



CORRELATION OF DIABETIC RETINOPATHY AND SERUM LIPID LEVELS

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ABSTRACT

Background: Diabetic Retinopathy (DR) is a leading cause of preventable blindness worldwide. High serum lipid levels have been projected as risk factor for DR. High serum lipid levels were recognized to cause endothelial dysfunction due to decreased bioavailability of nitric oxide and this endothelial dysfunction was proposed to playing a role in retinal exudate formation in DR. As different studies have found conflicting results of correlation of lipid profile with DR and CSME (Clinically significant Macular Edema), therefore current study was undertaken to document the role of serum lipid levels in diabetic retinopathy.

Objective: To study the correlation between DR and CSME with Serum Lipid Levels.

Methodology: Present study was conducted on 100 diagnosed cases of DR. Fundus showing features of diabetic retinopathy were graded into five classes based on of EDTRS classification: Mild NPDR, Moderate NPDR, Severe NPDR, Very severe NPDR and PDR. Patients with Diabetic Retinopathy were further sub classified into 2 groups based on presence or absence of CSME. Serum triglyceride, HDL cholesterol, LDL cholesterol, total cholesterol, blood sugar level and HbA1C was estimated using an auto analyzer.

Results: Present study has found that there was statistically highly-significant increase in mean \pm SD values of Serum total cholesterol and Serum triglyceride level with increasing the severity of diabetic retinopathy ($p < 0.001$). However, there was statistically non-significant relationship in mean \pm SD values of Serum LDL and Serum HDL cholesterol level with increasing the severity of diabetic retinopathy ($p > 0.05$). There was statistically significant relation between Serum triglyceride and CSME ($p < 0.05$). However, there was statistically non-significant relationship between Serum total cholesterol, Serum LDL, Serum HDL and CSME ($p > 0.05$).

KEYWORDS : Blindness, Diabetic Retinopathy, CSME, NPDR, PDR

INTRODUCTION

Diabetic Retinopathy (DR) is a major microvascular complication of diabetes which leads to irreversible blindness in diabetic patients worldwide⁽¹⁾. According to the WHO (World Health Organisation), India would become one of the major hubs of diabetic population during the next two decades⁽²⁾. A recent systematic review of 35 population-based studies shows that the prevalence of DR is 34.6%, proliferative diabetic retinopathy (PDR) is 7%, diabetic macular edema (DME) is 6.8% and vision-threatening diabetic retinopathy (VTDR) is 10.2% among individuals with diabetes. By extrapolating these results to the global number of diabetics, it is estimated that the number of people with DR would grow from 126.6 million in 2011 to 191 million in 2030⁽³⁾.

High serum lipid levels have been projected as risk factor for DR. High serum lipid levels were recognized to cause endothelial dysfunction due to decreased bioavailability of nitric oxide and this endothelial dysfunction was proposed to playing a role in retinal exudate formation in DR⁽⁴⁾. A hallmark of this disease is alterations in the blood-retinal barrier that is characterized by pericyte loss and endothelial cell junction breakdown⁽⁵⁾. Diabetic Retinopathy, a diabetic microangiopathy is characterized by micro-aneurysms (MAs), capillary non-perfusion, and ischemia within the retina. Capillary non-perfusion impairs the nutrition of the neuroglial tissues in the retinal parenchyma and the resultant hypoxia increases the expression of vascular endothelial growth factor (VEGF), which promotes both angiogenic responses and vascular permeability⁽⁶⁾.

DR might cause several complications, such as Diabetic Macular Ischemia (DMI) and Diabetic Macular Edema (DME). Diabetic Macular Edema (DME) is classified into focal and diffuse types. Focal macular edema is caused by foci of

vascular abnormalities, primarily microaneurysms, which leads to leakage of fluid whereas diffuse macular edema is caused by dilated retinal capillaries in the retina. Diabetic maculopathy is caused by a combination of both VEGF-mediated factors and inflammatory mediators⁽⁶⁾.

