagnosed with Meibomian Gland Dysfunction attending the ophthalmology outpatient department at Government Medical College, Patiala during a period of 1 year from 01-02-2021 to 31-01-2022. Ethical approval was obtained from the Institutional Ethics Committee. 71 consecutive patients diagnosed with MGD and 74 age and sex-matched controls were enrolled after they gave their informed consent. Inclusion criteria was all patients aged 18 years and above. Exclusion criteria included patients on systemic or topical antibiotics, steroids or glaucoma medication within 1 month before selection; contact lens wear, ocular diseases such as keratitis, episcleritis, scleritis; punctual occlusion, liver disease, pregnancy and breast feeding; treatment with drugs affecting tearing (antihypertensives/ OCPs/ isotretinoin); lipid lowering agents (statins/ fibrins), anticoagulants; allergic keratoconjunctivitis; ocular and orbital surgery of any kind, altered lid anatomy; allergy to any component of procedural medication such as stains.

Once patients were selected, baseline assessment included symptoms and signs scaled according to the following table (mild/moderate/severe).

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Symptom	Absent	Mild	Moderate	Severe
1. Itching	None	Awareness	Desire to rub	Frequent rub
2. Foreign Body Sensation	None	Awareness	Desire to rub	Desire to close eyelids
3. Dryness	None	Awareness	Need drops	Frequent drops
4. Burning	None	Awareness	Desire to rub	Frequent rub
5. Eyelid margin Swelling	None	Noticeable	Obvious	Decrease in palpebral fissure

Signs	Grade 0	Grade 1	Grade 2	Grade 3
1. MG secretion (central lower eyelid)	Clear	Cloudy	Turbid with clumps	Solid with paste
2. Plugged MG orifice (middle lower eyelid)	None	Less than 1/3	1/3-2/3	More than 2/3
3. Tear film breakup time (in seconds)	>10	8-10	5-7	<5
4. Numerical staining	Scores refer to a summed score of staining of the exposed cornea and conjunctiva. Fluorescein stain was used. The Oxford scale has a range of 0–15.[4]			

MGD was diagnosed based on having at least two symptoms and two signs (one must be the presence of Meibomian gland signs) with a minimum severity score of 2 for each. According to the report submitted by the International Workshop on Meibomian Gland Dysfunction and Management in 2011, MGD was divided into four stages, taking both the symptoms and clinical signs into consideration.[5]

Stage	MGD Grade	Symptoms	Corneal Staining
1	+ (minimally altered secretions, expressibility:1)	None	None
2	++ (mildly altered secretions, expressibility:1)	Minimal to mild	None to limited; Oxford Grade 0-3

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3	+++ (moderately altered secretions, expressibility:2)	Moderate	Mild to moderate; mainly peripheral; Oxford Grade 4-10
4	++++ (severely altered secretions, expressibility:3)	Marked	Marked; central in addition; Oxford Grade 11-15

Then, after overnight fasting. 2mL blood was drawn in plain vial and lipid profile was done. Parameters measured were:

- Triglycerides (TG): Hypertriglyceridemia >150 mg/dL
- Total cholesterol (TC): Hypercholesterolemia >200 mg/dL
- Low-density lipoprotein (LDL) cholesterol (LDL-C): High LDL >130 mg/dL
- High-density lipoprotein (HDL) cholesterol (HDL-C): Low HDL <40 mg/dL.

Statistical evaluation was done by calculating the prevalence of dyslipidaemia in patients with MGD using Chi-square test/Fisher's exact test/ANOVA test. A P-value of <0.05 was considered statistically significant. The data was entered in MS Excel spreadsheet and analysis was done using Statistical Package for the Social Sciences (SPSS).

RESULTS - The study consisted of 145 subjects with 71 MGD patients presenting to the outpatient department, and 74 age matched control group. The mean(SD) age of patients of MGD patients was 51.4(14.9) with a range of 27-68 years and control group was 48.4(11.50) with a range of 29-66 years.

