Dyslipidemia as Early Indicator of Diabetic Triopathy

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Abstract: _Background: Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease[1,2]. It is predicted that by 2O3O DM may afflict up to 79.4 million individuals in India[3,4], Few studies have assessed the relative associations of lipid fractions with diabetic microvascular events. Our aim was to determine a correlation between serum lipid profile and microvascular complication of DM patients. Material and methods: This retrospective study was done among 141T$_1$DM and 119T$_2$DM patients attending or enrolled in Medicine or Geriatric OPD or indoor patients at SP MC Bikaner Rajasthan from june2009 to Dec 2011. Statistical program SPSS 10, student t test and chi square test were employed for assessment of data. Results: There was statistically significant correlation between total cholesterol, LDL, VLDL and triglyceride with microvascular complications (p<.001).Low level of HDL cholesterol were highly significant in retinopathy and neuropathy (p<.001).while significant association was observed with nephropathy (p<.01). Conclusion: All microvascular complications were more with early onset and long duration of diabetes. Retinopathy was more in male as compared to females in T$_1$DM patients, whereas neuropathy was more in female as compared to male in T$_2$DM patients. Hence regular monitoring of lipid profile and screening for microvascular complication should be followed._

Keywords: Triglycerides (TG), Total Cholesterol (TC), Low Density Lipoproteins (LDL), microvascular complications.

1. Introduction

Diabetes is a group of chronic diseases characterized by hyperglycaemia. As of 2014, an estimated 387 million people have diabetes worldwide,[5] with type 2 diabetes making up about 90% of the cases.[6,7] This is equal to 8.3% of the adult population,[7] with equal rates in both women and men.[8] In the years 2012 to 2014, diabetes is estimated to have resulted in 1.5 to 4.9 million deaths per year.[5,9]Diabetes at least doubles the risk of death.[10]The importance of protecting the body from hyperglycaemia cannot be overstated; Generally, the injurious effects of hyperglycaemia are separated into macro vascular complications (coronary artery disease, peripheral arterial disease, and stroke) and microvascular complications (diabetic nephropathy, neuropathy, and retinopathy).Dyslipidemia may cause or exacerbate diabetic retinopathy and nephropathy by alterations in the coagulation-fibrinolytic system, changes in membrane permeability, damage to endothelial cells and increased atherosclerosis. Hyperlipidemia is associated with faster decline in glomerular filtration rate and progression of albuminuria and nephropathy. To date, few studies have investigated the relative magnitude of association between individual lipid sub fractions and diabetes-related MVCs. In recognition of that gap, this study was done to accessthe associations between the levels of lipid sub fractions (LDL-C, HDL-C, TG, and non-HDL-C) and MVCs of DM.

2. Material and Methods

This retrospective study was done among 141T$_1$DM and 119T$_2$DM patients with age group 15-65yrs attending or enrolled in Medicine or Geriatric OPD or indoor patients at SP MC Bikaner Rajasthan from June 2009 to Dec 2011.We followed revised ADA criteria for diagnosis of DM[11] , and those patient who were on lipid lowering therapy or familial history of hyperlipidemia,or terminally ill patients were excluded from the study. Information including age, sex, height, body weight (WT), body mass index (BMI), waist-hip ratio (WHR), and systolic and diastolic blood pressure was collected from each patient. Fasting plasma sugar, low density lipoprotein (LDL), triglyceride level (TG), high density lipoprotein (HDL), glycated haemoglobin (HbA1$_C$), creatinine, and 24 h urinary albumin excretion was done for each patient. Estimated glomerular filtration rate (eGFR) was measured by modification of diet in renal disease (MDRD)[12.] Neuropathy was diagnosed by history of numbness, paresthesia, and tingling sensation and confirmed by touch sensation by 10 gm microfilament vibration sense by tuning fork, ankle reflex and NCV. Funduscopy was done after dilatation using homatropine. Subjects with signs of micro-aneurysm, retinal dot blot hemorrhages, cotton wool spots, hard exudates is Non progressive Diabetic Retinopathy and neovascularisation progressive Diabetic Retinopathy were labeled as diabetic retinopathy.

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3. Statistical Analysis

Data was assessed using statistical program SPSS10.student t test and chi square test were employed to evaluate and establish correlation between lipid profile and microvascular complication in DM. P value of<0.05 was considered as significant.

