

## Influence of Serum Lipid Profile in Type 2 Diabetes Mellitus Patients with Diabetic Macular Edema

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### Abstract

**Background and Aim:** Diabetic macular edema, is major cause of vision loss. Association of lipids in pathogenesis of DR and DME has been less clear. This study is undertaken to determine association of serum lipid levels and diabetic macular edema.

**Materials and Methods:** An observational cross-sectional study was conducted from January 2021 to June 2022. Total 505 subjects were recruited based on inclusion and exclusion criteria, detailed history was elicited from patient about duration of DM, history of treatment received till now, presence of any other systemic illness. General ocular examination was done and anterior segment was evaluated by slit lamp biomicroscope, fundus examination was done by indirect ophthalmoscope and slit lamp biomicroscope using +90D lens. All patients of Type II Diabetes mellitus after examination were categorized into 3 groups, Subjects with no Macular Edema, Subjects with Nonclinically Significant Macular Edema, and Subjects with Clinically Significant Macular Edema.

Relevant laboratory investigation like blood sugar profile, serum lipid profile, renal profile were done and then the association of serum lipid levels with macular edema was studied.

**Result:** The mean total cholesterol and mean LDL among DM2 patients who had DME was 204.34 (19.27) mg/dl and 134.39 (19.12) mg/dl respectively and who didn't have DME was 189.56 (24.36) mg/dl and 120 (24.75) mg/dl respectively. The difference in mean LDL and total cholesterol were statistically significant between two groups ( $p < 0.01$ ).

**Conclusion:** Elevated serum lipid level showed a significant association with diabetic macular edema. Lipid lowering agents may help in reducing the occurrence of edema and vision loss in diabetic patients.

**Keywords:** Diabetes Mellitus, Retinopathy, Macular Edema, Lipid Profile.

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### Introduction

Diabetic macular edema is the accumulation of excess fluid in the extracellular space

within the retina in the macular area, typically in the inner nuclear, outer plexiform, and Henle's

fibre layer and subretinal space [1,2]. It is the most frequent cause of severe vision impairment in diabetic patient. The age and sex standardized prevalence of diabetic macular edema and CSME was found to be 13.5% and 7% [3]. Diabetic maculopathy alters the structure of macula resulting in blurring and distortion of central vision. Once diabetic maculopathy occurs, there is no satisfactory treatment available and the prognosis of visual outcome is also poor, so it is always better to prevent its development.

Diabetic macular edema can occur independently of DR, it appears to be strongly associated with the severity of diabetic retinopathy. DME share many risk factors with DR. Systemic risk factors for DME are hyperglycemia, diabetes duration, hypertension and dyslipidaemia. Macular edema has a complex multifactorial pathogenesis that is still poorly understood. Ganglion cells and the inner plexiform layer may be harmed by diabetes-accelerated neurotoxicity. The development of diabetic macular edema has also been linked to impairment of vascular autoregulation, capillary pericyte loss, thickening of capillary basement membranes, and delayed leukocyte migration [4].

Lipid exudation frequently coexists with diabetic retinopathy. In people with diabetic retinopathy, elevated serum lipid levels are linked to an increased incidence of retinal hard exudate. Increasing levels of exudate appear to be independently associated with an increased risk of visual impairment, even though retinal hard exudate typically coexists with diabetic macular edema. When it comes to the pathophysiology of diabetic retinopathy, especially in regard to the rupturing of the blood-retinal barrier, the high lipid levels are also linked to endothelial dysfunction. Pre- and intra-retinal alterations that occur at the macula are referred to as diabetic maculopathy. The main alterations occurring internally in diabetic retinal disease

are retinal ischemia caused by capillary and arteriolar non perfusion and collapse of blood-retinal barrier. Both structural and functional alterations to the macula are seen to be caused by diabetic macular edema, which can develop at any stage of retinopathy.

DME is divided into Centre involving (500 $\mu$ m) and Non center involving (outside 500 $\mu$ m), based on the criteria of involvement of fovea in Optical Coherence Tomography(OCT)

Few researches have looked into the relationship between blood lipid levels and diabetic macular edema . According to several research, the levels of low-density lipoprotein and serum cholesterol and retinal hard exudation are positively correlated. According to other research, serum triglyceride levels play a significant role in the development of macular edema. Other studies have found no connection between diabetic macular edema and serum lipid levels.

The goal of the current investigation was to identify the relationship between the serum lipid profile and the diabetic macular edema both clinically significant and non-significant. This investigation was necessary because of the contradictory data in the literature about the relationship between blood lipid levels and diabetic macular edema, as well as the dearth of studies in comparison to the volume of cases currently being treated.

### Aims

1. To estimate the prevalence of diabetic macular edema, both clinically significant macular edema (CSME) and non-clinically significant macular edema.
2. To analyze the association of serum lipid biomarkers in patients of diabetes mellitus with and without macular edema.

