



# International Journal of Clinical Endocrinology

## Research Article

## Variables Associated with Diabetic Maculopathy: A Cross Sectional Study from Basrah -

Zaid H. Abduljabbar<sup>1</sup>, Abbas A. Mansour<sup>2\*</sup>, Salah Z. Al Asady<sup>3</sup> and  
Wissam J. Alhamdani<sup>4</sup>

<sup>1</sup>*Dhi qar Health Directorate, Basrah, Iraq*

<sup>2</sup>*Diabetes, Endocrine and Metabolism Division, Department of Medicine, College of Medicine, University of Basrah, Basrah, Iraq*

<sup>3</sup>*Ophthalmology Division, Department of Surgery, Basrah College of Medicine, Basrah, Iraq*

<sup>4</sup>*Specialist Ophthalmologist, Basrah Health Directorate, Basrah, Iraq*

**\*Address for Correspondence:** Abbas Ali Mansour, Diabetes, Endocrine and Metabolism Division, Department of Medicine, College of Medicine, University of Basrah, Basrah, Hattin post office .P.O Box: 142, Basrah - 61013, Iraq, Tel: +009647801403706; E-mail: abbas.mansour@fdemc.iq

**Submitted:** 11 June 2018; **Approved:** 20 July 2018; **Published:** 24 July 2018

**Cite this article:** Abduljabbar ZH, Mansour AA, Al Asady SZ, Alhamdani WJ. Variables Associated with Diabetic Maculopathy: A Cross Sectional Study from Basrah. Int J Clin Endocrinol. 2018;2(1): 022-028.

**Copyright:** © 2018 Mansour AA, et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

## ABSTRACT

**Background:** Diabetic Maculopathy (DME) does not compulsorily fit the usual course of diabetic retinopathy advancement. This work aimed to study the variables associated with DME in a cohort of patients with type 2 diabetes mellitus from Basrah (Southern Iraq).

**Patients and Methods:** This was a cross sectional study from Faiha Specialized Diabetes, Endocrine and Metabolism Center (FDEMC) done over the period of January - April 2014. The study enrolled 197 patients with type 2 diabetes mellitus with at least 10 years duration and aged >30 years.

**Results:** No significant differences between those with DME and no maculopathy regarding age, gender, BMI, family history of diabetes, duration of diabetes, hypertension, systolic or diastolic blood pressure, current smoking, HbA1c, lipid profile, laser treatment, cataract surgery or drug treatment.

Comparison between maculopathy 1 and 2 was showed that all the studied variables were not significantly different except for Total Cholesterol (TC), which was higher in the maculopathy 2 (P value = 0.026) and High-Density Lipoprotein Cholesterol (HDL-C) higher among maculopathy 1 (p = 0.003). Furthermore comparing more severe maculopathy (M2) with no maculopathy only the TC remain significantly higher (p values = 0.032) among those with severe maculopathy (M2).

Only Duration of diabetes  $\geq$  13 years (odds ratio [OD], 0.53; 95% confidence interval [CI], 0.303 to 0.951; p = 0.032), TC  $\geq$  200mg/dL (OD, 0.25; 95% CI, 0.13 to 0.47; p < 0.0001), low-density lipoprotein cholesterol (LDL-C)  $\geq$  100 mg/dL (OD, 0.15; 95% CI, 0.08 to 0.31; p < 0.0001) were statistically associated with DME.

On logistic regression analysis, the TC  $\geq$  200 mg/dL (B = -0.734, Wald = 3.900, Exp (B) = 0.480, 95% CI = 0.232 to 0.994; p = 0.048) and LDL-C  $\geq$  100 mg/dL (B = -1.403, Wald = 12.664, Exp (B) = 0.246, 95% CI = 0.114 to 0.533; p < 0.0001) remains significantly associated with DME.

**Conclusion:** Only TC and LDL-C correlated with the presence of DME. No significant associated seen with age, gender, smoking state, duration of diabetes, hypertension, BMI, high density lipoprotein cholesterol (HDL-C), HbA1c, previous laser treatment, cataract surgery or treatment for diabetes.

**Keywords:** Diabetic Maculopathy; Type 2 diabetes; Dyslipidemia

## INTRODUCTION

Diabetic Maculopathy or Called Macular Edema (DME) is the major cause of visual loss in the working age in developed countries. According to the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), the prevalence of DME after 15 years of known diabetes was approximately 25% in patients with type 2 who were on insulin, and 14% of patients with type 2 diabetes who were not on insulin [1,2].

Despite the fact that DME is a common complication of diabetic retinopathy and shows a clear association with the systemic metabolic diversifications of diabetes, it does not compulsorily fit the usual course of diabetic retinopathy advancement. It may occur at any stage of diabetic retinopathy, whether non-proliferative, or proliferative, or even at the most advanced stages of the retinopathy [3].

