Abnormalities in Lipid Profile Amongst Type 1 and Type 2 Diabetes in North Indian Population

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Abstract- Diabetes mellitus is characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Lipid abnormalities which can occur in diabetes mellitus can further complicate management of patients and is believed to play an important role in the pathogenesis of atherosclerosis. Keeping the above in view the present study aims to look for association between the lipid profile amongst diabetic patients and normal healthy controls in the Punjabi population. To meet the above objective blood samples were collected from a total of 100 diabetic subjects (20 type 1 and 80 type 2 diabetes) visiting the OPD and ward of department of medicine, in Civil Hospitals of Kapurthala, Jalandhar and Amritsar and 100 normal healthy controls matched for age and sex. Each patient was investigated for plasma glucose fasting (FPG), glycosylated hemoglobin (HbA1c), serum cholesterol (TC), serum triglyceride (TG), high density lipoproteins (HDL) low density lipoproteins (LDL) and very low density lipoproteins (VLDL). The mean serum cholesterol, triglycerides, LDL cholesterol, VLDL cholesterol and HDL cholesterol in diabetic subjects were 191.27 ± 30.85 mg/dl, 159.11 ± 37.11 mg/dl, 115.80 ± 25.62 mg/dl, 31.48 ± 7.68 mg/dl and 43.22 ± 5.00 mg/dl while their levels in normal healthy individuals were 166.21 ± 9.67 mg/dl, 123.69 ± 15.87 mg/dl, 96.57 ± 7.97 mg/dl, 24.78 ± 3.15 mg/dl and 44.90 ± 1.49 mg/dl respectively. The mean serum cholesterol, triglycerides, LDL cholesterol and VLDL cholesterol was significantly higher while serum HDL value was significantly lower in diabetic subjects as compared to non diabetic subjects. This study shows dyslipidemia among diabetic patients and proposes that the failure to recognize the presence of abnormal lipid profile may be a primary cause of poor management often encountered in some of the treated diabetics.

*Keywords***:** Diabetes, Lipid Profile, Cholesterol, VLDL, LDL, HDL, triglycerides

I. INTRODUCTION

Diabetes Mellitus (DM) is a clinical syndrome characterized by hyperglycemia due to the absolute deficiency (type 1 diabetes) or relative deficiency of insulin (type 2 diabetes and gestational diabetes). The deficiency of insulin could be due to the genetic defect of β-cell function or insulin, pancreatic diseases, drug induced, viral infections, increased production of hormonal antagonist to insulin and specific syndrome [1]. Malfunctions like lipid abnormalities, renal diseases and liver diseases which can occur in diabetes mellitus can further complicate management of patients and escalate the cause of diabetes mellitus treatment. Estimation of lipid abnormalities needs to be targeted because persistent hyperglycemia causes glycosylation of all proteins especially collagen, and matrix proteins of arterial wall which eventually causes endothelial cell dysfunction contributing further to atherosclerosis [2]. Atherosclerosis is the most common complication of the diabetes mellitus with largest number of ischemic events occurring in people with type 2 diabetes. However the risk of atherosclerosis is also high in type 1 diabetes and may manifest at younger age. Coronary heart disease is a major cause of death in patients with type 1 diabetes.

The pathophysiology of underlying diabetic dyslipidemia is closely linked to insulin resistance, which in turn leads to increased release of fatty acid from adipose tissue [3]. Increased plasma levels of fatty acids increase production of VLDL, TG and cholesterol by the liver. Increased plasma TG levels are then the "driving force" for low HDL C and abnormal, small dense LDL. Insulin resistance fat cells first undergo breakdown of their stored triglycerides and greater release of free fatty acids into the circulation. Increased fatty acids in the plasma lead to increase fatty acid uptake by the liver. The liver takes those fatty acids and synthesizes them into triglycerides. The presence of increased triglycerides stimulates the assembly and secretion of the apolipoprotein (apo) B and very low density lipoprotein [4].