## Material and Methods

An observational cross sectional study was carried out at the Gandhi Memorial Hospital Rewa department of ophthalmology from January 2021 to September 2022. Both male and female patients with Type 2 Diabetes Mellitus (both inpatients and outpatients) were included. A sample of 505 individuals with diabetes mellitus were included in study

### Inclusion criteria:

- Type II diabetes mellitus patient

### Exclusion criteria:

- Accelerated hypertension
- Co-existing ocular disorder like uveitis, opaque or hazy media
- Retinal disorder like retinal vein/artery occlusion, retinitis pigmentosa
- Vitreoretinal degeneration and dystrophies
- Recent ocular surgeries

A detailed history was taken from patients. The duration of diabetes mellitus, history of treatment, presence of other systemic condition etc was recorded in predefined format. Anterior segment examination was done by slit lamp bio-microscope, fundus examination was done by indirect ophthalmoscopy and slit lamp examination using +90D lens. Diabetic retinopathy was classified according to modified ETDRS classification. The modified ETDRS classification was used to categorize diabetic retinopathy and macular edema. CSME was defined as presence of one of the following 1) any retinal thickening at or within 500microns of center of macula 2)hard exudates within 500 microns of center of macula with adjacent retinal thickening 3)retinal thickening of one disc diameter or

more any part of which is within one disc diameter from center of macula .

OCT was performed to measure and identify the kind of macular edema. Fasting blood sugar, lipid profile, and postprandial blood sugar were measured in the patients.

Informed consent was taken. The following information was obtained: 1) Demographic characteristics include age, gender and ethnicity; 2) Duration of diabetes; 3) Presence of other co-morbidities include hypertension, ischaemic heart disease, nephropathy, neuropathy; 4) Current treatment 5) history of smoking ,Systolic and diastolic blood pressures (BP) were measured one hour apart and average reading was recorded. Height and weight of the subject were measured and body mass index (BMI) calculated. Refractive assessment was performed by one optometrist and best corrected visual acuity (BCVA) was recorded. The following blood tests were carried out: 1) FBS and PPBS 2) Serum urea and creatinine 3) Serum lipid and its components include total cholesterol(>240mg/dl), low density lipoprotein (LDL>(>160mg/dl), high density lipoprotein (HDL>(>60mg/dl) and triglycerides (TG) (>200mg/dl) 5) HbA1c 6) Liver function tests including serum albumin . All the laboratory tests were performed with autoanalyser.

### Statistical analysis

Data was collected on predesigned proforma and was analyzed using chisquare and student t statistical test. Data was considered to be significant if  $p \leq 0.05$ .