DME is characterized by increased vascular permeability and the deposition of hard exudate in the central retina. This hard exudate is thought to be the result of lipoproteins leaking from retinal capillaries into the extra-cellular space of the retina with cystic retinal thickening or lipid deposition [4].

In the retina, there is a specialized structure, blood-retinal barrier (BRB) that regulates fluid movements into and out of the retinal tissue. Breakdown of the BRB is the cause of a leak, and it's mediated by ischemic oxygen free radicals and inflammatory mediators [5].

Retinal edema occurs when there is an increase of water in the retinal tissue, resulting in an increase in its thickness. This increase in water content of the retinal tissue may be initially intracellular (cytotoxic edema) or extra-cellular (vasogenic edema) [6].

In DME, extracellular edema resulting from the breakdown of the BRB is present [7]. All of these pathological changes were typical in diabetes, hypertension, and dyslipidemia.

DME is associated with dyslipidemia in diabetes mellitus, but the treatment of lipid disorder may not reduce these complications [8].

In the view of the increasing incidence of diabetes mellitus worldwide, DME is still representing a widespread cause of visual loss, and because of the difficulty of its treatment, it is important to identify the risk factors involved, to prevent it or get the right treatment options. The understanding of the main pathophysiologic mechanisms of this disease is demanding in the useful treatment option [9].

## AIM

This work aimed to study the variables associated with DME in a cohort of patients with type 2 diabetes mellitus from Basrah (Southern Iraq).

## PATIENTS AND METHODS

### Study design

This was a cross sectional study from Faiha Specialized Diabetes, Endocrine, and Metabolism Center (FDEMC) done over the period of January –April 2015.

### Participants

The total enrolled patients were 197 of them 104 (52.8%) females. All patients informed about the study and permission was taken.

### Inclusion criteria

- Type 2 diabetes.
- 10 years or more of diabetes duration.
- Adult's  $\geq$ 30 years of age.

### Exclusion criteria

- Type 1 diabetes.

- **Pregnant women.**
- **Those with no lipid profile or retinal examination.**
- **Patient's refusal.**
- **Patients on statin before lipid estimation.**
- **Diabetes less than 10 years.**
- **Amputation.**

We enrolled the first 2-3 patients seen in the center in the morning daily for four months (the study period) if they are fulfilled the inclusion criteria.

Patients with inclusion criteria were assessed by a single doctor for full history and examination. Including measurement of height, weight and blood pressure, which was measured in the right arm after 5 minutes rest.

Variables: age, gender, duration of diabetes, Oral Antidiabetic Drugs (OAD), insulin alone, and insulin with OAD.

Blood pressure systolic and diastolic, weight, height, family history of diabetes, previous LASER, cataract surgery.

Hypertension was defined as a doctor's diagnosis with a drug used in the past or an average of two readings of blood pressure measurement of 140/90 or more for new cases.

**Eye examination**

The full Ophthalmological examination was done in the form of; best corrected visual acuity (BCVA), slit-lamp examination and intraocular pressure measurement, fundus examination using indirect slit-lamp biomicroscopy to determine the presence or absence of maculopathy, and optical coherence tomography (OCT) was done when indicated.

Maculopathy (M) was divided according to grading scheme of the Scottish Diabetic Retinopathy Screening Collaboration [10].

**M1 (observable):**

- Lesions within a radius of >1 but < - 2 disc diameters of the center of the fovea
- Any hard exudates

**M2 (referable):**

- Lesions within a radius of < - 1 disc diameter of the center of the fovea
- Any blot hemorrhages
- Any hard exudates

For all patients fasting lipid profile was done at 8:00 a.m. advising the patient to omit statin therapy two weeks before the day of the test for those taking statin.

**Biochemical testing**

HbA<sub>1c</sub> was done using Bolyzer 300 chemistry analyzer and D-10 hemoglobin testing system by Bio-Rad Laboratories, Inc., Hercules, CA 94547 respectively.

Serum lipid profile was measured in the early morning after at least 10 hours fasting using 5 ml of venous blood and, the measurement was done using Fully Automated Clinical Chemistry Analyzer Bolyzer<sup>®</sup> 300. Lipid profile abnormalities were classified

according to National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) [11].

**STATISTICAL ANALYSIS**

All data were entered into SPSS-15. Continuous variables expressed as mean ± SD categorical variables as number and percent accordingly. Chi squared ( $\chi^2$ ) test, and Student t-test was used to studying the difference between variables. All continuous variables were put into categorical variables to be used for univariate analysis. Variables significantly associated with maculopathy on univariate analysis were entered into a logistic regression analysis to see which variable remains statistically significantly associated with maculopathy. A P values less than 0.05 were reported as statistically significant.