Several studies have reported a correlation between diabetes and lipid profile. In recent cross sectional study

from Turkey [5], abnormalities in lipid profile has been reported in type 2 diabetic patients. There were significantly higher levels of TC, TG and LDL while there was a significantly lower level of HDL in diabetes. In addition significant correlation was observed between HbA1C and TC, TG and LDL. Similarly an altered plasma lipid profile was observed in the UK Prospective Diabetes Study [6]. In this study, women with type 2 DM had markedly higher LDL-cholesterol levels than women who were not diabetic. The plasma triglyceride levels of patients with type 2 DM were substantially increased, whereas HDL-cholesterol levels were markedly reduced in both men and women with diabetes mellitus compared with the non diabetic controls. Total cholesterol levels of those with diabetes mellitus and control individuals did not differ. The relationship between diabetes mellitus and lipid profile has not been extensively studied in Punjab although the prevalence of diabetes mellitus is very high and increasing. It is possible that there are diabetic patients who might have lipid dysfunction which may greatly affect their glycemic control. Due to the lack of adequate information about the two conditions, preventive management is difficult to plan. Keeping the above in view the present study aims to estimate & compare the Lipid profile in diabetics (type 1 and type 2) and non diabetics subjects. In addition efforts will be to look for any association between lipid profile and diabetes in the targeted group population.

II.   MATERIALS AND METHODS

The subjects were selected from the cases presenting with diabetes mellitus in the OPD and ward of department of medicine, in Civil Hospitals of Kapurthala, Jalandhar and Amritsar. An informed verbal consent was taken from each and every patient. The study population consisted of 100 diabetic (20 type 1 and 80 type 2) and 100 non diabetic subjects. The criteria for diagnosis of diabetes were the American Diabetic Association criteria; Fasting Plasma Glucose (FPG) level of 110mg/dl or higher, at more than two occasions and were receiving treatments such as insulin, oral hypoglycemic drugs and or physical exercise for diabetic mellitus. The criteria used for separating type 1 and type 2 subjects were the physician classification based on age of onset of diabetes and dependence on Insulin Therapy alone to achieve normal plasma concentration of glucose. The non diabetes volunteers without history of DM whose

FPG were less than 110 mg /dl on two occasions were taken as the control samples. These volunteers included non-diabetic subjects who came in the hospitals for routine checkups as advised by their attending physicians. The controls were not taking any drugs. The study excluded subjects suffering from rheumatoid arthritis, tuberculosis, collagen disorders, liver diseases, renal diseases, cardiac failure and gout. Blood samples were collected from all the 200 subjects. They were kept on over night fast at least for 10 hrs before blood collection. 5 ml of venous blood was taken in dry disposable syringe under aseptic conditions in sterile, dry vial for biochemical analysis. The samples were assayed for biochemical investigation including FPG, HbA1c and lipid profile. FPG (normal range 70-110mg/dl), HbA1c (normal range 4.2-6.2%), serum cholesterol (normal range150-200 mg/dl), serum triglycerides (normal range 100-150 mg/dl), serum HDL (normal range 35-48 mg/dl), serum LDL (normal range <130) and serum VLDL (normal range 5-35 mg/dl) were determined on semi automated clinical chemistry analyzer.

Statistical Analysis

The results obtained from the above investigation were analysed and expressed as mean $\pm$ SD. The comparison was done by student t test on number of variable of each parameter using SPSS version 10.

III.   RESULTS

In order to meet the proposed objectives of this study, whole blood samples were collected from 100 diabetic and 100 non-diabetic subjects. Among the 100 diabetic subjects, 48 were male and 52 were female. Similarly among the 100 non-diabetic subjects 48 were male and 52 were females. When categorized on the basis of type of diabetes 20 were type 1 diabetic and 80 were type 2 diabetes. The mean age of diabetic subjects was 40.95±11.2 years with range between 18-57 years. Mean age of non-diabetic subjects was 41.09±11.1 years and range between 17-58 years. There was no statistically significant difference between both groups with respect to mean age (p value= 0.93). As shown in table 1 the mean FPG levels (157.45±14.41 mg/dl) in diabetic subjects was significantly (p=<.0001) higher than the mean (88.52±6.72 mg/dl) value in non-diabetic subjects. Similarly mean value of HbA1C (7.18±0.73 %) in diabetic subjects was significantly (p=<.0001) higher than mean (5.01±0.22 %)   in   non-diabetic   subjects.