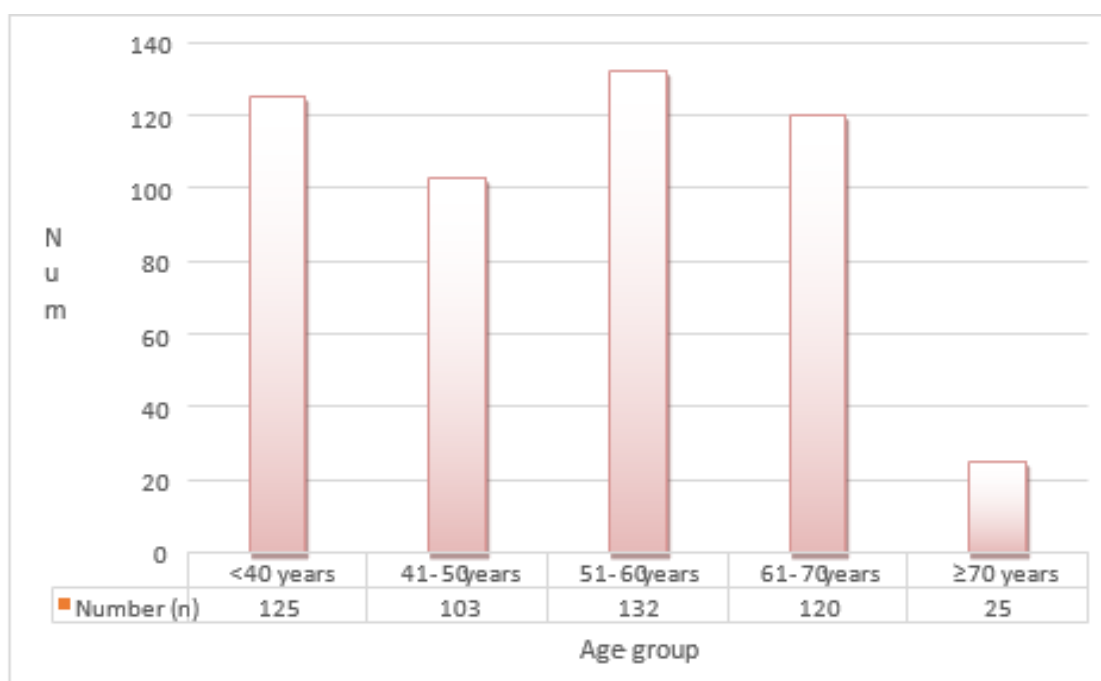
### Results

Data were collected from 505 participants. Data are as follows-

**Table 1: Distribution of participants according to age (n= 505)**

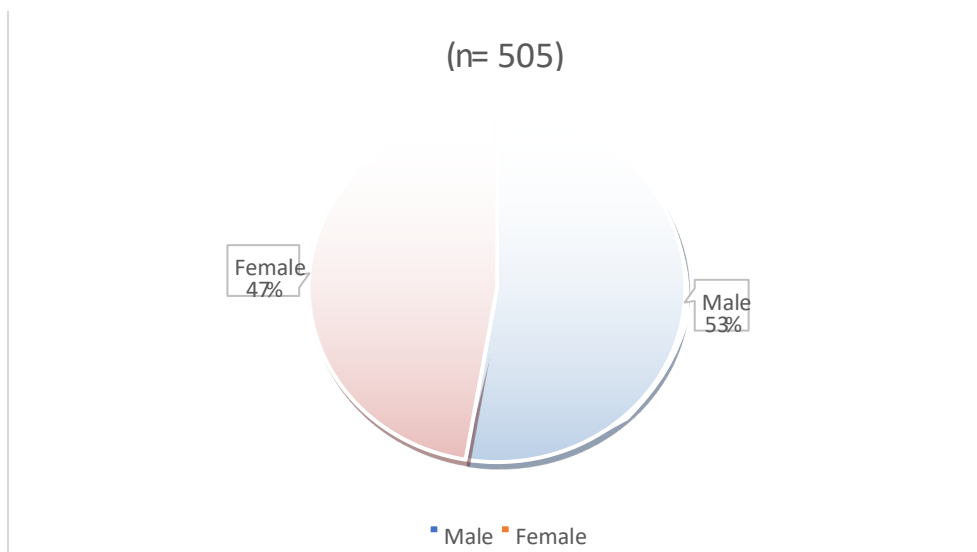
Years	Number (n)	Percent (%)
< 40 years	125	24.8
41- 50 years	103	20.4
51- 60 years	132	26.1
61- 70 years	120	23.8
≥70 years	25	5.0
Mean (SD)	51.44	12.62

Table 1 & figure 1 show age distribution of the participants. The mean (SD) of the participants was 51.44 (12.62) years. About one fourth participants were less than 40 years old. Five percent participants were more than 70 years old.

**Figure 1: Distribution of participants according to age (n= 505)****Table 2: Distribution of participants according to gender (n= 505)**

Gender	Number (n)	Percent (%)
Male	266	52.7
Female	239	47.3

Table 2 & figure 2 show gender distribution of the participants. They show that about 53% participants were male and 47% were female.

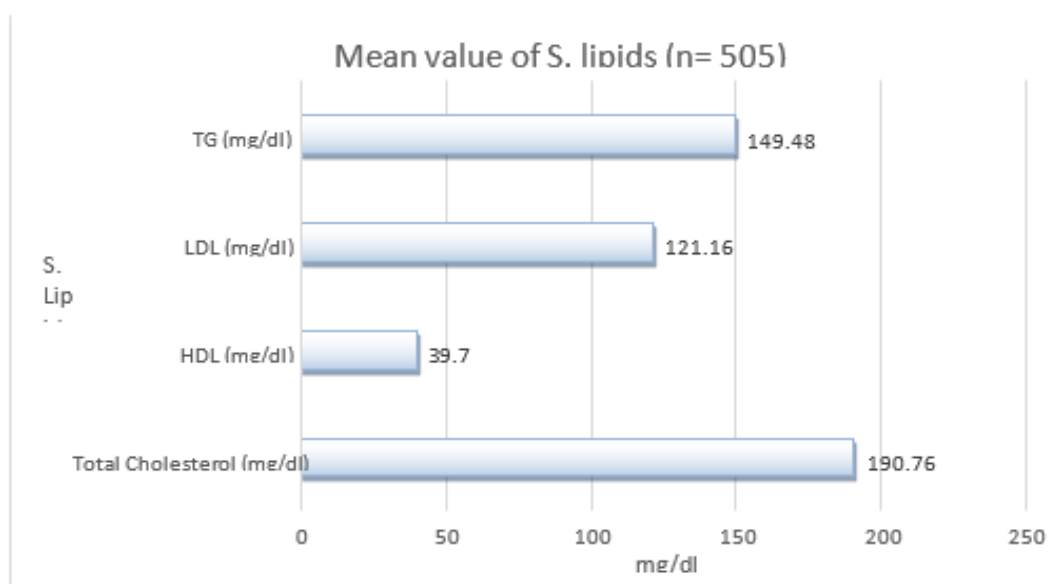


**Figure 2: Distribution of participants according to gender (n= 505)**

**Table 3: Mean values of Serum lipids among participants (n= 505)**

	Mean	SD
Total Cholesterol (mg/dl)	190.76	24.32
HDL (mg/dl)	39.70	9.39
LDL (mg/dl)	121.16	24.64
TG (mg/dl)	149.48	51.11