	MGD	Controls	P value
Age in years (mean ± SD)	51.9 (11.5)	47.7 (12.6)	0.07
Age Range (years)	25-75	20-78	
Gender distribution	Males= 40 Females= 31	Males= 38 Females= 36	0.36
Total Cholesterol mg/dL mean(SD)	209.2(35.4)	161.1(37.3)	0.001
LDL mg/dL mean(SD)	137.2(26.7)	107.5(25.5)	0.001
HDL mg/dL mean(SD)	44.2(8.2)	55.7(9.2)	0.001
TG mg/dL mean(SD)	150.8(22.9)	114.6(11.5)	0.003

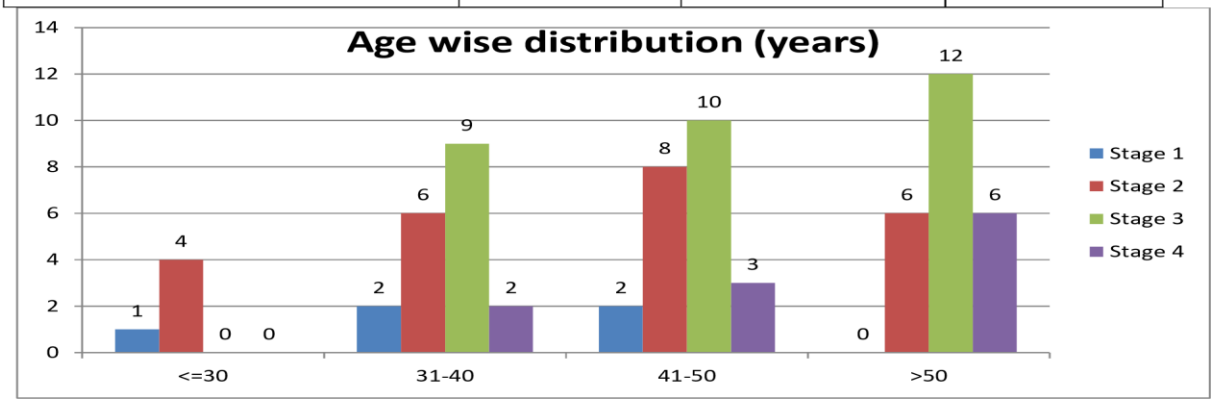

Table1 – The Corelation between the age, gender and cholesterol levels with severity of Meibomian Gland Dysfunction (MGD)

Figure 1 – Corelation between the age of patients and severity of MGD.

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The mean(SD) age of patients of MGD patients was 51.4(14.9) with a range of 27-68 years and control group was 48.4(11.50) with a range of 29-66 years. The maximum number of MGD patients belonged to Stage 3 MGD and Stage 1 had minimum number of patients. Similarly, >50 age group had maximum number of patients and <30 age group had the least number of patients. The mean(SD) age for stage 1, 2, 3 and 4 MGD patients is 33.2(7.3), 49.7(9.4), 51.2(10.0) and 59.1(13.6) respectively; p-value< 0.001. The mean cholesterol levels in MGD patients was 209.2(35.4) and in controls was 161.1(37.3); p<0.001. The mean triglycerides and LDL were also significantly higher in MGD, while HDL was significantly lower; p<0.001 in each.

MGD □	Stage 1	Stage 2	Stage 3	Stage 4	P value
Number	5	24	31	11	0.69
Gender	M=3; F=2	M=13; F=11	M=17; F=14	M=7; F=4	
Age (Range)	33.2 (7.3) (25-43)	49.7(9.4) (36-70)	51.2(10.0) (38-73)	59.1 (13.6) (39-75)	0.001

Table 2- The Corelation between age and gender of patients with severity of MGD.

There were 38 males and 36 females in the control group whereas 40 males and 31 females in the MGD group. In the MGD group, the maximum number of male and female patients belonged to stage 3 MGD group; p-value =0.69.