Table 1: Biochemical parameters in diabetic and non-diabetics					
Parameters(mg/dl)	**Diabetic (N=100)**	**Non-diabetic (N=100)**	**t value**	**S E**	**p value**
	Mean ± SD	**Mean ± SD**			
FPG	157.45 ± 14.41	88.52 ± 6.72	43.35	1.590	<0.0001**

HbA1c(%)	7.18 ± 0.73	5.01 ± 0.22	28.46	0.076	<0.0001**
Cholesterol	191.27 ± 30.85	166.21 ± 9.67	7.75	3.23	<0.0001**
Triglycerides	159.11 ± 37.11	123.69 ±15.87	8.77	4.03	<0.0001**
HDL-cholesterol	43.22 ± 5.00	44.90 ±1.49	2.83	0.522	0.005**
LDL-cholesterol	115.80 ± 25.62	96.57 ± 7.97	7.167	2.683	<0.0001**
VLDL-cholesterol	31.48 ± 7.68	24.78 ± 3.15	8.071	0.830	<0.0001**

** Highly Significant

Lipid profile in Diabetes vs non diabetes

The levels and comparison of mean serum concentration of lipid profile in diabetic and non-diabetic subjects is shown in Table 1. The mean serum cholesterol (191.27±30.85 mg/dl) in diabetic subjects was very significantly (p=<.0001) higher than the mean values (166.21±9.67 mg/dl) in non-diabetic subjects. The mean (159.11±37.11 mg/dl) triglycerides in diabetic subjects was higher than the mean (123.69±15.87 mg/dl) in non-diabetic subjects and difference was statistically very significant (p=<.0001). The mean serum HDL-cholesterol in diabetic and non-diabetic subjects was (43.22±5.00 mg/dl) and (44.90±1.49 mg/dl) respectively. Serum HDL value was lower in diabetic subjects as compared to non-diabetic subjects and this difference was statistically very significant (p=0.005). There was very high significant difference (p=<.0001) between the mean (115.80±25.62 mg/dl) of LDL-cholesterol in diabetic subjects compared with mean (96.57±7.97mg/dl) in non-diabetic subjects. The mean VLDL-cholesterol (31.48±7.68 mg/dl) in diabetic subjects was very significantly (p=<.0001) higher than the mean values (24.78±3.15 mg/dl) in non-diabetic subjects.

Table 2 : Levels of lipid profile in diabetic male and diabetic female groups					
Parameters (mg/dl)	**Diabetic male (N = 48)**	**Diabetic female (N = 52)**			
	Mean ± SD	Mean ± SD	**t value**	**S E**	**p value**
Cholesterol	183.81 ± 28.86	198.15 ± 31.30	2.375	6.036	0.0195**
Triglycerides	163.92 ± 32.43	154.67 ± 40.77	1.248	7.407	0.2147
HDL-cholesterol	41.50 ± 3.61	44.81 ± 5.59	3.485	0.950	0.0001**
LDL-cholesterol	108.71 ± 23.92	122.35 ± 25.61	2.746	4.967	0.0072**
VLDL-cholesterol	32.00 ± 7.15	31.00 ± 8.18	0.648	1.542	0.5181

** Highly Significant

The levels and comparison of mean serum concentration of lipid profile in diabetic male and female subjects are shown in Table 2. The mean serum cholesterol (183.81±28.86 mg/dl) in diabetic male subjects was significantly (p=.0195) lower than the mean values (198.15±31.30 mg/dl) in diabetic female subjects. The mean (163.92±32.43 mg/dl) triglycerides in diabetic male subjects was higher than the mean (154.67±40.77 mg/dl) in diabetic female subjects but difference was statistically insignificant (p=.214). The mean serum HDL-cholesterol in diabetic male and female subjects was (41.50±3.61 mg/dl) and (44.81±5.59 mg/dl) respectively. Serum HDL value was lower in diabetic male subjects as compared to diabetic female subjects and this difference was statistically very significant (p=.0001). There was significant (p=.0072) difference between the mean (108.71 ± 23.92 mg/dl) LDL-cholesterol in diabetic male subjects compared with mean (122.35±25.61 mg/dl) in female diabetic subjects. The mean VLDL-cholesterol (32.00±7.15 mg/dl) in diabetic male subjects was insignificantly (p=0.5181) higher than the mean values (31.00±8.18 mg/dl) in female diabetic subjects.