Table 3 & figure 3 show mean value of serum lipids. The mean (SD) total cholesterol among participants was 190.76 (24.32) mg/dl. The mean (SD) HDL among participants was 39.70 (9.39) mg/dl. The mean (SD) LDL among participants was 121.16 (24.64) mg/dl. The mean (SD) triglyceride among participants was 140.48 (51.11) mg/dl.



**Figure 3: Mean values of Serum lipids among participants (n= 505)**

**Table 4: Distribution of participants according to HBA1c (n= 505)**

HBA1c	Number (n)	Percent (%)
<8 %	239	47.3
≥ 8%	266	52.7
Mean (SD) %	7.79	1.03

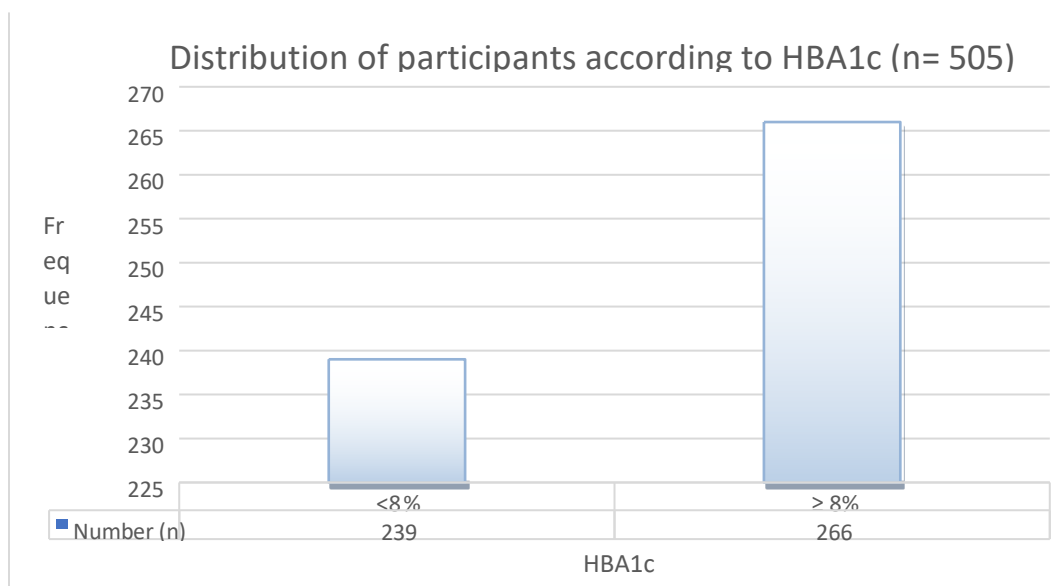
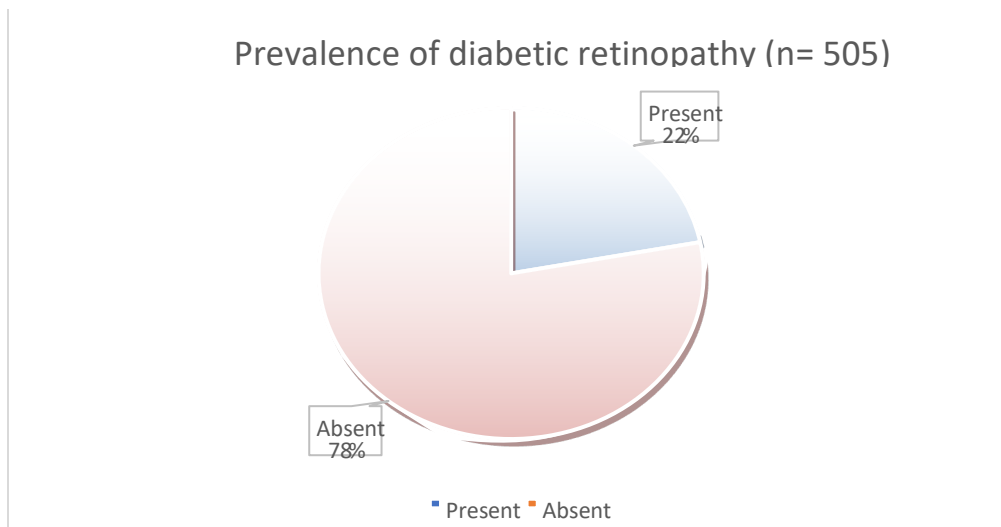
**Figure 4: Distribution of participants according to HBA1c (n= 505)**

Table 4 & figure 4 show distribution of participants according to HBA1c. About 47.3% participants had <8% HBA1c, and 52.7 participants had ≥ 8%% HBA1c. The mean (SD) HBA1c was 7.79 (1.03) %.