**RESULTS**

Table 1 show basic characteristics. The mean age was 56.8 ± 7.7 years, ranged between 36 and 82 years. Of them, 52.8% were men with a mean duration of diabetes was 14.3 ± 5.2 years, ranged between 10 and 45 years. The Family history of diabetes was positive in 63.5% ,and 45.2% were hypertensive. The mean of BMI (Kg/m<sup>2</sup>) was 29.9 ± 4.8. We have 66 patients (33.5%) with varying degree of DME. There were 41 patients (62.1%) exhibited grade 1 maculopathy (M1), and 25 patients (37.9%) had grade 2 maculopathy (M2).

**Table 1:** Demographic characteristics of 197 patients with type 2 diabetes mellitus.

Variables	Mean ± SD or number (%)
Age (years)	56.8 ± 7.7
Male gender	104 (52.8)
Female gender	93(47.2)
Duration of DM (years)	14.3 ± 5.2
Current smoker	51 (25.9)
Family history of diabetes mellitus	125 (63.5)
Hypertension	89(45.2)
Systolic BP (mmHg)	137.7 ± 18.9
Diastolic BP (mmHg)	81.0 ± 9.6
Body mass index (BMI) - kg/m <sup>2</sup>	29.9 ± 4.8
HbA1c (%)	10.4 ± 2.0
High density lipoprotein cholesterol (HDL-C) mg/dL	46.6 ± 16.9
Triglycerides (TG) mg/dL	197.2 ± 139.7
Very-low-density lipoprotein cholesterol (VLDL-C) mg/dL	39.0 ± 27.9
No maculopathy	131.0 (66.5)
Maculopathy (any)	66(33.5)
*Maculopathy 1	41 (62.1)
*Maculopathy 2	25 (37.9)
Laser Treatment	9(4.6)
Cataract Surgery	18 (9.1)
Oral Antidiabetic Drugs (OAD)	58 (29.4)
Insulin alone	4 (2.0)
OAD+ insulin	135 (68.5)
*Of those with maculopathy	

Differences between 197 patients with maculopathy and no maculopathy are present in Table 2. No significant differences between the two groups regarding age, gender, BMI, family history of diabetes, duration of diabetes, hypertension, systolic or diastolic blood pressure, current smoking, HbA1c, lipid profile, laser treatment, cataract surgery or drug treatment.

Comparison between maculopathy 1 and 2 was made in Table 3. Again, all the studied variables were not significantly different except for Total Cholesterol (TC), which was higher in the maculopathy 2 (P value = 0.026) and high-density Lipoprotein Cholesterol (HDL-C) higher among maculopathy 1 (p = 0.003).

When we compared more severe Maculopathy (M2) with no maculopathy only the TC remain significantly higher (p values = 0.032) among those with severe maculopathy (M2) in table 4.

All variables changed to categorical variables to study the association with maculopathy using univariate analysis (Table 5). Only duration of diabetes  $\geq 13$  years (odds ratio [OD], 0.53; 95% confidence interval [CI], 0.303 to 0.951; p = 0.032), TC  $\geq 200$ mg/dL (OD, 0.25; 95% CI, 0.13 to 0.47; p <0.0001), low-density lipoprotein cholesterol (LDL-C)  $\geq 100$  mg/dL (OD, 0.15; 95% CI, 0.08 to 0.31; p <0.0001) were statistically associated with DME.

Variables that's statistically significant on univariate analysis were entered into the logistic regression analysis. After this analysis, the TC  $\geq 200$  mg/dL (B = -0.734, Wald = 3.900, Exp (B) = 0.480, 95% CI = 0.232 to 0.994; p =0.048) and LDL-C  $\geq 100$  mg/dL (B = -1.403, Wald = 12.664, Exp (B) = 0.246, 95% CI = 0.114 to 0.533; p < 0.0001) remains significantly associated with DME (Table 6).

