

A Study of Lipid Profile in Diabetic Retinopathy in Type 2 Diabetic Patients

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Abstract: Aim of this study is to establish role of hyperlipidemia in diabetic retinopathy. **Method:** A cross sectional study with 200 patients (Group 1 with 100 diabetic patients with diabetic retinopathy, Group 2 with 100 diabetic patients without retinopathy) of type 2 diabetes mellitus for more than 10 years (diabetic age) were included in the study with 100 (Group 3) normal age and sex matched controls. All subjects were investigated for total lipid profile, blood sugar levels along with complete ophthalmic assessment. **Results:** Mean values of total cholesterol in Group 1, Group 2, and Group 3 were 229.86 ± 30.25 mg/dl, 218.15 ± 49.19 mg/dl and 152.55 ± 26.53 mg/dl respectively. **Conclusion:** This study suggests that diabetic retinopathy patients have high serum lipid levels compared to diabetic patients without retinopathy.

Keywords: Hyperlipidemia, Diabetic Retinopathy

1. Introduction

Diabetes Mellitus (DM) is leading cause of increasing mortality and morbidity due to fatal complications. Chronic complications of DM include macrovascular manifestations like coronary artery disease, cerebrovascular disease and peripheral vascular disease. Microvascular complications like retinopathy, nephropathy and neuropathy.

Diabetic retinopathy (DR) is a vascular disorder affecting the microvasculature of the retina. Progressive microvascular ischemia with vascular leak occurring within the ischemic retina or, in more severe cases, new vessel proliferation and vitreous hemorrhage, are the main features of diabetic retinopathy. Diabetic retinopathy has become the leading cause of blindness in both developed and developing countries.^[1,2,3]

Diabetic retinopathy is frequently accompanied by lipid exudation^[4]. There have been several conflicting reports in relation to role of hyperlipidemia in development of diabetic retinopathy. Studies are also going on to assess the efficacy of lipid lowering drugs in progression of diabetic retinopathy so as to decrease the need for interventions to decrease ocular morbidity.

In this study, role of hyperlipidemia in diabetic retinopathy is assessed.

2. Literature Survey

Even though numerous studies have explored the associations between DR and lipid abnormalities, the results obtained remain inconsistent in contrast to other definite risk factors for DR such as blood sugar and blood pressure control. In Triglycerides, only 2 studies show an association with DR^{[5], [6]}. With regard to Low Density Lipoprotein (LDL), there are 3 studies^{[7], [8], [9]} showing a significant association with DR and 8 studies demonstrating an association with Diabetic Macular Edema (DME)^{[13], [6]} or retinal hard exudates^{[10], [11], [12], [13], [14], [15]}. There is no single lipid measure consistently found to be associated with DR.

However, more evidence has been obtained that links total cholesterol or LDL with the presence of hard exudates^{[16], [17], [11], [12], [13], [14]} since retinal exudates are often due to leakage of lipid from abnormal retinal capillaries and are usually associated with DME.

3. Material and Methods

A total of 300 subjects, both males and females, attending department of ophthalmology at South central Railway hospital, Telangana, India were included in this cross sectional observational study. Subjects were allocated to one of the following three groups:

Group I: 100 Diabetic patients with different stages of retinopathy

Group II: 100 Diabetic patients without retinopathy

Group III: 100 Non-diabetics as controls

A detailed ophthalmic assessment was done in each patient including complete ophthalmic and systemic history (the duration of diabetes), followed by a complete ocular examination including determination of visual acuity, intraocular pressure, fundus examination by direct and indirect ophthalmoscope. Based on the ETDRS criteria, patients will be graded according to their severity of retinopathy to corresponding lipid levels.

5ml of fasting blood sample was collected with sterile measures from the anterior cubital vein using disposable syringe to assess lipid profile and blood sugar level. Postprandial blood sugar (2 hours after meal) level estimation was also done. The following tests were carried out by enzymatic method using auto analyzer in the Central Laboratory with the help of the department of Biochemistry, South Central Railway Hospital, Telangana, India.

- 1) Serum fasting total cholesterol
- 2) Serum fasting triglyceride
- 3) Serum fasting low density lipoprotein
- 4) Serum fasting high density lipoprotein
- 5) Fasting Blood Sugar and Postprandial blood sugar.
- 6) Hb1Ac

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Dyslipidemia was defined using NCEP ATP III guidelines^[18] as:

- Total cholesterol \geq 200 mg/dl
- HDL cholesterol $<$ 40 mg/dl
- LDL cholesterol \geq 100 mg/dl
- Triglycerides \geq 150 mg/dl

Statistical Analysis

The data collected was entered into Microsoft excel spreadsheet and analyzed using IBM SPSS Statistics, Version 22 (Armonk, NY: IBM Corp). Descriptive data were presented in the form of mean, median, standard deviation and quartiles for continuous variables. Comparisons of the categorical variables between the study groups were performed using the chi square test and fishers test. The continuous variables following normal distribution were compared between the study groups using Independent sample test and Analysis of variance (ANOVA) with Tukey Post hoc test. The continuous variables not following normal distribution were compared between the study groups using Kruskal wallis test followed by Mann whitney U test. P value $<$ 0.05 was considered as statistically significant.