Lipid profile in type 1 Diabetes vs non diabetes

The levels and comparison of mean serum concentration of lipid profile in type 1 diabetic and non-diabetic subjects are shown in Table 3. The mean serum cholesterol (178.95±17.86 mg/dl) in type 1 diabetic subjects was significantly (p=<.0001) higher than the mean values (166.21±9.67 mg/dl) in non-diabetic subjects. The mean (145.6±32.40 mg/dl) triglycerides in type 1 diabetic patients was higher than mean (123.69±15.87 mg/dl) in non-diabetic subjects and this difference was statistically very significant (p=<.0001). The mean serum HDL-cholesterol in type 1 diabetic and non-diabetic subjects was (40.6±4.37 mg/dl) (44.90±1.49 mg/dl) respectively. Serum HDL value was lower in type 1 diabetic subjects as compared to non-diabetic subjects and this difference was statistically very significant (p=<.0001). There was very high significant (p=<.0001) difference between the mean (107.55±13.41 mg/dl) of LDL-cholesterol in type 1diabetic subjects compared with mean (96.57±7.97 mg/dl) in non-diabetic subjects. The mean VLDL-cholesterol (26.95±6.54 mg/dl) in type 1 diabetic

subjects was significantly (p=0.0249) higher than the mean

values (24.78±3.15 mg/dl) in non-diabetic subjects.

Table 3: Levels of lipid profile in type 1 diabetic and non-diabetic groups					
Parameters (mg/dl)	**Type 1diabetic (N =20)**	**Non-diabetic (N = 100)**	**t value**	**S E**	**p value**
	Mean ± SD	**Mean ± SD**			
Cholesterol	178.95 ± 17.86	166.21 ± 9.67	4.564	2.031	<0.0001**
Triglycerides	145.6 ± 32.40	123.69 ± 15.87	4.585	4.778	<0.0001**
HDL-cholesterol	40.6 ± 4.37	44.90 ±1.49	7.532	0.544	<.0001**
LDL-cholesterol	107.55 ± 13.41	96.57 ± 7.97	4.882	2.202	<.0001**
VLDL-cholesterol	26.95 ± 6.54	24.78 ± 3.15	2.271	0.955	0.0249*

** Highly Significant, * Significant

Lipid profile in type 2 Diabetes vs non diabetes

The levels and comparison of mean serum concentration of lipid profile in type 2 diabetic and non-diabetic subjects are shown in Table 4. The mean serum cholesterol (191.57±29.64 mg/dl) in type 2 diabetic subjects was significantly (p=<.0001) higher than the mean values (166.21±9.67 mg/dl) in non-diabetic subjects. The mean

(163.20±34.92 mg/dl) triglycerides in type 2 diabetic subjects was higher than the mean (123.69±15.87 mg/dl) in non-diabetic subjects and this difference was statistically very significant (p=<.0001). The mean serum HDL-cholesterol in type 2 diabetic and non-diabetic subjects was (43.74±4.88 mg/dl) and (44.90±1.49 mg/dl) respectively.

Table 4: Levels of lipid profile in type 2 diabetic and non-diabetic groups					
Parameters(mg/dl)	**Type 2 diabetic (N =80)**	**Non-diabetic (N = 100)**	**t value**	**S E**	**p value**
	Mean ± SD	**Mean ± SD**			
Cholesterol	191.57 ± 29.64	166.21 ± 9.67	8.042	3.163	<0.0001**
Triglycerides	163.20 ± 34.92	123.69 ± 15.87	10.091	3.915	<0.0001**
HDL-cholesterol	43.74 ± 4.88	44.90 ±1.49	1.862	0.515	0.064
LDL-cholesterol	115.09 ± 25.48	96.57 ± 7.97	6.789	2.694	<0.0001**
VLDL-cholesterol	32.74 ± 7.02	24.78 ± 3.15	10.139	0.785	<0.0001**