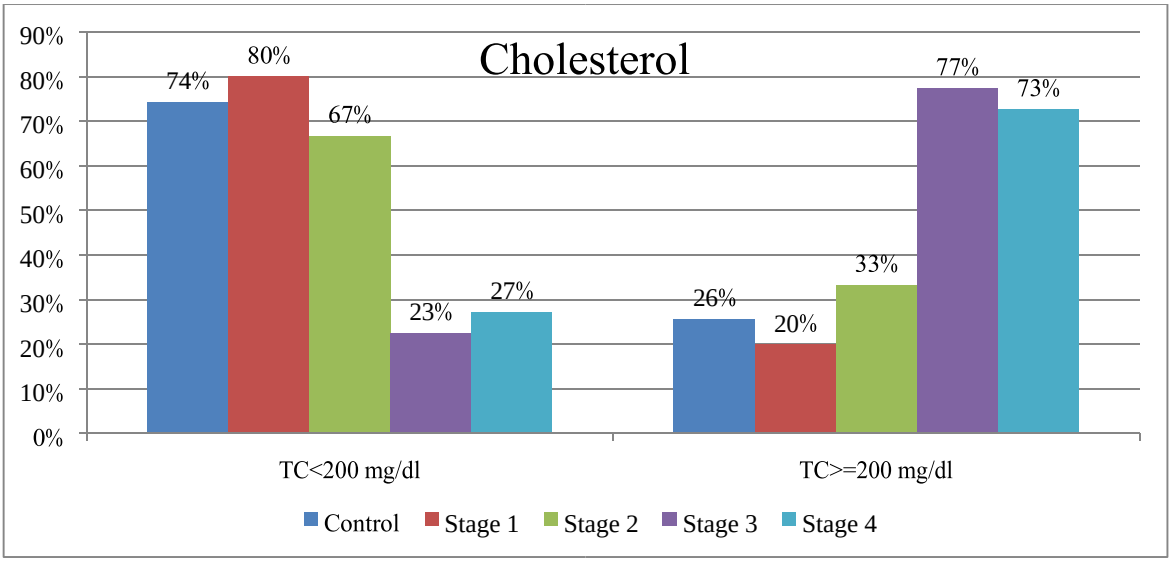

Figure 2 – Corelation between the Total Cholesterol levels and severity of MGD

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The patients with total cholesterol <200 mg/dl with MGD were 30 and ≥200 mg/dl with MGD were 41. The maximum difference between the number of patients with total cholesterol ≥200 mg/dl and <200 mg/dl was found to be in Grade 3 MGD. The p-value was 0.01 which indicates that there is a significant correlation between increasing grade of MGD and elevated serum total cholesterol levels.

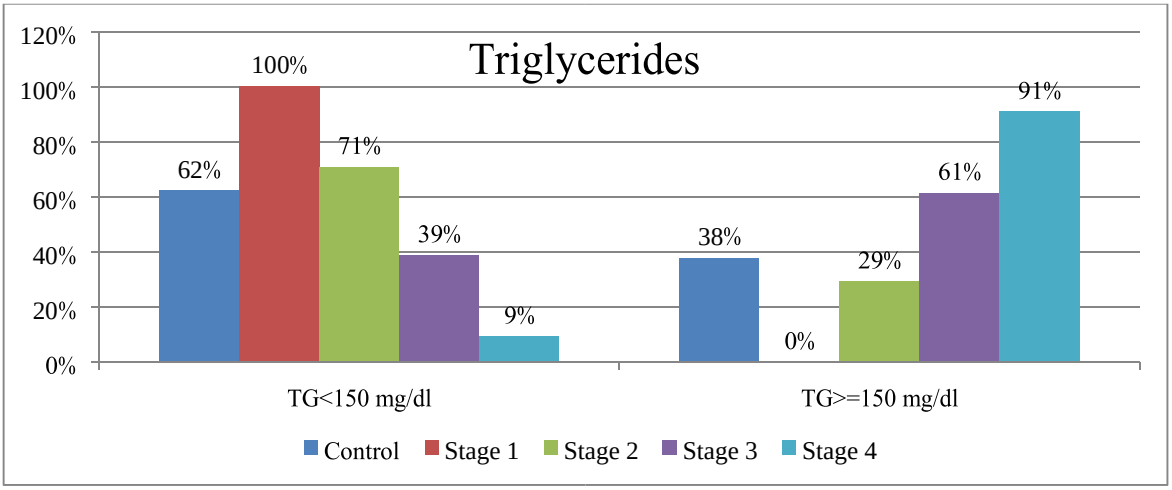

Figure 3 – Corelation between Triglyceride levels with severity of MGD

The patients with Triglycerides <150 mg/dl with MGD were 35 and ≥150 mg/dl with MGD were 36; p-value =0.0005 which indicates that there is a significant correlation between increasing grade of MGD and elevated serum triglyceride levels.