4. Results

A total of 300 subjects were studied.

- Subjects in all the three groupshad a near equal sex distribution with only a slight male predominance. The Male to Female ratio [M:F] was 54 : 46. However the difference with respect to the sex distribution was not statistically significant in the current study (p =.99).
- The Mean age in Group1, Group 2 and Group3 were 65.48 ± 6.705 , 64.57 ± 6.456 and 64.66 ± 6.889 years respectively. The study showed slightly higher mean age, in Group 1 (DR) compared to other but it is not statistically significant.
- The mean duration of diabetes is 13.38 years and 10.67 years in Group 1 and 2 respectively which is statistically significant(p $<$ 0.001).
- The mean visual acuity in the three group is Right eye in Log mar unit 0.45, 0.18, 0.19 and in Left eye 0.43,0.18,0.25 respectively.The present study showed the mean visual acuity in (RE)(Table 1) and (LE) (Table 2) in Log MAR units have found to be higher in Group 1 compared to other groups and a statistically significant difference is noted (p= $<$ 0.001).

Table 1: Comparison of Visual acuity in Right eye (RE) inLog mar units amongst different groups

Group	BCVA(RE)		Kruskall wallis test		Mann whitney U test			
	N=100	Mean (SD)	Median (Q1 – Q3)	Chi square value	p-value	Group 1 vs Group 2	Group 1 vs Group 3	Group 2 vs Group 3
1		0.45 (0.29)	0.50 (0.30- 0.60)	57.19	$<$ 0.001*	$<$ 0.001*	$<$ 0.001*	0.51(NS)
2		0.18 (0.28)	0(0 - 0.30)					
3		0.19 (0.26)	0(0 - 0.45)					

*P $<$ 0.05 Statistically significant

p $>$ 0.05 non significant, NS

BCVA Best corrected visual acuity

Log MAR-Logarithm of Minimum Angle of Resolution

Table 2: Comparison of Visual acuity in Left eye (LE) inLog mar units amongst different groups

Group	BCVA(LE)		Kruskall wallis test		Mann whitney U test			
	N=100	Mean (SD)	Median (Q1 – Q3)	Chi square value	p-value	Group 1 vs Group 2	Group 1 vs Group 3	Group 2 vs Group 3
1		0.43 (0.28)	0.50 (0.18- 0.60)	41.47	$<$ 0.001*	$<$ 0.001*	$<$ 0.001*	0.07(NS)
2		0.18 (0.27)	0 (0 - 0.30)					
3		0.25 (0.29)	0 (0 - 0.50)					

*P $<$ 0.05 statistically significant

p $>$ 0.05 non significant, NS

- The present study showed statistically significant difference between serum lipid levels in Group 1, Group 2 & Group 3. The mean values of total cholesterol in Group 1, Group 2, and Group 3 were 229.86 ± 30.25 mg/dl, 218.15 ± 49.19 mg/dl and 152.55 ± 26.53 mg/dl respectively with statistically significant difference (p= $<$ 0.001).
- The mean triglyceride level was also higher in Group 1 as compared to Group 2 and Group 3 with mean values 240.08 ± 66.35 mg/dl, 179.93 ± 20.49 mg/dl and 129.11 ± 15.68 mg/dl respectively, with a statistically significant difference (p $<$ 0.001).
- The values of HDL in Group 1, Group 2 and Group 3 were 47.75 ± 9.17 mg/dl, 51.33 ± 13.67 mg/dl, 53.38 ± 7.98 mg/dl respectively and a statistically significant difference was noted (p=0.001).
- The values of LDL in Group 1, Group2 and Group3 were 131.93 ± 16.39 mg/dl, 100.49 ± 18.83 mg/dl and 98.19 ± 26.34 mg/dl respectively. A statistically significant difference (p= $<$ 0.001) was observed.
- In the present study most of the subjects in the Group 1 had poor glycemc control, suggested by raised FBS, PPBS and HbA1c (p= $<$ 0.001) levels. The mean values of FBS, PPBS (short term glycemc marker) and HbA1c (long term glycemc control marker) were higher in Group 1 than in Group 2.