** Highly Significant

Comparison of lipid profile amongst type 1 and type 2 Diabetes

The levels and comparison of mean serum concentration of lipid profile in type 1 diabetic and type 2 diabetic subjects are shown in Figure 1. The mean serum cholesterol (178.95±17.86 mg/dl) in type 1 diabetic subjects was insignificantly (p=.0719) different than the mean values (191.57±29.64 mg/dl) in type 2 diabetic subjects. The mean (145.6±32.41 mg/dl) triglycerides in type 1 diabetic patients was lower than the mean (163.20±34.92 mg/dl) in type 2 diabetic subjects and difference was statistically significant

(p=.0437). The mean serum HDL-cholesterol in type 1 diabetic and type 2 diabetic subjects was (40.6±4.37 mg/dl) and (43.74±4.88 mg/dl) respectively. Serum HDL value was lower in type 1 diabetic subjects as compared to type 2 diabetic subjects and this difference was statistically very significant (p=.0101). There was insignificant (p=.2048) difference between the mean (107.55±13.41 mg/dl) of LDL-cholesterol in type 1diabetic subjects compared with mean (115.09 ±25.48 mg/dl) in type 2 diabetic subjects. The mean VLDL-cholesterol (26.95±6.54 mg/dl) in type 1 diabetic subjects was significantly (p=.0012) lower than the mean values (32.74±7.02 mg/dl) in type 2 diabetic subjects.
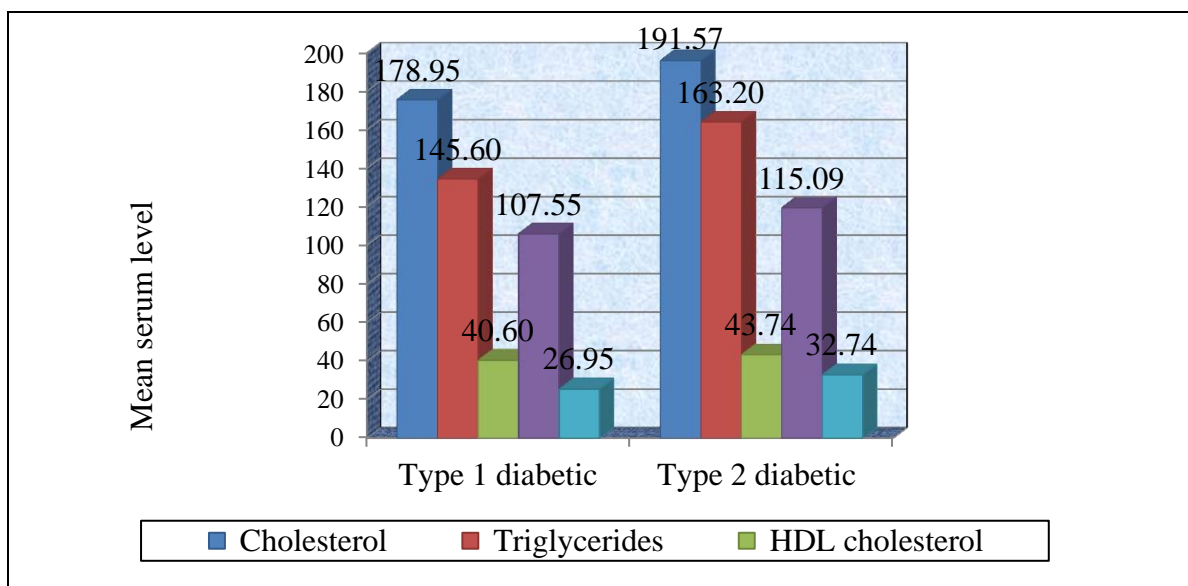
Figure 1: Mean lipid profile levels in type 1 and type 2 diabetic subjects

IV. DISCUSSION

Diabetic dyslipidemia is a hall mark of metabolic syndrome and is believed to play an important role in the pathogenesis of atherosclerosis [7]. Thus it has become major cause for higher cardiovascular morbidity and mortality. Cardiovascular diseases (CVD) are the most prevalent cause of death and disability in both developed as well as developing countries [8]. South Asians around the globe have the highest rates of coronary artery disease (CAD) [9]. CAD is usually due to atherosclerosis of large and medium sized arteries and diabetic dyslipidemia has been found to be one of the most important contributing factor [2].