**Table 5: Prevalence of diabetic retinopathy among patients (n= 505)**

DR	Number (n)	Percent (%)
Present	111	22.0
Absent	394	78.0



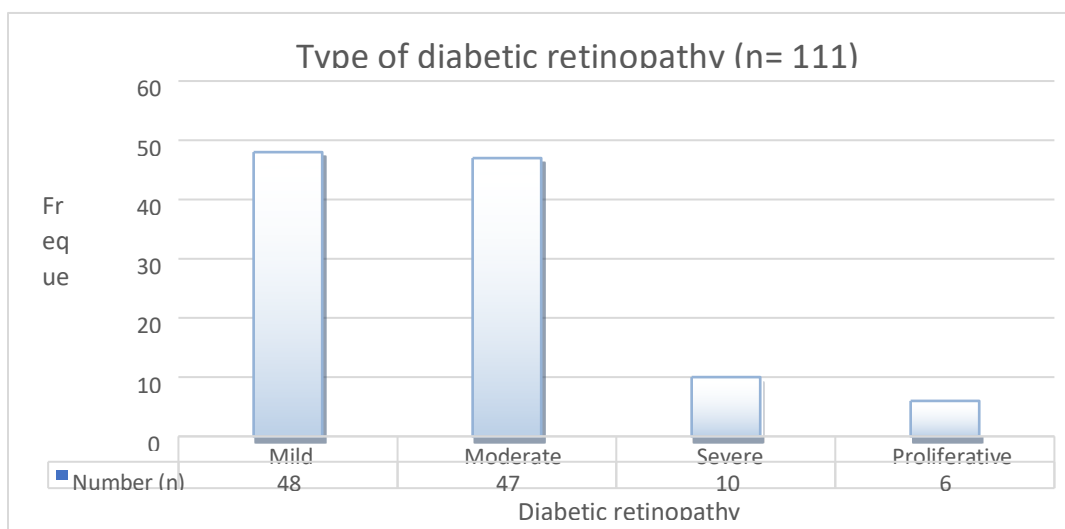
**Figure 5: Prevalence of diabetic retinopathy among patients (n= 505)**

Table 5 & figure 5 show prevalence of diabetic retinopathy. About 22% patients had diabetic retinopathy.

**Table 6: Distribution of participants according to type of diabetic retinopathy (n= 111)**

DR	Number (n)	Percent (%)
Mild	48	43.2
Moderate	47	42.3
Severe	10	9.0
Proliferative	6	5.5

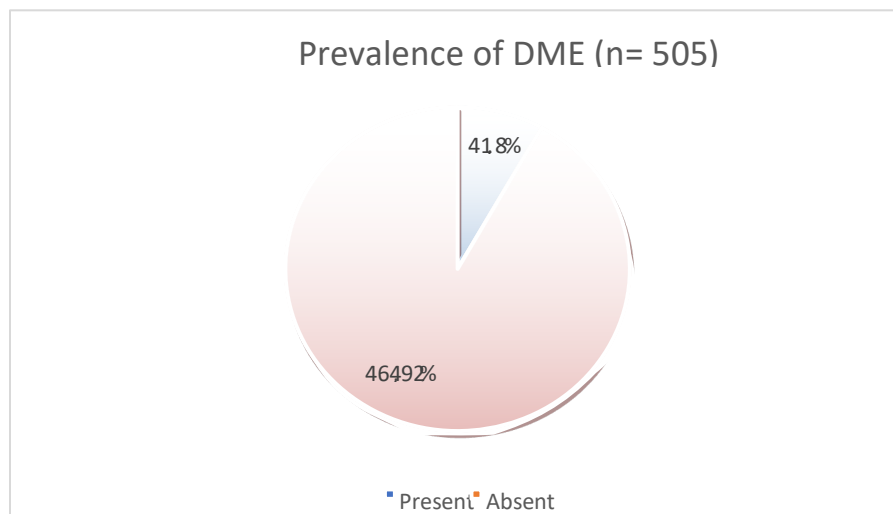
Table 6 & figure 6 show types of diabetic retinopathy among diabetic retinopathy patients. About 43.2% (n=48) had mild, 42.3% (n=47) had moderate, 9% (n=10) had severe and 5.5% (n=6) had proliferative diabetic retinopathy.