## DISCUSSION

The prevalence of maculopathy has varied widely depending

**Table 2:** Clinical and biochemical characteristics of the study groups with and without maculopathy.

Variables	No maculopathy 131(66.5)	Maculopathy 66 (33.5)	P value
	Mean $\pm$ SD or Number (%)	Mean $\pm$ SD or Number (%)	
Age (Years)	56.7 $\pm$ 8.0	57.1 $\pm$ 7.1	0.181
Male gender	55.0(52.9)	49.0(47.1)	0.501
Current smoker	25.0 (49.0)	26.0(51.0)	0.220
Family history of diabetes mellitus	69.0 (55.2)	56(44.8)	0.669
Duration of diabetes	13.7 $\pm$ 5.2	15.4 $\pm$ 5.0	0.542
Hypertension	49 (55.1)	40(44.9)	0.774
Systolic BP (mmHg)	136.5 $\pm$ 17.7	140.0 $\pm$ 21.0	0.187
Diastolic BP (mmHg)	80.8 $\pm$ 9.1	81.6 $\pm$ 10.6	0.176
Body mass index (BMI) - kg/m <sup>2</sup>	30.0 $\pm$ 4.8	29.7 $\pm$ 4.8	0.627
HbA1c (%)	10.1 $\pm$ 1.9	11.0 $\pm$ 2.0	0.806
Total cholesterol (TC) mg/dL	209.4 $\pm$ 52.9	212.1 $\pm$ 45.1	0.262
Low-density lipoprotein cholesterol (LDL-C) mg/dL	103.7 $\pm$ 34.4	112.0 $\pm$ 33.9	0.748
High density lipoprotein cholesterol (HDL-C) mg/dL	46.1 $\pm$ 16.4	47.5 $\pm$ 18.0	0.311
Triglycerides (TG) mg/dL	196.7 $\pm$ 152.0	198.2 $\pm$ 112.3	0.720
Very-low-density lipoprotein cholesterol (VLDL-C) mg/dL	39.1 $\pm$ 30.5	38.6 $\pm$ 22.1	0.598
Laser treatment	5.0(55.6)	4.0(44.4)	0.961
Cataract surgery	8.0 (44.4)	10.0(55.6)	0.286
Oral antidiabetic drugs (OAD)	35.0 (59.3)	24 (40.7)	0.310
Insulin alone	4.0 (100.0)	0.0(0.0)	
OAD+ insulin	72.0 (53.7)	62.0 (46.3)	

**Table 3:** Maculopathy 1 vs. maculopathy 2 among 66 patients with maculopathy.

Variable	Maculopathy 1 41 (62.1)	Maculopathy 2 25 (37.9)	P value
	Mean $\pm$ SD or Number (%)	Mean $\pm$ SD or Number (%)	
Age (Years)	56.6 $\pm$ 7.1	57.8 $\pm$ 7.1	0.718
Male gender	33 (31.7)	16(15.4)	0.501
Current smoker	18.0 (35.3)	8.0(15.7)	
Family history of diabetes mellitus	36.0 (28.8)	20.0(16)	
Duration of diabetes	15.3 $\pm$ 4.9	15.6 $\pm$ 5.3	0.573
Hypertension	26.0(29.2)	14.0(15.7)	
Systolic BP (mmHg)	136.8 $\pm$ 19.9	145.2 $\pm$ 22.1	0.659
Diastolic BP (mmHg)	80.7 $\pm$ 10.0	83.2 $\pm$ 11.4	0.235
Body mass index (BMI) - kg/m <sup>2</sup>	29.7 $\pm$ 5.0	29.8 $\pm$ 4.6	0.823
HbA1c %	11.1 $\pm$ 2.0	11.0 $\pm$ 2.0	0.381
Total cholesterol (TC) mg/dL	211.1 $\pm$ 51.5	213.8 $\pm$ 32.8	0.026
Low-density lipoprotein cholesterol (LDL-C) mg/dL	106.9 $\pm$ 34.3	120.2 $\pm$ 30.5	0.501
High density lipoprotein cholesterol (HDL-C) mg/dL	50.8 $\pm$ 20.6	42.0 $\pm$ 11.0	0.003
Triglycerides (TG) mg/dL	191.0 $\pm$ 127.9	210.1 $\pm$ 81.7	0.451
Very-low-density lipoprotein cholesterol (VLDL-C) mg/dL	36.7 $\pm$ 25.0	41.9 $\pm$ 16.3	0.630
Laser treatment	3.0 (33.3)	1.0(11.1)	
Cataract surgery	8.0 (44.4)	2.0(11.1)	
Oral antidiabetic drugs (OAD)	20.0 (33.9)	4.0(6.8)	
Insulin alone	0.0 (0.0)	0.0(0.0)	
OAD+ insulin	40.0 (29.9)	22.0(16.4)	