As different studies have found conflicting results of correlation of lipid profile and DR, therefore current study has been undertaken to document the role of serum lipid levels in diabetic retinopathy, its relationship with clinically significant macular edema (CSME) and visual acuity in patients of DR

Aim

- To study Diabetic Retinopathy and its association with Serum Lipid Levels

Material and methodology

Cross sectional study done in Rohilkhand Medical college and hospital, Bareilly. Study was done in period between November 2018 – October 2019. Subjects were Randomly selected Diabetic Retinopathy patients consenting to participate

Study tools:

Pre-designed semi-structured questionnaire and laboratory investigations
Sample size: 100 patients

INCLUSION CRITERIA:

- Diagnosed cases of Diabetic Retinopathy
- Age more than 40 years

EXCLUSION CRITERIA:

- Patients in whom dilatation of the pupil was contraindicated e.g. angle-closure glaucoma

- Patients with hazy media which makes visualization of fundus difficult
- Patients on hypolipidemic drugs
- Patients who have been treated earlier with either laser or intravitreal anti-VEGF injections
- Participant Enrollment:
- All the patients were enrolled after their written and informed consent. First, all the patients were asked for basic information on pre-designed semi-structured questionnaire and then they underwent required investigations.
- A detailed ocular examination was undertaken employing slit lamp bio-microscopy for anterior segment
- Best corrected visual acuity of each eye was examined using Snellen's chart
- Detailed fundus examination after mydriasis with 1% tropicamide and 5% phenylephrine eye drops was done using direct and indirect ophthalmoscopy with +20D lens and stereoscopic slit lamp biomicroscopy of disc and macula using +90D lens
- Those fundus showing features of diabetic retinopathy were graded into five classes based on of EDTRS classification:
 1. Mild NPDR
 2. Moderate NPDR
 3. Severe NPDR
 4. Very severe NPDR
 5. PDR
- Patients with Diabetic Retinopathy were further sub classified into 2 groups based on presence or absence of CSME

LABORATORY PROCEDURES

- Fasting and random blood glucose levels were tested
- Fasting serum lipid levels were tested
- HbA1C levels were tested
- Specimen to be collected: 3ml of fasting blood sample was collected to assess lipid profile and blood sugar level.
- Serum triglyceride, HDL cholesterol, LDL cholesterol, total cholesterol, blood sugar level and HbA1C was estimated using an auto analyzer.
- Dyslipidemia was defined using NCEP ATP III guidelines⁽⁷⁾

Observation

A cross-sectional study was conducted in diabetic patients for studying diabetic retinopathy and its association with serum lipid levels at Rohilkhand Medical College and Hospital, Bareilly. Total 100 patients were included in study and evaluated for diabetic retinopathy. Details of patients such as socio-demographic profile, diabetes duration, HbA1c level, serum lipid level, DR staging and visual acuity were collected. All the data entered into Microsoft excel spreadsheet and analyzed with the help of SPSS software version 20.0. Following were the results of the present study In the current study, mean age of the patients was 55.4 ± 9.6 years with minimum 40 years and maximum 88 years. Majority of the patients (38%) were 40 – 50 years old, followed by 51 – 60 years old (36%), 61 – 70 years old (20%) and >70 years old (6%). In the current study, more than half of the patients (57%) were females (n=57) with male – female ratio of 1: 1.3. Among males (n=43), majority of the patients (39.5%) were 40 – 50 years old, followed by 61 – 70 years old (30.2%), 51 – 60 years old (23.3%), and >70 years old (7%). However, among females (n=57), majority of the patients (45.6%) were 51 – 60 years old, followed by 40 – 50 years old (36.8%), 61 – 70 years old (12.3%) and > 70 years old (5.3%). By applying chi-square test the relationship of age and gender was found to be statistically non-significant ($p > 0.05$).

