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Association of Diabetic Retinopathy and Lipid Profile in Diabetic Patients in Mathura District

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Abstract

Background: It is estimated that diabetes mellitus affects 4 percent of the world's population, almost half of whom have some degree of diabetic retinopathy at any given time. Elevated serum lipid levels are associated with an increased risk of retinal hard exudate in persons with diabetic retinopathy. Therefore the current study was undertaken to determine the association of serum lipid profile with diabetic retinopathy and its severity. **Subjects and Methods:** One hundred fifty diabetic patients, out of these, 75 diabetic patients with retinopathy served as the study group I and 75 diabetic patients with no retinopathy formed group II (control group). Simultaneously, 75 age and sex matched healthy subjects were also studied as controls (group III). Serum total cholesterol, serum triglyceride, serum low density lipoprotein and serum high density lipoprotein were measured by using enzymatic method and autoanylyser. Fasting blood sugar and post prandial blood sugar were estimated by using GOD POD method. **Results:** Most of the patients in Group I had some degree of visual impairment. However there was no statistical significance with $p > 0.05$. The mean value of total cholesterol was higher in both group I and group II with value being higher in group1 (229.09mg/dl) as compared to group II (215.32mg/dl). Triglyceride levels also followed the similar trend with group I having mean value of 238.95mg/dl and group II having 179.93 mg/dl. But only total cholesterol value had statistical significance $p < 0.05$. **Conclusion:** The present study demonstrated statistically significant correlation between diabetic retinopathy and hypercholesterolemia. Increased cholesterol level was significantly associated with the occurrence of all grades of retinopathy especially severe NPDR, very severe NPDR and PDR. No correlation was found between lipid profile and visual acuity. These data suggest that hyperlipidaemia should be promptly treated in diabetic patients.

Keywords: Diabetes mellitus, Diabetic retinopathy, Hyperlipidaemia.

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Introduction

It is estimated that diabetes mellitus affects 4 percent of the world's population, almost half of whom have some degree of diabetic retinopathy at any given time.[1,2] According to WHO, diabetic retinopathy is responsible for 3-7% of the total blindness in Asia.[3] In India the prevalence of diabetic retinopathy in general population is 3.5%. and the prevalence of diabetic retinopathy in the population with diabetes mellitus is 18.0%.[4] In a population-based study in South India, diabetic retinopathy was detected in 1.78% of the diabetic patients screened.[5,6] According to the World Diabetes Atlas, India is projected to have around 51 million people with diabetes. 7 There is a growing concern for Asia being the region for diabetic epidemic.[7,8]

Diabetic retinopathy is a very common, potentially preventable, long-term, microvascular complication of diabetes mellitus and a leading cause of visual disability and blindness. 9 While there are multiple risk factors which have been associated with the development and progression of diabetic retinopathy. However, dyslipidemia, microalbuminuria, BMI and smoking are some of the factors whose role as predictors of diabetic retinopathy is not well established.[10-12]

Diabetic retinopathy is frequently accompanied by lipid exudation.[13] Elevated serum lipid levels are associated with an increased risk of retinal hard exudate in persons with diabetic retinopathy.[14] The elevated lipid levels are also associated with endothelial dysfunction, which appears to play an important role in the pathogenesis of diabetic retinopathy, particularly in relation to the breakdown of blood-retinal barrier.

The association between serum lipid levels and diabetic retinopathy has been investigated in few studies. Some studies show a positive relationship between serum cholesterol and low-density lipoprotein levels and retinal hard exudation. Other studies show serum triglyceride levels as being important in the progression of retinopathy. Certain other studies show no relationship between serum lipid levels and diabetic retinopathy.[15]

The conflicting reports in the literature regarding the association between serum lipid levels and diabetic retinopathy and the paucity of studies relative to the existing case load warrants this study. Therefore the current study

was undertaken to determine the association of serum lipid profile with diabetic retinopathy and its severity.

Subjects and Methods

This study was carried out in the department of Ophthalmology, department of Ophthalmology at KD Medical College, Mathura, from March 2018 to August 2018.

One hundred fifty (150) diabetic patients, out of these, 75 diabetic patients with retinopathy served as the study group I and 75 diabetic patients with no retinopathy formed group II (control group). Simultaneously, 75 age and sex matched healthy subjects were also studied as controls (group III).

Patients with age of more than 40 years with duration of diabetes more than 5 years were included in the study. Patients with significant hazy media which impairs visualization of the fundus and patients with pupillary abnormalities which prevent adequate dilatation for fundus visualisation or patients on hypolipidemic drugs were excluded from the study.