**Table 4:** No maculopathy vs. maculopathy 2 among patients among 156 patients.

Variable	No Maculopathy 131(66.5)	Maculopathy 2 25(12.7)	P value
	Mean $\pm$ SD or Number (%)	Mean $\pm$ SD or Number (%)	
Age (Years)	56.7 $\pm$ 8.0	57.8 $\pm$ 7.1	0.273
Male gender	55(52.9)	16(15.4)	
Current smoker	25(49.0)	8(15.7)	
Family history of diabetes mellitus	69(55.2)	20(16)	
Duration of diabetes	13.7 $\pm$ 5.2	15.6 $\pm$ 5.3	0.542
Hypertension	49(55.1)	14(15.7)	
Systolic BP (mmHg)	136.5 $\pm$ 17.7	145.2 $\pm$ 22.1	0.187
Diastolic BP (mmHg)	80.8 $\pm$ 9.1	83.2 $\pm$ 11.4	0.176
Body mass index (BMI) - kg/m <sup>2</sup>	30.0 $\pm$ 4.8	29.8 $\pm$ 4.6	0.852
HbA1c %	10.1 $\pm$ 1.9	11.0 $\pm$ 2.0	0.390
Total cholesterol (TC) mg/dL	209.4 $\pm$ 52.9	213.8 $\pm$ 32.8	0.032
Low-density lipoprotein cholesterol (LDL-C) mg/dL	103.7 $\pm$ 34.4	120.2 $\pm$ 30.5	0.554
High density lipoprotein cholesterol (HDL-C) mg/dL	46.1 $\pm$ 16.4	42.0 $\pm$ 11.0	0.094
Triglycerides (TG) mg/dL	196.7 $\pm$ 152.0	210.1 $\pm$ 81.7	0.496
Very-low-density lipoprotein cholesterol (VLDL-C) mg/dL	39.1 $\pm$ 30.5	41.9 $\pm$ 16.3	0.490
Laser treatment	5(55.6)	1(11.1)	
Cataract surgery	8(44.4)	2(11.1)	
Oral hypoglycemic agent (OAD)	35(59.3)	4(6.8)	
Insulin alone	4(100)	0(0.0)	
OAD+ insulin	72(53.7)	22(16.4)	

on the methodology and populations. In this study, the overall prevalence of diabetic maculopathy was 33.5%, which is comparable to Raman et al., study [12] and Al Till et al., [13], was 31.76%, 30.8% respectively. Several studies show a lower prevalence of maculopathy; like Zander et al., Study [14], which reported the prevalence of

**Table 5:** Univariate analysis, among those with maculopathy and those without among 197 patients with type 2 diabetes mellitus.

Variable	No maculopathy No. (%)	Maculopathy No. (%)	OR Maculopathy vs. no maculopathy (95% Confidence interval)	P value
	Mean ± SD or Number (%)	Mean ± SD or Number (%)		
Age ≥60 years	45(40.5)	37(43.0)	0.903(0.510, 0.598 )	0.726
Male gender	55(49.5)	49(57.0)	0.742(0.421, 1.306)	0.300
Current smoker	25 (22.5)	26 (30.2)	0.671 (0.354,1.273)	0.220
Family history of diabetes mellitus	69(62.2)	56 (65.1)	0.880(0.490,1.582)	0.669
Duration of diabetes≥ 13 years	47 (42.7)	50 (58.1)	0.537(0.303,0.951)	0.032
Hypertension	49 (44.1)	40 (46.5)	0.909 (0.516,1.600)	0.741
Systolic BP (mmHg) ≥ 140	61 (55.0)	39 (45.3)	1.470 (0.835,2.589)	0.181
Diastolic BP (mmHg) ≥ 90	24 (21.6)	19 (22.1)	0.973(0.492, 1.922)	0.937
Body mass index (BMI) - kg/m <sup>2</sup> ≥ 25	95(85.6)	76 (88.4)	0.781(0.335,1.820)	0.567
HbA1c % ≥10	61 (55.0)	58 (67.4)	0.589 (0.328,1.058)	0.076
Total cholesterol (TC) mg/ dL ≥ 200	49 (44.1)	65 (75.6)	0.255 (0.138,0.474)	<0.0001
Low-density lipoprotein cholesterol (LDL-C) mg/ dL ≥ 100	50(45.0)	72 (83.7)	0.159 (0.080,0.316)	<0.0001
High density lipoprotein cholesterol (HDL-C) mg/ dL <40	47 (42.3)	33 (38.4)	1.179 (0.664, 2.096)	0.574
Triglycerides (TG) mg/ dL ≥ 150	62 (55.9)	51 (59.3)	0.868 (0.491, 1.536)	0.628
Very-low-density lipoprotein cholesterol (VLDL-C) mg/ dL >30	61 (55.0)	50 (58.1)	0.878 (0.497, 1.551)	0.655
Laser treatment	5 (4.5 )	4 (4.7)	0.967 (0.252, 3.715)	0.961
Cataract surgery	8 (7.2)	10(11.6)	0.590 (0.222, 1.566)	0.286
OAD+ insulin	72 (53.7)	62 (46.3)	0.715 (0.388,1.317)	0.356

**Table 6:** logistic regression analysis for variables significantly associated with maculopathy on univariate analysis.

	B	S.E.	Wald	df	P value	Exp (B)	95% Confidence interval for EXP (B)	
							Lower	Upper
Duration of diabetes≥ 13 years	-0.532	-0.532	2.757	1	0.097	0.587	0.313	1.101
Total cholesterol (TC) mg/dL ≥200 mg/dl	-0.734	0.372	3.900	1	0.048	0.480	0.232	0.994
Low-density lipoprotein cholesterol (LDL-C) mg/dl ≥100 mg/dL	-1.403	0.394	12.664	1	<0.0001	0.246	0.114	0.533
Constant					<0.0001	31.202		

maculopathy in the type 2 diabetic cohort was 23%, whereas Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) found a DME prevalence of 28% among 1121 people whose age at diagnosis was 30 years or older whose duration of diabetes was 20 or more years. In Salem et al. study the prevalence of maculopathy was (17%) [15] and the prevalence was 6.3% by Khanekar et al. Study [16]. This variation may reflect the poor glycemic control of Iraqis in addition to socioeconomic and racial factor with food habits. In this study, there is no significant association between DME and age. The similar finding also reported by others [17,18].