1. Comparison of lipid profile with DR staging

Table 1: Comparison of lipid profile with DR staging

Diabetic Retinopathy staging	Lipid profile			
	Cholesterol (Mean \pm SD)	Triglyceride (Mean \pm SD)	LDL (Mean \pm SD)	HDL (Mean \pm SD)
Mild NPDR	186.9 \pm 43.21	149.4 \pm 52.2	92.1 \pm 27.8	45.6 \pm 12.6
Moderate NPDR	232.4 \pm 34.1	217.7 \pm 72.6	103.9 \pm 29.8	51.5 \pm 14.8
Severe NPDR	259.5 \pm 43.7	348.4 \pm 191.4	96.6 \pm 23.7	49.9 \pm 13.2
Very severe NPDR	280.6 \pm 38.5	249.4 \pm 116.3	106.1 \pm 39.3	48.0 \pm 15.5
PDR	286.5 \pm 43.5	413.7 \pm 241.8	99.5 \pm 32.7	49.0 \pm 17.8
One- way ANOVA	F value	20.599	14.402	0.909
	P value	<0.001	<0.001	0.462

By applying one-way ANOVA test, present study has found there was statistically highly-significant increase in mean \pm SD values of Serum total cholesterol and Serum triglyceride level with increasing the severity of diabetic retinopathy ($p < 0.001$). However, there was statistically non-significant relationship in mean \pm SD values of Serum LDL and Serum HDL cholesterol level with increasing the severity of diabetic retinopathy ($p > 0.05$).

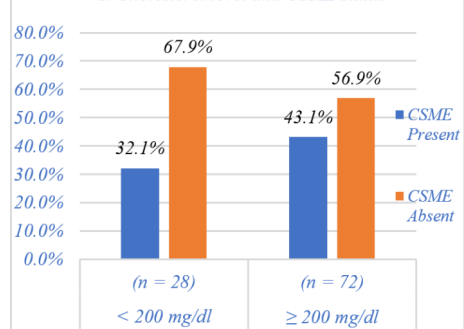
Distribution of all patients based on S. Cholesterol level and CSME status

Table 2: Distribution of all patients based on S. Cholesterol level and CSME status			
CSME status	Serum Cholesterol level (mg/dl)		Total (%)
	<200 (%)	\geq 200 (%)	
Present	9 (32.1)	31 (43.1)	40 (40.0)
Absent	19 (67.9)	41 (56.9)	60 (60.0)
Total	28 (100.0)	72 (100.0)	100 (100.0)

Chi square test = 1.00, df = 1, p value = 0.317

Among patients with Serum cholesterol level <200 mg/dl (n=28), 32.1% patients had presence of CSME and 67.9% had absence of CSME. While among patients with Serum cholesterol level \geq 200 mg/dl (n=72), 43.1% had presence of CSME and 56.9% had absence of CSME. By applying chi-square test, the relationship of S. Cholesterol level and CSME status was statistically non-significant ($p > 0.05$).

Chart 1: Distribution of all patients based on S. Cholesterol level and CSME status

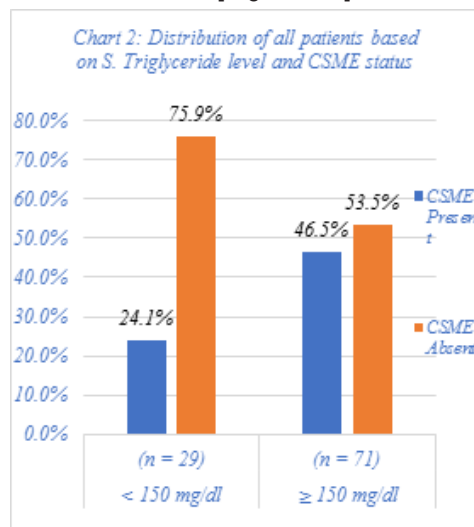


Distribution of all patients based on S. Triglyceride level and CSME status

Table 3: Distribution of all patients based on S. Triglyceride level and CSME status			
CSME status	Serum Triglyceride level (mg/dl)		Total (%)
	<150 (%)	\geq 150 (%)	
Present	7 (24.1)	33 (46.5)	40 (40.0)
Absent	22 (75.9)	38 (53.5)	60 (60.0)
Total	29 (100.0)	71 (100.0)	100 (100.0)