**Figure 6: Distribution of participants according to type of diabetic retinopathy (n= 111)**

**Table 7: Prevalence of diabetic macular edema among patients (n= 505)**

DME	Number (n)	Percent (%)
Present	41	8.1
Absent	464	91.9

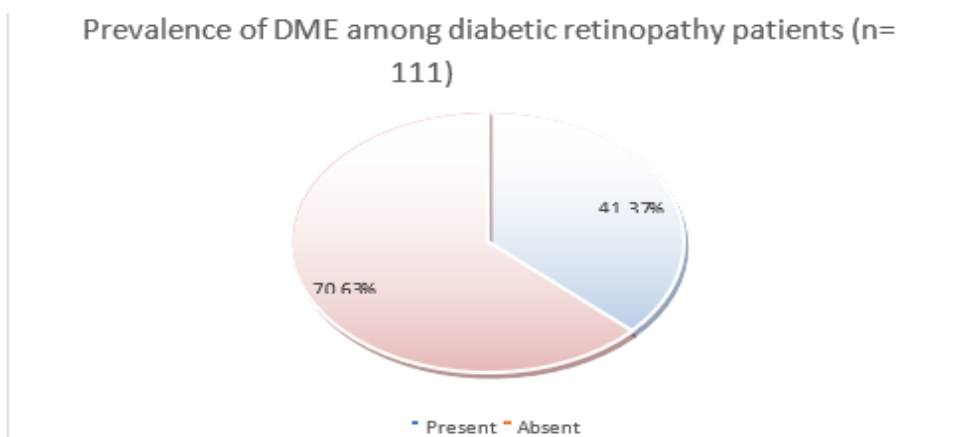


**Figure 7: Prevalence of diabetic macular edema among patients (n= 505)**

Table 7 & figure 7 show prevalence of diabetic macular edema among diabetic patients. The prevalence of DME among DM2 patients was found 8.1%.

**Table 8: Prevalence of diabetic macular edema among diabetic retinopathy patients (n= 111)**

DME	Number (n)	Percent (%)
Present	41	36.9
Absent	70	63.1



**Figure 8: Prevalence of diabetic macular edema among diabetic retinopathy patients (n= 111)**

Table 8 & figure 8 show prevalence of DME among diabetic retinopathy patients. About 36.9% diabetic retinopathy patients had DME.



**Table 9: Distribution of participants according to type of diabetic macular edema (n= 41)**

DME	Number (n)	Percent (%)
Non- CSME	32	78.1
CSME	9	21.9

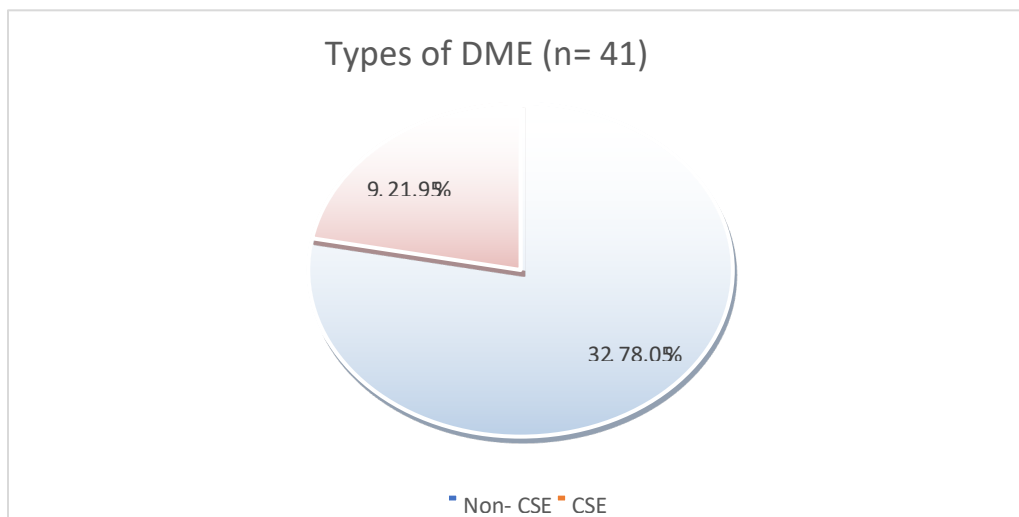
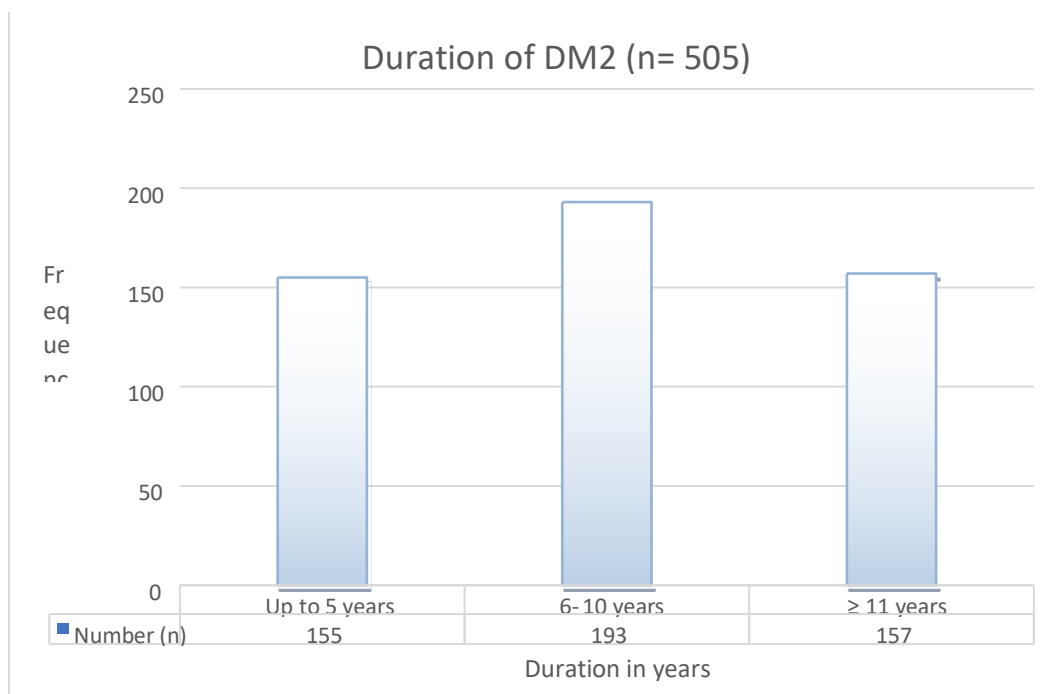
**Figure 9: Distribution of participants according to type of diabetic macular edema (n= 41)**