Gender is not identified as a risk factor in our study, which was also seen in previous studies [12,17,19].

BMI showed no significant association with maculopathy; a similar finding reported before [20,21]. On the other hand, cross sectional study done by Van Leiden et al., [22] and Laila H.M. El-Shazly et al., [23] both reported association of macular edema and increased BMI. However Looker et al., [24] found that lower BMI was associated with increased severity of retinopathy.

The relationship between smoking and DME is not well understood. Smoking in this study was not associated with maculopathy that, a similar finding to others [17,25,26]. An analysis of data from the Wisconsin Epidemiologic Study of Diabetic Retinopathy found that smoking status was not related to the incidence and progression of DR over 4 years. [27] Similarly, a more recent analysis of 25-year data from the same Wisconsin study found a univariate relationship of a higher incidence of macular edema in diabetic persons who smoked more than 15 pack-years after diabetes diagnosis; however, this relationship was not significant in multivariate analyzes. [28]. The reasons for not finding a relation are not known. Regardless, smoking should be avoided due to its relation to increased risk of death and other systemic complications.

Because of the cross sectional design in our study, the relation between maculopathy and hyperglycemia (as measured by HbA1C), was not seen like that was seen in prospective studies [29]. Yet, there was an association between maculopathy and the duration of DM (as demonstrated by univariate analysis) and hence with exposure to hyperglycemia. Zander et al. Study [14] found the same results.

Regarding the duration of diabetes, it was found to be significantly higher in patients with maculopathy on univariate analysis, but the relationship was no longer significant in a multivariate logistic regression analysis in this study. Few previous studies showed the duration of diabetes as a risk factor for diabetic macular edema [14,30,31]. Wisconsin Epidemiologic Study of Retinopathy also exhibited the importance of the diabetic duration, which showed an increased prevalence of diabetic maculopathy of 28% of patients whose age at the time of diagnosis was 30 years or older and whose diabetes duration was 20 years or longer [32] This discrepancy could be explained as the macular edema may occur at any stage of diabetic retinopathy even in the absence of severe retinopathy and sometimes can present as early diabetic sign. Our finding correlates with the study reported by Sasaki et al., [18].

Previous studies have found that serum lipids were associated with macular hard exudate and DME [12,33-38].

The Early Treatment Diabetic Retinopathy Study (ETDRS) reported an association of total cholesterol and LDL -C levels in the presence of hard exudates in the macula in patients with DR [35]. Idiculla et al., [36] reported that cholesterol levels were associated with hard exudates in the center of the macula, and LDL cholesterol levels were associated with CSME in patients with type 2 diabetes. The Chennai Urban Rural Epidemiology Study (CURES) Eye Study also found a correlation between LDL -C level and CSME and DME [39].

The Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Study13 reported that total cholesterol related to severe maculopathy and that LDL cholesterol related to DME [12].

The WESDR also reported an association between serum cholesterol and severity of hard exudates [29]. Our results are consistent with findings from these studies. Our study observed the association of serum lipids with maculopathy. Concerning the no maculopathy versus maculopathy group, increasing proportions with elevated levels was noted for serum total cholesterol and serum LDL cholesterol in univariate analysis. Even, after adjusting the confounding variables, the multivariate analysis identified two variables associated with maculopathy; serum total cholesterol and LDL-C. As mentioned above, the ETDRS was reported that higher baseline total and LDL -C levels increased the risk of retinal exudation by two-fold [35].

## CONCLUSION

Only TC and LDL-C correlated with the presence of DME. No significant associated seen with age, gender, smoking state, duration of diabetes, hypertension, BMI, HDL-C HbA1c level, previous laser treatment, cataract surgery, or treatment for diabetes. However, larger studies may give more information.