Data was collected using a piloted performa meeting the objectives of the study after an informed consent. A detailed history of each patient was obtained regarding the age, duration of diabetes, the anti-diabetic treatment they were on and any associated illness. The duration of diabetes was reckoned from the time of diagnosis.

Ophthalmic evaluation

All the study subjects had a thorough ophthalmic evaluation which included slit-lamp biomicroscopic examination of anterior segment, best corrected visual acuity (BCVA) of each eye recorded using Snellen chart, detailed fundus examination after mydriasis with 1% tropicamide and 5% phenylephrine eye drops using direct ophthalmoscopy, indirect ophthalmoscopy with +20D lens and stereoscopic slit lamp biomicroscopy of the disc and macula using + 78D Volk lens. All cases were examined for the presence or absence of diabetic retinopathy. Those cases with fundus showing features of diabetic retinopathy were graded into five classes on the basis of ETDRS classification.[16]

Biochemical Parameters

5ml of fasting blood sample was collected under asepsis from the anterior cubital vein using disposable syringe to assess lipid profile and blood sugar level. Postprandial blood sugar level estimation was also done. The following tests were carried out by enzymatic method using autoanylyser in the Central Laboratory with the help of the department of Biochemistry

Serum total cholesterol, serum triglyceride, serum low density lipoprotein and serum high density lipoprotein were measured by using enzymatic method 17 and autoanylyser. Fasting blood sugar and post prandial blood sugar were estimated by using GOD POD method.[17]

Statistical analysis

All group data were presented as frequency distribution (proportion) and the average value was presented as means ± SD for the normal distribution data. ANOVA and Chi-square were used to interpret the results of the study. The p value 0.05 was considered as significant. Data was analysed by using SPSS for windows software (version 16.0).

Results

Most of the patients had cataract of different grades and types. The percentage of subjects with normal anterior segment in group I, II and III were 20.0%, 28.0% and 22.66%. There was no significant difference in anterior segment features in different groups. [Table 1]

Table 1: Anterior segment features in different groups

Anterior segment	Group I	Group II	Group III	Total
Normal	15(20%)	21(28%)	17 (22.66%)	53 (23.55%)
Cataract	40(53.33 %)	44 (58.66%)	44 (58.66%0	128 (56.88%)
Pseudophakia	20 (26.66%)	10 (13.33%)	14 (18.66%)	44 (19.55%)

Most of the patients in Group I had some degree of visual impairment. However there was no statistical significance with p >0.05. [Table 2]

Table 2: Visual acuity distribution in each group.

Visual Acuity	Group I	Group II	Group III	Total
6/6	10 (13%)	49 (65%)	52 (69.33%)	111 (49.33%)
6/9-6/12	29 (38%)	11 (14%)	7 (9.33%)	47 (20.88%)
6/18-6/36	33 (44%)	13 (17%)	14 (18.67)	60 (26.66%)
≤6/60	3 (4%)	1 (1.3%)	2 (2.6%)	6 (2.6%)

In the group I, Mild NPDR retinopathy was present in 44 % of patients, moderate NPDR in 29 % of patients, severe NPDR retinopathy in 10% of patients, very severe NPDR in 5% and proliferative retinopathy in 7% of patients. Among these 22 patients (29.33%) had CSME. [Table 3]

Table 3: Distribution of severity of diabetic retinopathy and presence of CSME

Diabetic retinopathy grade	Frequency	CSME
Mild NPDR	33 (44%)	11 (50%)
Moderate NPDR	22 (29%)	7 (31.81%)
Severe NPDR	8 (10%)	2(11%)
Very Severe NPDR	5 (6.66%)	1(5.5%)
PDR	7 (9.33%)	1(5.5%)
Total	75 (100%)	22 (100%)

It is evident from fig 1 that the mean value of total cholesterol was higher in both group I and group II with value being higher in group1 (229.09mg/dl) as compared to group II (215.32mg/dl). Triglyceride levels also followed the similar trend with group I having mean value of 238.95mg/dl and group II having 179.93 mg/dl. But only total cholesterol value had statistical significance p < 0.05.