Table 9 & figure 9 show types of DME. About 21.9% (n=9) had CSE, and 78.1% (n= 32) had non-CSE.

**Table 10: Distribution of participants according to duration of DM-2 (n= 505)**

Duration of DM	Number (n)	Percent (%)
Up to 5 years	155	30.7
6- 10 years	193	38.2
≥ 11 years	157	31.1
Mean (SD) (years)	8.16	3.84

Table 10 & figure 10 show distribution of participants according to duration of DM2. About 30.7 participants had DM2 for up to 5 years. About 38.2% had for 6-10 years, 31.1% had for ≥ 11 years. The mean (SD) duration was 8.16 (3.84) years.



**Figure 10: Distribution of participants according to duration of DM-2 (n= 505)**

**Table 11: Association between DME and fasting glucose (n=505)**

	DME		Mean Difference (95% CI)	p-value
	Yes (n= 41)	No (n= 70)		
Fasting blood glucose (mg/dl) Mean (SD)	168.78 (21.39)	159.75 (23.25)	-9.030 (-17.833-0.22)	0.04

Table 11 shows association between diabetic macular edema (DME) and fasting blood glucose. The mean (SD) fasting blood glucose among DM2 patients who had DME was 168.78 (21.39) mg/dl. The mean (SD) fasting blood glucose among DM2 patients who didn't have DME was 159.75 (23.25) mg/dl. The difference in mean fasting blood glucose was statistically significant between two groups. (p= 0.04)

**Table 12: Association between DME and HBA1c (n=505)**

	DME		Mean Difference (95% CI)	p-value
	Yes (n= 41)	No (n= 70)		
HBA1c Mean (SD)	8.07 (1.00)	7.96(1.04)	-0.11 (-0.50- 0.28)	0.58

Table 12 shows association between diabetic macular edema (DME) and HBA1c. The mean (SD) HBA1c among DM2 patients who had DME was 8.07 (1.00) mg/dl. The mean (SD) HBA1c among diabetic retinopathy patients who didn't have DME was 7.96 (1.04) mg/dl. The difference in mean HBA1c was not statistically significant between two groups. (p= 0.58)

**Table 13: Association between DME and blood lipid levels (n=111)**

(mg/dl)	DME		Mean Difference (95% CI)	p- value
	Yes (n= 41)	No (n= 70)		
Total Cholesterol	204.34 (19.27)	192.06 (29.86)	12.28 (3.54- 21.02)	0.006
HDL	37.17 (10.98)	40.73 (9.86)	-3.56 (-7.56- 0.45)	0.081
LDL	134.39 (19.12)	122.84 (24.78)	11.55 (2.63- 20.46)	0.012
TG	163.90 (55.46)	142.43 (47.74)	21.47 (1.71- 41.23)	0.033

Table 13 shows association between diabetic macular edema (DME) and blood lipids. The mean (SD) total cholesterol among DR patients who had DME was 204.34 (19.27) mg/dl. The mean (SD) total cholesterol among DR patients who didn't have DME was 192.06 (29.86) mg/dl. The difference in mean total cholesterol was statistically significant between two groups. (p=0.006)