## REFERENCES

1. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy. II. Prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years. *Arch Ophthalmol*. 1984; 102: 520-526. <https://goo.gl/vm5RtB>
2. Williams R, Airey M, Baxter H, Forrester J, Kennedy-Martin T, Girach A. Epidemiology of diabetic retinopathy and macular oedema: a systematic review. *Eye (Lond)*. 2004; 18: 963-983. <https://goo.gl/eVYjD1>
3. Klein BE, Klein R, Lee KE. Components of the metabolic syndrome and risk of cardiovascular disease and diabetes in Beaver Dam. *Diabetes Care*. 2002; 25: 1790-1794. <https://goo.gl/eTF2g5>
4. Zhang X, Zeng H, Bao S, Wang N, Gillies MC. Diabetic macular edema:

- new concepts in patho-physiology and treatment. *Cell Biosci*. 2014; 4: 27. <https://goo.gl/Xf4NsC>
5. Bhagat N, Grigorian RA, Tutela A, Zarbin MA. Diabetic macular edema: pathogenesis and treatment. *Surv Ophthalmol*. 2009; 54: 1-32. <https://goo.gl/RDXPnp>
  6. Cunha-Vaz J. Diabetic macular edema. *Eur J Ophthalmol*. 1998; 8: 127-130. <https://goo.gl/EX47VK>
  7. Cunha-Vaz J, Faria de Abreu JR, Campos AJ. Early breakdown of the blood-retinal barrier in diabetes. *Br J Ophthalmol*. 1975; 59: 649-656. <https://goo.gl/5kAZoG>
  8. Das R, Kerr R, Chakravarthy U, Hogg RE. Dyslipidemia and Diabetic Macular Edema: A Systematic Review and Meta-Analysis. *Ophthalmology*. 2015; 122: 1820-1827. <https://goo.gl/9hnTVj>
  9. Christina Antonopoulos and Manju Subramanian. *Diabetic Macular Edema, Diabetic Retinopathy*, Dr. Mohammad Shamsul Ola (Ed.), 2012; ISBN: 978-953-51-0044-7. <https://goo.gl/WxeLUE>
  10. The Scottish Diabetic Retinopathy Grading Scheme. 2007.
  11. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). *JAMA*. 2001; 285: 2486-2497. <https://goo.gl/9KynJB>
  12. Raman R, Rani PK, Kulothungan V, Racheppalle SR, Kumaramanickavel G, Sharma T. Influence of serum lipids on clinically significant versus nonclinically significant macular edema: SN-DREAMS Report number 13. *Ophthalmology*. 2010; 117: 766-772. <https://goo.gl/8vhVT2>
  13. Al-Till MI, Al-Bdour MD, Ajlouni KM. Prevalence of blindness and visual impairment among Jordanian diabetics. *Eur J Ophthalmol*. 2005; 15: 62-68. <https://goo.gl/o8QbhS>
  14. Zander E, Herfurth S, Bohl B, Heinke P, Herrmann U, Kohnert KD, et al. Maculopathy in patients with diabetes mellitus type 1 and type 2: associations with risk factors *Br J Ophthalmol*. 2000; 84: 871-876. <https://goo.gl/UXE4FD>
  15. Salem M, Ajlouni K. Diabetic retinopathy among Jordanians: It's patterns, severity, and some associated risk factors. *Diabetologia Croatica*. 1999; 28: 17-23. <https://goo.gl/ovkmBJ>
  16. Khandekar R, Al Lawatii J, Mohammed AJ, Al Raisi A. Diabetic retinopathy in Oman: a hospital based study. *Br J Ophthalmol*. 2003; 87: 1061-1064. <https://goo.gl/87EMYF>
  17. Jew OM, Peyman M, Chen TC, Visvaraja S. Risk factors for clinically significant macular edema in a multi-ethnics population with type 2 diabetes. *Int J Ophthalmol*. 2012; 5: 499-504. <https://goo.gl/PNco6m>
  18. Sasaki M, Kawashima M, Kawasaki R, Uchida A, Koto T, Shinoda H, Tsubota K, Wang JJ, Ozawa Y. Association of serum lipids with macular thickness and volume in type 2 diabetes without diabetic macular edema. *Invest Ophthalmol Vis Sci*. 2014; 55: 1749-1753. <https://goo.gl/mHnSD9>
  19. Rasmieh M Al-Amer, Yousef Khader, Samer Malas, Nakhleh Abu-Yaghi, Muawyah Al-Bdour, Kamel Ajlouni. Prevalence and risk factors of diabetic retinopathy among Jordanian patients with type 2 diabetes. *Digital Journal of Ophthalmology*. 2008; 14. <https://goo.gl/qwF8uj>
  20. Raman R, Rani PK, Gnanamoorthy P, Sudhir RR, Kumaramanickavel G, Sharma T. Association of obesity with diabetic retinopathy: Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study (SN-DREAMS Report no. 8). *Acta Diabetol*. 2010; 47: 209-215. <https://goo.gl/85qvHR>
  21. Knudsen LL, Lervang HH, Lundbye-Christensen S, Gorst-Rasmussen A. Non-ophthalmic parameters and clinically significant macular oedema. The North Jutland County Diabetic Retinopathy Study (NCDRS) 2. *Br J Ophthalmol*. 2007; 91: 1593-1595.
  22. Van Leiden HA, Dekker JM, Moll AC, Nijpels G, Heine RJ, Bouter LM, et al. Risk factors for incident retinopathy in a diabetic and nondiabetic population: the Hoorn study. *Arch Ophthalmol*. 2003; 121: 245-251. <https://goo.gl/h7Hfy7>
  23. Laila HM EL-Shazly, Nadia S Ahmad H, Fatma EL-Sebayee. Risk factors association with diabetic retinopathy and maculopathy in Egyptian type 2 diabetics. *Med J Cairo Univ*. 2011; 79: 1-6. <https://goo.gl/NkWLq7>
  24. Looker HC, Knowler WC, Hanson RC. Changes in BMI and weight before