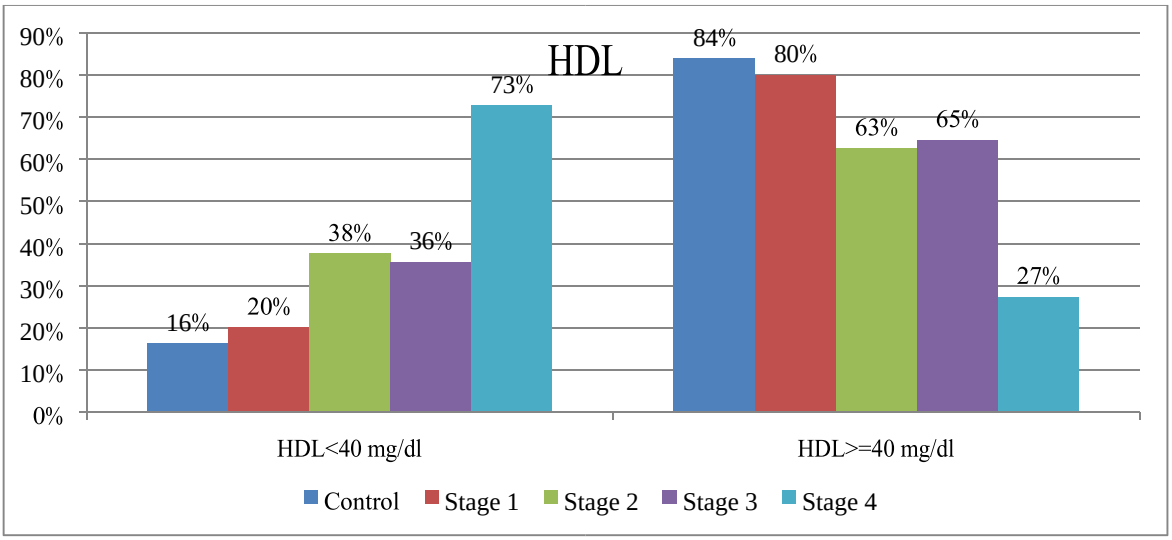

Figure 4 – Corelation between HDL levels and severity of MGD

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The patients with HDL <40 mg/dl with MGD were 29 and ≥40 mg/dl with MGD were 42. The maximum difference between the number of patients with HDL ≥40 mg/dl and <40 mg/dl was found to be in Grade 3 MGD; p value=0.23 which indicates that there is no significant correlation between increasing grade of MGD and decreased serum HDL levels.

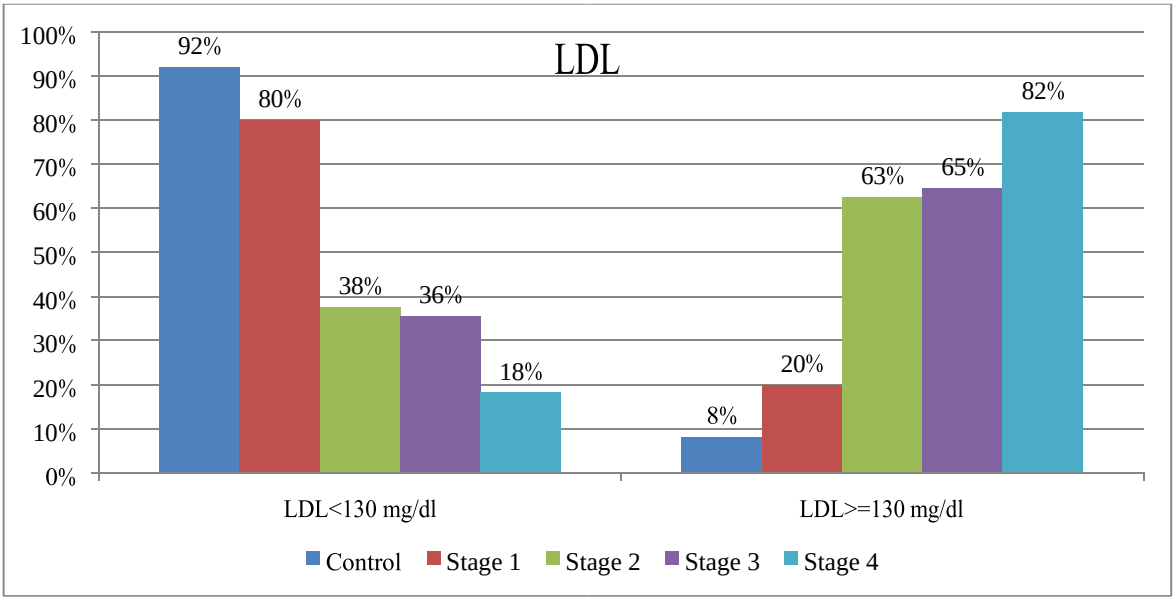

Figure 5 – Corelation between LDL levels and severity of MGD

The patients with LDL <130 mg/dl with MGD were 26 and ≥130 mg/dl with MGD were 45. The maximum difference between the number of patients with LDL ≥130 mg/dl and <130 mg/dl was found to be in Grade 3 MGD; p-value was 0.22 which indicates that there is no significant correlation between increasing grade of MGD and elevated serum LDL levels.