4. Results

In our study a total of 260 patients were enrolled and evaluated, among them there were 141 T_1DM (53 male and 88 female) patients and 119 T_2DM(41 male and 78 female) patients.

In T_1DM patients, 38 patients have neuropathy, 14 patients had their TC $\leq$250 mg /dl while 24 patients had their TC>250mg/dl. 31patients have HDL<40, whereas 7 patient have HDL within normal limit and none have HDL above baseline.7 patients have LDL <100mg/dl, 19 have between 100-129mg/dl whereas 12 patient have LDL$\geq$129mg/dl and finally all these 38 patients have their VLDL and TG levels below 40 and 200 respectively.33 patients who had nephropathy, 12 patients had TC$\leq$250 mg/dl while 21 patients had TC >250mg/dl 28 patients have HDL<40, whereas 5 patient have HDL within normal limit and none have HDL above baseline.4 patients have LDL <100mg/dl, 11 have between 100-129mg/dl whereas 18 patient have LDL$\geq$129mg/dl and finally all these 33 patients have their VLDL and TG levels below 40 and 200 respectively. Among 70 retinopathy patients, 24 patients had TC$\leq$250mg/dlwhile 46 patients had TC >250 mg/dl. 57 patients have HDL<40, whereas 13 patient have HDL within normal limit and none have HDL above baseline.9 patients have LDL <100mg/dl, 36 have between 100-129mg/dl whereas 25 patient have LDL$\geq$129mg/dl.64 patients have VLDL level $\leq$ 40mg/dl and 6 patients have$\geq$40mg/dl and finally 64 patients have TG $\leq$200mg/dl, 3patients have between 200-239 mg/dl whereas 3patients had >239 mg/dl.(table no 1)

Table 1: Type 1 DM patients and their lipid profile

COMPLICATION	TC		LDL			VLDL		TG		
	$\leq$250	$\geq$250	<100	100-129	>129	$\leq$40	$\geq$40	<200	200-239	>239
NEUROPATHY	14	24	7	19	12	38	0	38	0	0
NEPHROPATHY	12	21	4	11	18	33	0	33	0	0
RETINOPATHY	24	46	9	36	25	64	6	64	3	3

In T_2DM patients, 48 patients have neuropathy, 27 patients had their TC $\leq$250 mg /dl while 21 patients had their TC>250mg/dl. 32patients have HDL<40, 14 patient have HDL within normal limit and2 patients have HDL above baseline.4 patients have LDL <100mg/dl, 4 have between 100-129mg/dl whereas 40 patient have LDL$\geq$129mg/dl.36 patients have VLDL $\leq$40mg/dl, and 12 patients have >40mg/dl. TG levels were below200mg/dl among 4 patients, 11 patient have 200-239 mg/dl and finally 33 patients have TG >239 mg/dl. Among 18 patients who had nephropathy, 4 patients had TC$\leq$250 mg/dl while 14 patients had TC >250mg/dl, 15 patients have HDL<40, whereas 3 patient have HDL within normal limit and none have HDL above baseline.1 patients have LDL <100mg/dl, none between 100-129mg/dl whereas 17 patients have LDL$\geq$129mg/dl. .13 patients have VLDL $\leq$40mg/dl, and 5 patients have >40mg/dl. TG levels were below200mg/dl among 1 patient, 6 patient have 200-239 mg/dl and finally 11 patients have TG >239 mg/dl. Among 70 retinopathy patients, 22 patients had TC$\leq$250mg/dlwhile 31 patients had TC >250 mg/dl. 30 patients have HDL<40, whereas 21 patient have HDL within normal limit and 2 patients have HDL levels above baseline.5 patients have LDL <100mg/dl, 6 have between 100-129mg/dl whereas 42 patient have LDL$\geq$129mg/dl.35 patients have VLDL level $\leq$ 40mg/dl and 18 patients have >40mg/dl and finally 4 patients have TG $\leq$200mg/dl, 32 had between 200-239mg/dl whereas 17 patients have >239md/dl(table no 2).