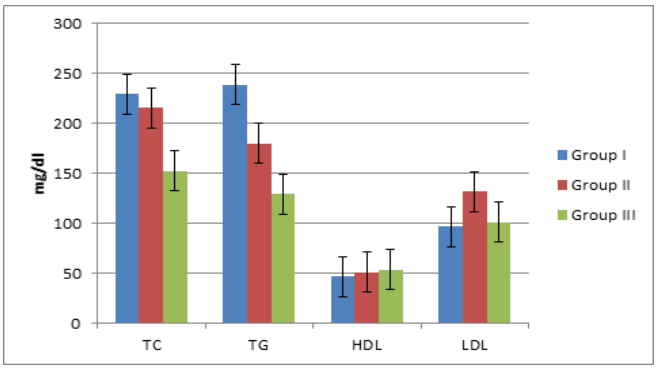

Figure 1: Mean values of lipid subfraction in each group.

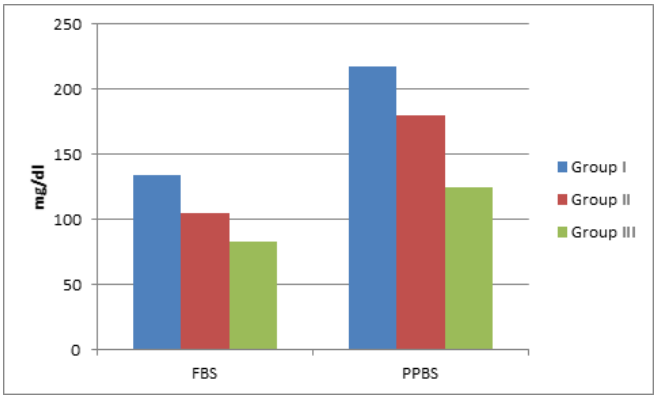

Figure 2: Mean values of blood sugar level in each group.

[Figure 2] shows that FBS was significantly high in group I compare to group II and III. Similarly, PPBS level was significantly high in group II and III compare to diabetic retinopathy group I.

In group I, most of the patients, in all severity groups had raised total cholesterol (72%) and raised triglyceride levels (92%). However, only the rise in total cholesterol was statistically significant ($p < 0.05$). [Table 4]

Table 4: Lipid profile and severity of diabetic retinopathy.

Lipid profile	Category	Diabetic Retinopathy					Total	P value
		Mild NPDR	Moderate NPDR	Severe NPDR	Very severe NPDR	PDR		
TC	High	25(75.75%)	12 (54.54%)	7 (87.5%)	4(80%)	6(88.9%)	54	<0.05
	Normal	8(24.24%)	10(45.45%)	1(12.5%)	1 (20%)	1 (14.2%)	21	
TG	High	30 (90%)	20(90.9%)	7 (87.5%)	5 (100%)	7 (100%)	69	>0.05
	Normal	3 (10%)	2 (9.09%)	1(12.5%)	0 (0%)	0 (0%)	6	
HDL	Low	3 (10%)	2 (9.09%)	2 (25%)	2 (40%)	3(42.5%)	12	>0.05
	Normal	30 (90%)	20(90.9%)	6 (75%)	3 (60%)	4(47.5%)	63	
LDL	High	1 (3.03%)	3 (12.1%)	1(12.5%)	1 (20%)	0 (0%)	6	>0.05
	Normal	32(96.9%)	19(86.36%)	7 (87.5%)	4(80%)	7 (100%)	69	

Table 5: Mean values of the lipid subfractions in subjects categorized according to severity of diabetic retinopathy

Lipid profile	Mild NPDR	Moderate NPDR	Severe NPDR	Very severe NPDR	PDR	Group II
TC	215.6± 30.6	221.3± 49.4	235.0± 39.7	234.4± 44.7	254.67± 35.6	229.0± 30.0
TG	241.1± 16.9	232.4± 18.8	245.7± 22.2	231.0± 26.7	243.0±1 3.6	179.9± 20.4
HDL	48.7±9. 1	47.5±4. 9	45.72± 10.8	40.4±7. 8	42.56±1 0.8	51.3±1 3.7
LDL	92.1±1 8.9	106.03 ±20	80.45± 22.3	97.8±1 3.7	166.22± 27.0	131.9± 16.3

[Table 5] shows serum total cholesterol concentrations were higher in subjects with severe NPDR, very severe NPDR and PDR compared with subjects without DR ($p < 0.05$).

Discussion

Hyperglycemia and dyslipidemia are two major metabolic disorders seen in patients with diabetes mellitus. Despite considerable progress in understanding of hyperglycemia-induced disease over the past decade, the link between diabetic metabolic disorders and retinopathy still eludes us. 18 This study aimed to determine the relationship between serum lipid profile and the severity of diabetic retinopathy in type 2 diabetes patients.