Chi square test = 4.282, df = 1, p value = 0.039

Among patients with Serum Triglyceride level <150 mg/dl (n=29), 24.1% patients had presence of CSME and 75.9% had absence of CSME. While among patients with Serum Triglyceride level \geq 150 mg/dl (n=71), 46.5% had presence of CSME and 53.5% had absence of CSME. By applying chi-square test, the relationship of Serum Triglyceride level and CSME status was statistically significant ($p < 0.05$).



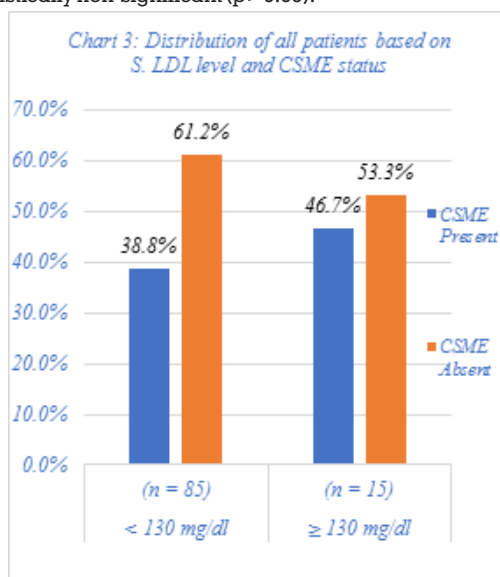
Distribution of all patients based on S. LDL level and CSME status

Table 4: Distribution of all patients based on S. LDL level and CSME status

CSME status	Serum LDL level (mg/dl)		Total (%)
	<130 (%)	\geq 130 (%)	
Present	33 (38.8)	07 (46.7)	40 (40.0)
Absent	52 (61.2)	08 (53.3)	60 (60.0)
Total	85 (100.0)	15 (100.0)	100 (100.0)

Chi square test = 0.327, df = 1, p value = 0.568

Among patients with Serum LDL level <130 mg/dl (n=85), 38.8% had presence of CSME and 61.2% had absence of CSME. While among patients with Serum LDL level \geq 130 mg/dl (n=15), 46.7% had presence of CSME and 53.3% had absence of CSME. By applying chi square test the relationship of Serum LDL level and CSME status was found to be statistically non-significant ($p > 0.05$).



Distribution of all patients based on S. HDL level and CSME status

Table 5: Distribution of all patients based on S. HDL level and CSME status

CSME status	Serum HDL level (mg/dl)		Total (%)
	<40 (%)	\geq 40 (%)	
Present	12 (48.0)	28 (37.3)	40 (40.0)
Absent	13 (52.0)	47 (62.7)	60 (60.0)
Total	25 (100.0)	75 (100.0)	100 (100.0)

Chi square test = 0.889, df = 1, p value = 0.346

Among patients with Serum HDL level <40 mg/dl (n=25), 48% had presence of CSME and 52% had absence of CSME. While among patients with Serum HDL level \geq 40 mg/dl (n=75), 37.3% had presence of CSME and 62.7% had absence of CSME. By applying chi-square test the relationship of Serum HDL level and CSME status was found to be statistically non-significant ($p > 0.05$).