Table 2: Type 2 DM Patient and their lipid profile

COMPLICATION	TC		LDL			VLDL		TG		
	$\leq$250	$\geq$250	<100	100-129	>129	$\leq$40	$\geq$40	<200	200-239	>239
NEUROPATHY	27	21	4	4	40	36	12	4	11	33
NEPHROPATHY	4	14	1	0	17	13	5	1	6	11
RETINOPATHY	22	31	5	6	42	35	18	4	32	17

5. Discussion

Various studies have proven the role of elevated serum lipids with macro vascular complications of DM like coronary artery disease but, studies of association of lipids with specific micro vascular complications of DM have shown varying results. Hiraga[13] et al, Hernandez[14] et aland ogbera[15] et al established in their respective studies that lipoproteins are independent risk factor for CAD in diabetic patients. There are few studies available which have dealt with serum lipid and its association with microvascular complication with diabetes.

The present study was conducted in Department of Medicine, Sardar Patel Medical College, Bikaner. 260 patient having diabetes (141 T_1DM and 119 T_2DM patients) was enrolled for our study. The mean age for type 1 DM subgroup was 32.4$\pm$6.4yrs whereas for type 2 DM subgroup was 56.8$\pm$8.2 yrs.The average duration of diabetes was 10.3$\pm$5.4 yrs.The mean value of fasting and post prandial blood sugar was 182$\pm$56 and 255.9$\pm$80mg/dl respectively. Thus we see there is predilection of development of microvascular complication with the poorer control of diabetes. Duration of diabetes also seemed to play a role as nearly all the patient had either one or another form of microvascular complication.Our study results showed a positive correlation of microvascular complication with total cholesterol ,LDL,VLDL, and triglyceride(p<0.001).it was observed that retinopathy was more common in male in comparison to female in type 1 DM. Neuropathy was more common in female in comparison to male in type 2 DM patients. Low level of HDL cholesterol were highly significant in both retinopathy (p<0.001) andneuropathy

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(p<0.001) while association with nephropathy was also significant (p<0.01).(Table no 3 and 4)

Table 3: Statistical analysis of lipid profiles with microvascular complication

	NEUROPATHY				NEPHROPATHY				RETINOPATHY			
	TYPE1DM		TYPE2DM		TYPE1DM		TYPE2DM		TYPE1DM		TYPE2DM	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
TC	194.4	26.8	232.8	39.3	203.4	24.2	256.3	32.8	191.9	22.3	244.5	54.0
LDL	124.3	25.2	161.6	33.5	135.4	25.9	183.2	26.9	123.3	22.1	172.0	48.1
VLDL	25.7	4.9	38.1	6.9	26.2	4.7	39.4	5.9	27.9	7.5	38.8	6.7
TG	133.1	26.6	190.3	34.7	135.9	25.4	196.3	29.6	141.9	37.7	193.8	33.3
HDL	43.8	6.7	39.1	7.9	43.7	5.5	34.7	4.9	42.7	6.7	39.2	2.6

Table 4: Statistical analysis of lipid profiles with microvascular complication

	NEUROPATHY		NEPHROPATHY		RETINOPATHY	
	t	P	t	P	t	P
TC	5.090	<0.001	6.565	<0.001	7.359	<0.001
LDL	5.678	<0.001	6.225	<0.001	7.512	<0.001
VLDL	9.291	<0.001	8.770	<0.001	8.391	<0.001
TG	8.337	<0.001	7.644	<0.001	7.954	<0.001
HDL	3.124	0.002	5.823	<0.001	2.603	0.010

Table 5: Variation of HDL with type 1DM and type 2 DM

COMPLICATION	TYPE 1 DM			TYPE 2 DM		
	<40	40-60	>60	<40	40-60	>60
NEUROPATHY	27	21	4	36	12	4
NEPHROPATHY	4	14	1	13	5	1
RETINOPATHY	22	31	5	35	18	4

6. Conclusion

Lipid abnormalities were associated with an increased risk of all three diabetic complications studied, i.e. diabetic nephropathy, retinopathy, and incident CAD events. This study demonstrates correlation among HDL-C, TG and non-HDL-C with risk for microvascular events following the diagnosis of DM. Numerous studies have shown decreased risk in macro vascular disease in patients with diabetes who are treated with lipid-lowering agents, especially statins. As these microvascular complications were more with poorer glycaemia control and deranged lipid profile hence patient of DM should be regularly monitored for fasting/PP sugar, lipid profile and should be subjected to regular screening for microvascular complication.

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