The present study showed statistically significant correlation between diabetic retinopathy and raised total cholesterol level ($p < 0.05$). Increased cholesterol level was significantly associated with the occurrence of all grades of retinopathy. The mean value of total cholesterol in group I was higher comparing to group II and group III. The mean triglyceride level was also higher in group I as compared to group II and group III. However, this correlation was not statistically significant ($p > 0.05$). These findings are very similar to the previous study of Al-Bdour et al.[11] as they observed positive relation between diabetic retinopathy and hypercholesterolemia ($p < 0.05$). Similarly, Larsson et al,[19] also found significant correlation between higher levels of serum total cholesterol and retinopathy. Alike, Rema et al,[20] recorded the association of serum lipids with diabetic retinopathy in urban South Indians. The serum triglyceride ($p= 0.001$) levels and total cholesterol ($P= 0.014$) were higher in patients with diabetic retinopathy as compared to those without diabetic retinopathy. This association was maintained even after adjusting for age, as age by itself is a significant risk factor for hyperlipidemia. Similar results were obtained by Haddad et al.[21] In the present study although both total cholesterol and triglyceride levels were

elevated in group I as compared to group II and group III, only hypercholesterolemia was statistically significant.

The Hoorn Study, a large population based study to determine the potential risk factors for retinopathy in diabetic and nondiabetic individuals showed that retinopathy, and hard exudates in retinopathy in particular, are related to elevated serum total and LDL cholesterol levels.[22] Agarwal et al,[23] and Sachdev et al,[24] also observed raised level of total and LDL cholesterol and reduced level of HDL/LDL cholesterol ratio in patients with diabetic retinopathy. These results are partly in concordance with the present study as hypercholesterolemia but not hypertriglyceridemia was found to be a risk factor for retinopathy in the current study.

In the present study serum total cholesterol concentrations were higher in subjects with severe NPDR, very severe NPDR and PDR compared with subjects without DR ($p< 0.05$). Except for this parameter, there were no significant differences in the lipid concentrations with the severity of DR. Elevated triglyceride were found to be a significant risk factor for moderate and severe non-proliferative retinopathy and proliferative retinopathy even after adjustment for age, duration of diabetes, HbA1c, and albumin excretion rate in EURODIAB study.[25] In CURES eye study serum cholesterol concentrations were higher in subjects with moderate NPDR compared with subjects without DR ($p <0.05$). Triglyceride concentrations were higher in those with mild NPDR compared with those without DR ($p <0.05$).[26]

The present study found a significant association between hypercholesteremia and CSME ($p < 0.05$). This was in accordance with the study by Al-Bdour et al,[11] who found significant association between the development of diabetic maculopathy and hypercholesteremia. Similarly, higher total cholesterol level was positively associated with presence of CSME, in a cross-sectional analysis of participants with diabetes in the Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR).[26] Alike, CURES eye study also showed an association of Diabetic macular edema in type 2 diabetic subjects with increased cholesterol level.[20] In a prospective analysis of ETDRS data, the development of CSME was 50% faster among subjects with elevated baseline levels of total cholesterol and triglycerides.[27] Ucgun et al also showed a positive relationship between CSME and hypercholesteremia.[28]

The present study did not show any trend of increase in the severity of diabetic retinopathy with the increasing levels of different serum lipid subfractions. Larsson et al,[19] showed a linear relationship of serum cholesterol levels with severity of diabetic retinopathy. WESDR study also found that there was a significant trend for increasing severity of diabetic retinopathy with increasing cholesterol.[20]

Most of the diabetics in the present study had poor glycemic control. Hyperglycemia is also associated with dyslipidemia, specifically increased levels of total cholesterol and triglycerides, a slight elevation of LDL, but generally little if any change in HDL. Consequently hyperglycemia may be an important confounding factor in the study with respect to both diabetic retinopathy and hypercholesterolemia.[16,19,22]

Conclusion

The present study demonstrated statistically significant correlation between diabetic retinopathy and hypercholesterolemia. Increased cholesterol level was significantly associated with the occurrence of all grades of retinopathy especially severe NPDR, very severe NPDR and PDR. It also showed that hypercholesterolemia is significantly associated with CSME. No correlation was found between lipid profile and visual acuity. These data suggest that hyperlipidaemia should be promptly treated in diabetic patients. However, further studies are required to establish the causal relationship between dyslipidemia and diabetic retinopathy.

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