- and after the development of type 2 diabetes. *Diabetes Care*. 2001; 24: 1917-1922. <https://goo.gl/NuyDZt>
25. Varma R, Bressler NM, Doan QV, Gleeson M, Danese M, Bower JK, et al. Prevalence of and risk factors for diabetic macular edema in the United States. *JAMA Ophthalmol*. 2014; 132: 1334-1340. <https://goo.gl/cCpdw3>
26. West KM, Erdreich LS, Stober JA. Absence of a relationship between smoking and diabetic microangiopathy. *Diabetes Care*. 1980; 3: 250-252. <https://goo.gl/Kp2NSf>
27. Klein R, Knudtson MD, Lee KE, Gangnon R, Klein BE. The Wisconsin epidemiologic study of diabetic retinopathy XXII. The twenty-five-year progression of retinopathy in persons with type 1 Diabetes. *Ophthalmology*. 2008; 115: 1859-1868. <https://goo.gl/w3FGoG>
28. Klein R, Knudtson MD, Lee KE, Gangnon R, Klein BE. The wisconsin epidemiologic study of diabetic retinopathy XXIII: the twenty-five-year incidence of macular edema in persons with type 1 diabetes. *Ophthalmology*. 2009; 116: 497-503. <https://goo.gl/TgkFu>
29. Klein R, Klein BE, Moss SE, Cruickshanks KJ. The Wisconsin epidemiologic study of diabetic retinopathy: XVII. The 14-year incidence and progression of diabetic retinopathy and associated risk factors in type 1 diabetes. *Ophthalmology*. 1998; 105: 1801-1815. <https://goo.gl/sp7Ykf>
30. Asensio-Sánchez VM, Gómez-Ramírez V, Morales-Gómez I, Rodríguez-Vaca I. Clinically significant diabetic macular edema: systemic risk factors. *Arch Soc Esp Oftalmol*. 2008; 83: 173-176. <https://goo.gl/trVpC4>
31. Ozer PA, Unlu N, Demir MN, Hazirolan DO, Acar MA, Duman S. Serum lipid profile in diabetic macular edema. *J Diabetes Complications*. 2009; 23: 244-248. <https://goo.gl/4Fk8qE>
32. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy. III. Prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. *Arch Ophthalmol*. 1984; 102: 527-532. <https://goo.gl/KCM4vQ>
33. Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care*. 2012; 35: 556-564. <https://goo.gl/ERXCSe>
34. Benarous R, Sasongko MB, Qureshi S, Fenwick E, Dirani M, Wong TY, et al. Differential association of serum lipids with diabetic retinopathy and diabetic macular edema. *Invest Ophthalmol Vis Sci*. 2011; 52: 7464-7469. <https://goo.gl/CHKZuM>
35. Chew EY, Klein ML, Ferris FL 3rd, Remaley NA, Murphy RP, Chantry K, et al. Association of elevated serum lipid levels with retinal hard exudate in diabetic retinopathy. *Early Treatment Diabetic Retinopathy Study (ETDRS) Report 22*. *Arch Ophthalmol*. 1996; 114: 1079-1084. <https://goo.gl/v1gqY8>
36. Idiculla J, Nithyanandam S, Joseph M, Mohan VA, Vasu U, Sadiq M. Serum lipids and diabetic retinopathy: A cross-sectional study. *Indian J Endocrinol Metab*. 2012; 16: S492-4. <https://goo.gl/PFUQt6>
37. Sasaki M, Ozawa Y, Kurihara T, Kubota S, Yuki K, Noda K, et al. Neurodegenerative influence of oxidative stress in the retina of a murine model of diabetes. *Diabetologia*. 2010; 53: 971-979. <https://goo.gl/b9ntMx>
38. Sasaki M, Kawasaki R, Noonan JE, Wong TY, Lamoureux E, Wang JJ. Quantitative measurement of hard exudates in patients with diabetes and their associations with serum lipid levels. *Invest Ophthalmol Vis Sci*. 2013; 54: 5544-5550. <https://goo.gl/nEk4TR>
39. Rema M, Srivastava BK, Anitha B, Deepa R, Mohan V. Association of serum lipids with diabetic retinopathy in urban South Indians--the Chennai Urban Rural Epidemiology Study (CURES) Eye Study-2. *Diabet Med*. 2006; 23: 1029-1036. <https://goo.gl/cc8bVP>