Table 3: Distribution of study parameters among the study groups

Group	N=100	Mean	Std. Deviation	ANOVA
				P-value
TCL	1	229.86	30.25	$<$ 0.001*
	2	218.15	49.19	
	3	152.55	26.53	
TG	1	240.08	66.35	$<$ 0.001*
	2	179.93	20.49	
	3	129.11	15.68	
HDL	1	47.75	9.17	0.001*
	2	51.33	13.76	
	3	53.38	7.98	
LDL	1	131.93	16.39	$<$ 0.001*

	2	100.49	18.83	
	3	98.19	26.34	
FBS	1	134.66	56.32	<0.001*
	2	103.62	34.13	
	3	83.08	12.66	
PPBS	1	218.4	87.77	<0.001*
	2	178.83	75.8	
	3	124.88	12.17	
HbA1c	1	8.9	0.54	<0.001*
	2	7.34	0.41	
	3	5.36	0.24	

*p<0.05 statistically significant

p>0.05 non significant, NS

- TCL Total cholesterol
- TG Triglycerides
- HDL High density lipoprotein
- LDL Low density lipoprotein
- FBS Fasting blood sugar
- PPBS Post prandial blood sugar
- HbA1c Glycated hemoglobin

5. Discussion

In the present study, there was nearly equal distribution of male and female in all the three groups. The mean age in group1, group 2 and group3 were 65.48±6.705, 64.57±6.456 and 64.66 ± 6.889 years respectively. The relationship of retinopathy with age was found in many other epidemiological studies, this study also showed slightly higher mean age, in group 1(DR) compared to other but it was not statistically significant. Dondana et al^[19] & CURES Eye Study^[6] had found significant correlation between the patient age and diabetic retinopathy.

The mean duration of diabetic age in group 1 and group 2 were 13.38±4.29 and 10.67±1.05years respectively. Longer duration was associated with a higher risk of DR(p<0.001). It is in accordance with previously published reports WESDR^[10] ; UKPDS^[20] ;DCCT^[13]. Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) also found that risk of retinopathy was directly related to the duration of diabetes^[10]. The CURES Eye study had found that for every five years increase in duration of diabetes, the risk of DR was increased by 1.89 times^[6].

The mean visual acuity in (RE) and (LE) in Log mar units were found to be higher in group 1 compared to other groups and a statistically significant difference was noted(p=<0.001). ETDRS study had found that elevated serum cholesterol at baseline increased the risk of visual loss by 50%.^[21]

The mean values of total cholesterol in group1, group2, and group 3 were 229.86±30.25mg/dl, 218.15±49.19 mg/dl and 152.55± 26.53mg/dl respectively with statistically significant difference (p=<0.001). Findings of the present study were in concordance with the investigation done by Al-Bdour et al^[22] while investigating the risk factors associated with diabetic retinopathy. Early Treatment Diabetic Retinopathy Study (ETDRS) showed that patients with elevated total serum cholesterol levels were twice as likely to have diabetic retinopathy as compared to patients with normal levels^[21]. In the CHS study^[7] and Hoorn

study^[12], mean plasma total cholesterol level was higher in patients with diabetes than in patients without diabetes. The patients who presented with diabetic retinopathy had significantly higher values of total cholesterol (P= 0.014) in CURES study^[6] and study from Romania^[9].

The values of LDL in group1 ,group2 and group3were 131.93 ±16.39mg/dl ,100.49 ±18.83mg/dl, 98.19 ± 26.34 mg/dl respectively and a statistically significant difference (p=<0.001) was observed. Early Treatment Diabetic Retinopathy Study (ETDRS) showed that patients with elevated serum low-density lipoprotein cholesterol levels were twice as likely to have diabetic retinopathy compared to patients with normal levels^[21]. The CHS study^[7], Hoorn study^[12], SMES study^[8] and a study from Romania^[9] also showed higher LDL values in patients with diabetic retinopathy. Sachdev et al^[15] also observed raised level of total and LDL cholesterol and reduced level of HDL/LDL cholesterol ratio in patients with diabetic retinopathy.

In the present study most of the subjects in the group 1 had poor glycemic control, suggested by raised FBS,PPBS and HbA1c(p=<0.001) levels. The mean values of FBS, PPBS(short term glycemic marker) and HbA1c (long term glycemic control marker) were higher in group 1 than in group 2, reinforcing the fact that the development and progression of DR is influenced by the level of blood glucose. Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) also found that risk of retinopathy is related to the control of blood glucose levels^[10]. The UKPDS (UK Prospective Diabetes Study) also showed that intensive glucose control reduced the risk of two-step change in retinopathy by 21% at 12 years follow up^[20]. Intensive glycemic control was effective in substantially reducing the incidence and progression of retinopathy in the Diabetes Control and Complication Trial (DCCT)^[13]. The CURES Eye Study observed a linear trend between prevalence of DR and poor glycemic control^[6].

6. Conclusion

This study suggests that diabetic retinopathy patients have high serum cholesterol levels and they need assessment of serum lipids regularly. Patients with diabetic retinopathy may need lipid lowering agents to halt the progression of diabetic retinopathy and prevent systemic and ocular morbidity of hyperlipidemia. High HbA1c level is also an important risk factor for the development of the retinopathy, this underlines that the need for better glycemic control in the prevention of complications of diabetic retinopathy. It would be better to consider Non-HDL cholesterol levels in future studies. Non-HDL cholesterol levels are also important predictors for progression of Diabetic maculopathy.

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