The results of the present study showed significantly increased level of cholesterol (P=<.0001), triglycerides (P=<.0001), LDL-cholesterol (P=<.0001) and VLDL-cholesterol (P=<.0001) and significantly decreased value of HDL-cholesterol (P=<.0001) in diabetic subjects compared to non-diabetic control subjects (Table 1).

These results are in good agreement with the study by [10],[11]. The main cause of the three cardinal features of diabetic dyslipidemia is the increased free fatty-acid release from insulin-resistant fat cells [11]. The increased flux of free fatty acids into the liver in the presence of adequate glycogen stores promotes triglyceride production, which in turn stimulates the secretion of apolipoprotein B (ApoB) and VLDL-cholesterol. The impaired ability of insulin to inhibit free fatty-acid release leads to enhanced hepatic VLDL-cholesterol production [12], which correlates with the degree of hepatic fat accumulation [13].

Hyperinsulinemia is also associated with low HDL-cholesterol levels [14]. The increased number of VLDL-cholesterol particles and increased plasma triglyceride levels decrease the level of HDL-cholesterol and increase the concentration of small dense LDL-cholesterol particles via several processes: VLDL-transported triglyceride is exchanged for HDL transported cholesterol ester through the action of the cholesterol ester transfer protein (CETP), which results in increased amounts of both atherogenic cholesterol-rich VLDL remnant particles and triglyceride-rich, cholesterol-depleted HDL particles. The increased concentration of small dense LDL-cholesterol particles is explained by a similar lipid exchange. Increased levels of VLDL transported triglyceride enable CETP to promote the transfer of triglyceride into LDL in exchange for LDL transported cholesterol ester. The triglyceride-rich LDL undergoes hydrolysis by hepatic lipase or lipoprotein lipase, which results in lipid-depleted small dense LDL particles [15].

Diabetic females have significantly higher serum cholesterol (P=<0.0001), HDL-cholesterol (P=<0.0001), LDL-cholesterol (P=0.007) and lower triglycerides as compared to diabetes males (Table 2). These results are in agreement with the studies o[16] although reports from Turkey [5]did not find any difference among cholesterol, triglycerides, HDL in diabetic males and females.

Among the type 1 diabetic subjects (Table 3) also mean levels of cholesterol (P=<0.0001), triglycerides (P=<0.0001), LDL-cholesterol (P=<0.0001), VLDL-cholesterol (P=0.024) were significantly higher where as HDL-cholesterol were significantly lower P=<0.0001 as

compared to non-diabetic subjects. The present data was in agreement with some previous reports [17] although other [18] have reported total serum cholesterol to be similar in type 1 and control groups. Possible reasons for difference in reports includes case selection criteria, nature of control population, diet of the general population, the duration and severity of diabetes, the degree of glycemic control and variation in laboratory methods.

In subgroup type 2 diabetic subjects (Table 4) mean cholesterol (P=<0.0001), triglycerides (P=<0.001), LDL-cholesterol (P=<0.0001), VLDL-cholesterol (P=<0.0001) were significantly higher where as HDL-cholesterol was marginally significantly lower as compared to non-diabetic subjects. Our results are consistent with previous report [19].

Type 2 diabetics has significantly higher cholesterol (P=0.007), triglycerides (P=0.04), HDL (P=0.01), VLDL (P=0.0001) but LDL-cholesterol is not significantly higher than type 1 diabetic subjects (Figure 1). These results are partially consistent with the study of [20], who found cholesterol, triglycerides and LDL-cholesterol were significantly higher in type 2 diabetic patients than in type 1 diabetic patients but HDL-cholesterol were same in both types of diabetic patients.

V.   CONCLUSION

The present study reports Dyslipidemia among diabetic patients and proposes that the failure to recognize the presence of abnormal lipid profile in diabetic patients may be the main reason of poor management often encountered in some of the treated diabetics. The early detection and treatment of dyslipidemia may help in reducing the risk of cardio vascular disorders. Hence there is need for the routine assay of lipid profile in diabetic, particularly in those patients whose conditions are difficult to manage.

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