DISCUSSION - Meibomian Gland Dysfunction occurs as a result of terminal duct obstruction by thickened meibum. Theoretically, presence of Cholesterol in the meibum will increase the density of meibum and also, increase the melting point of meibum as the melting point of cholesterol is around 148^0C as compared to around 30^0C to 34^0C for meibomian secretions[9]. This will clog the meibomian gland openings and change the tear film composition with reduced lipids and thus, increase evaporation of the tears causing evaporative dry eye. Previous studies have tried to prove increased cholesterol levels in meibomian gland secretions to be a risk factor for MGD.[8,15,16] So we conducted this study to find any correlation between the serum levels of cholesterol, triglycerides, HDL and LDL and the severity of MGD.

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This was a hospital based cross sectional study where consecutive patients above 18 years of age diagnosed with MGD were included in the study. The diagnosis of MGD in our study was made on the basis of presence of two symptoms and two signs (including MG secretion or plugging).[19] This diagnostic criterion makes sure that only the symptomatic patients of MGD have been included in the study. The MGD patients were then classified into grade 1,2,3 and 4 based on the severity of symptoms and signs. Then, after overnight fasting, lipid profile testing was done for serum total cholesterol, triglycerides, HDL and LDL levels.

The mean(SD) age of patients in our study was 49.7(12.2) with a range of 20-78 years of age. This is comparable to the mean(SD) age in studies conducted by Bukhari et al., Irfan KSA et al. and Braich et. al. with 49.4, 48.86(12.11) and 46.7(9.2) respectively.[15,22,15] In our study, we found that there is a significant correlation between severity of MGD and increasing age. Irfan KSA et al. also found a very strong association between increasing age and increasing severity of the stage of MGD.[21] A study by Gao et al showed that the prevalence of MGD increases with age, significantly and is most prevalent in 50-59 year age group.[20] Villani et al. evaluated age-related Meibomian Gland changes using in-vivo laser scanning confocal microscopy. They demonstrated that meibomian gland density and diameter significantly decreased with age.[18]

There was a male predominance in our study in the MGD group with 40 males as compared to 31 females. A few studies have previously found higher MGD prevalence in males.[21] Hassanzadeh et al studied the global prevalence of Meibomian Gland Dysfunction and found a wide variation all over the world with a pooled prevalence of 35% in clinical studies. They also found that men were more prone to having MGD than women.[23] With increasing grade of MGD, the male predominance increased with 33.7% patients being males with Grade 3 and 4 MGD as compared to 25.3% females. Irfan KSA et. al. and Braich et. al. also had more males in their study.[21,13]

We found that the levels of serum cholesterol, triglycerides and LDL were significantly high with mean(SD) values of 209.2(35.4), 150.8(22.9) and 137.2(26.7) mg/dL as compared to 161.1(37.3), 114.6(11.5) and 107.5(25.5) mg/dL in the control group. The serum HDL values were significantly lower in MGD patients with 44.2(8.2) mg/dL as compared to 55.7(9.2) mg/dL in the control group. This is in conformity with the study conducted by Braich et. al. who also had similar results when they compared 109 MGD patients with 115 control group participants.[13] Pinna et. al. also found higher levels of cholesterol, HDL and LDL in blood of MGD patients as compared to normal control.[15] There was a significant correlation found in our study between the serum levels of total cholesterol, triglycerides, LDL and HDL showing that higher grades of MGD had significantly higher serum levels of total cholesterol, triglycerides and LDL and significantly lower serum levels of HDL. Dao et. al. found that there was a significantly

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higher level of serum cholesterol in MGD patients as compared to controls in both 20-44 years and 45-64 years age group.[8] Irfan KSA et. al. found positive association between the severity of MGD and increasing levels of LDL, total cholesterol and Triglycerides.[21]

The strengths of this study are that it is a hospital based, cross sectional prospective trial with an adequate sample size. The study not only compares the clinical parameters in MGD patients with the control group, but also measures the changes in values with increasing severity of MGD. The limitations of the study includes a hospital based sample and homogeneity of the patients as they were all Indians and genetic profile and dietary factors affect the lipid profile of a person.

CONCLUSION - The results of this study suggest a strong correlation between incidence of MGD and serum levels of total cholesterol, triglycerides, HDL and LDL. There is also a strong correlation of increasing severity of MGD with increasing age, serum total cholesterol, triglycerides, and LDL; and decreasing serum HDL levels. So, an ophthalmologist should suspect dyslipidaemia in a MGD patient. However, studies on a larger population and different ethnicities need to be conducted in order to prove that this association is causal and universal.

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