DISCUSSION

Diabetic retinopathy (DR) remains a leading cause of visual disability and blindness and major microvascular complication of diabetes and is frequently accompany by lipid exudation. DR relationship with serum lipid levels was studied in many studies. Some studies have shown positive relationship between serum cholesterol and low-density lipoprotein levels and retinal hard exudates. While other studies have shown serum triglyceride levels as being important in the development of retinopathy

In the current study, 40% patients had CSME, while remaining 60% patients did not have CSME. A study by Hedge et al⁽⁸⁾ had found that 30% patients had CSME, among them 56.7% patients had mild NPDR, 30% had moderate NPDR, 6.7% had severe NPDR, 3.3% had very severe NPDR and 3.3% had PDR.

In the present study, among patients with S. cholesterol level <200 mg/dl, 32.1% patients had presence of CSME, while among patients with S. cholesterol level \geq 200 mg/dl, 43.1% had presence of CSME. This relationship of S. Cholesterol level and CSME status was statistically non-significant ($p > 0.05$).

In Hedge et al⁽⁸⁾ study significantly higher level of serum cholesterol was found among CSME patients (239.2 ± 25.5 mg/dl) compared to without CSME patients (205 ± 53.2 mg/dl, $p < 0.05$). Benarous et al⁽⁹⁾ had found significantly higher level of serum Cholesterol level in CSME patients (5.2 ± 1.4 mmol/L) compared to diabetic patients without CSME (4.6 ± 1.2 mmol/L, $p < 0.05$).

In the current study, among patients with S. TG level <150 mg/dl, 24.1% had presence of CSME, while among patients with TG level \geq 150 mg/dl, 46.5% had presence of CSME. This relationship of Serum Triglyceride level and CSME status was statistically significant ($p < 0.05$). A study by Hedge et al⁽⁸⁾ had found higher level of serum triglyceride among CSME patients (249.1 ± 70.6 mg/dl) compared to without CSME patients (234.5 ± 64.7 mg/dl). Benarous et al⁽⁹⁾ had found non-significantly higher level of serum Triglyceride level in CSME patients (2.1 ± 1.8 mmol/L) compared to diabetic patients without CSME (1.8 ± 1.1 mmol/L, $p > 0.05$).

In this study, among patients with S LDL level <130 mg/dl, 38.8% had presence of CSME, while among patients with LDL level \geq 130 mg/dl, 46.7% had presence of CSME. This relationship of Serum LDL level and CSME status was statistically non-significant ($p > 0.05$). A study by Hedge et al⁽⁸⁾ had found higher level of serum LDL among CSME patients (99.3 ± 34.3 mg/dl) compared to without CSME patients (95.6 ± 23.4 mg/dl). Benarous et al⁽⁹⁾ had found significantly higher level of serum LDL level in CSME patients (2.9 ± 1.2 mmol/L) compared to diabetic patients without CSME (2.4 ± 1 mmol/L, $p < 0.05$).

In the current study, among patients with S. HDL level <40 mg/dl, 48% had presence of CSME, while among patients with HDL level \geq 40 mg/dl, 37.3% had presence of CSME. This relationship of Serum HDL level and CSME status was statistically non-significant ($p > 0.05$). A study by Hedge et al⁽⁸⁾ had found higher level of serum HDL among CSME patients (50.4 ± 9.1 mg/dl) compared to patients without CSME (45.3 ± 8.7 mg/dl). Benarous et al⁽⁹⁾ had found almost similar level of serum HDL level in CSME patients (1.3 ± 0.5 mmol/L) compared to diabetic patients without CSME (1.3 ± 0.4 mmol/L).

Limitations of the study

- Every diabetic patient should be routinely examined for Retinal changes and Lipid profile. As this is a cross-sectional study strict follow up was not followed in the study.
- This study also done in a single hospital set up, so generalization of study findings will be doubtful.

CONCLUSION

The current cross-sectional study was conducted in diabetic patients has found relationship of DR with dyslipidemia. Adults at fifth decade and female gender were commonly found with diabetic retinopathy in our study. The relationship of serum cholesterol level, serum LDL and serum HDL level with CSME status was statistically non-significant, while serum triglyceride level had statistically significant relationship with CSME status.

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