The mean (SD) HDL among DR patients who had DME was 37.17 (10.98) mg/dl. The mean (SD) HDL among DR patients who didn't have DME was 40.73 (9.86) mg/dl. The difference in mean HDL was not statistically significant between two groups. (p= 0.081)

The mean (SD) LDL among DR patients who had DME was 134.39 (19.12) mg/dl. The mean (SD) LDL among DR patients who didn't have DME was 122.84 (24.78) mg/dl. The difference in mean LDL was statistically significant between two groups. (p=0.012)

The mean (SD) triglyceride among DR patients who had DME was 163.90 (55.46) mg/dl. The mean (SD) triglyceride among DR patients who didn't have DME was 142.43 (47.74) mg/dl. The difference in mean triglyceride was statistically significant between two groups. (p= 0.033)

### Discussion

Diabetes Mellitus is the most common metabolic disorder globally. Diabetes is also

called silent killer due to its systemic complications. Diabetes has a significant influence on the society because it affects the most useful and productive period of the patient. Among microvascular complications of diabetes, Diabetic retinopathy is the most common, which can lead to severe visual loss. Severe visual impairment among diabetes mellitus patients may also be caused by diabetic maculopathy [5,6].

Several previous studies have suggested that abnormal serum lipid levels, are important risk factors for the development of CSME. Hence, this study was undertaken to find out the association between abnormal serum lipids and development of CSME. Most common age group of patients in this study was between 51-60 years. This shows that CSME becomes more evident as the age advances. Prakash GS *et al* [5] reported the mean age of the patients in the study group (with CSME) was  $57.02 \pm 9.75$ . Seyed Ahmad *et al* [6] found mean age as 53.22 with the age range of 18-77 years. We included 266 (53%) males and 239 (47%) females. We found male predominance in our study. Studies by Asensio-Sanchez Vm *et al* [7] who reported 60% women and 40% men with CSME 1 and Ong Ming Jew *et al* [4] reported 42% males and 58% females with CSME in their study, which is in contrast to our present study. We found statistically significant association between the incidence of dyslipidaemia in CSME patients with

moderate visual loss than with mild or severe form with p value of  $< 0.0005$ . In the present study, the severity of diabetic retinopathy (according to worst eye), found to have maximum number of patients with mild NPDR (43.2%), followed by moderate NPDR (42.3%). Severe NPDR was seen only in 9% patients, PDR was seen in 5% patients. Rajiv Raman *et al* [8] reported 6.3% mild NPDR, 25% moderate NPDR, 50% severe NPDR and 18.8% PDR among CSME patients.

We observed mean FBS of  $168.78 \pm 21.39$ , which is higher than the normal values of FBS. In the study done by Rajiv Raman *et al* [8] they reported mean fasting plasma glucose of  $217.94 \pm 80.42$ . This supports the fact that hyperglycemia is one of the risk factors for development of CSME. Increased blood glucose levels for a long period of time can cause alterations in pericytes and basic membrane, contributing to endothelial barrier dysfunction.

The mean (SD) total cholesterol among DM2 patients who had DME was  $204.34 (19.27)$  mg/dl. The mean (SD) total cholesterol among DM2 patients who didn't have DME was  $189.56 (24.36)$  mg/dl. The difference in mean total cholesterol was statistically significant between two groups. ( $p < 0.01$ ) The mean (SD) HDL among DM2 patients who had DME was  $37.17 (10.98)$  mg/dl. The mean (SD) HDL among DM2 patients who didn't have DME was  $39.92 (9.21)$  mg/dl. The difference in mean HDL was not statistically significant between two groups. ( $p = 0.0720$ ). The mean (SD) LDL among DM2 patients who had DME was  $134.39 (19.12)$  mg/dl. The mean (SD) LDL among DM2 patients who did not have DME was  $120 (24.75)$  mg/dl. The difference in mean LDL was statistically significant between two groups. ( $p < 0.01$ ). The mean (SD) triglyceride among DM2 patients who had DME was  $163.90 (55.46)$  mg/dl. The mean (SD) triglyceride among DM2 patients who

didn't have DME was  $39.92 (9.21)$  mg/dl. The difference in mean triglyceride was not statistically significant between two groups. ( $p = 0.059$ ).

This shows that dyslipidaemia is significantly associated with development of CSME. Finally the present study has shown that serum lipids, especially LDL, was largely associated with CSME (67.3%), but not with the severity of DR, suggesting a differential impact of dyslipidemia in the pathogenesis of DR and CSME, similar to the fact said by Rebab Benarous *et al* [9] in their study

### Conclusion

Elevated serum lipid level showed a significant association with diabetic macular edema. Lipid lowering agents may help in reducing the occurrence of edema and vision loss in diabetic patients.

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