COMPARISON OF LIPID PROFILE OF OBESE AND NON-OBESE TYPE 1 DIABETES MELLITUS PATIENTS

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ABSTRACT: *Present study was carried out to identify the effect of diabetes on the lipid profile of obese and non-obese type 1 diabetes mellitus (T1DM) patients and their comparison with control subjects. Blood samples of 30 obese T1DM patients and 70 non-obese T1DM patients were collected from Services Hospital Lahore. Twenty blood samples of obese and 26 blood samples of non-obese control subjects were collected from different areas of Lahore. All samples were tested by enzymatic photometric assay technique to estimate the levels of serum cholesterol, triglyceride, HDL-C, LDL-C, VLDL-C, and total lipid. It was found that the levels of serum cholesterol, triglyceride, and VLDL-C and total lipid were non-significantly higher while levels of HDL-C and LDL-C were non-significantly lower in obese and non-obese T1DM patients as compared to control subjects. Results were discussed in the light of previous reports of different populations. These results suggested that T1DM patients are prone to develop hyperlipidemia and it can predispose these patients to develop atherosclerosis and other complications of cardiovascular diseases.*

Key Words: Obesity, T1DM, Lipid profile.

INTRODUCTION

Diabetes mellitus is a chronic disease of metabolism causing abnormal glucose homeostasis [1]. Diabetes mellitus is a syndrome of impaired carbohydrate, fat, and protein metabolism caused by either lack of insulin secretion or decreased sensitivity of the tissues to insulin [2]. Diabetes is the most common metabolic disorder all over the world. More than 171 million people are globally affected by diabetes mellitus, and the figure is expected to rise up to 366 million by 2030 [3]. The incidence of diabetes showing an alarming rise in the developed countries [4]. It is ranked seventh among the leading causes of death, and third when all its fatal complications are taken into account [5]. Uncontrolled diabetes with increased blood glucose is strongly correlated to causing long-term micro vascular complications such as retinopathy, neuropathy, coronary artery disease, stroke, and cerebrovascular disease [6-9].

T1DM is caused by a lack of insulin secretion and by autoimmune destruction of beta cells in the pancreatic islet [10]. All aspects of fat breakdown and use for providing energy are greatly enhanced in the absence of insulin. It becomes extreme in diabetes mellitus when the secretion of insulin is almost zero. Insulin deficiency causes lipolysis of storage fat and release of free fatty acids**.** The excess of fatty acids in the plasma associated with insulin deficiency also promotes the liver conversion of some of the fatty acids into phospholipids and cholesterol, two of the major products of fat metabolism. These two substances, along with excess triglycerides formed at the same time in the liver then discharged into the blood in the lipoproteins [2]. In the past 20 years, the prevalence of obesity has tripled worldwide [11] and the trend of increasing obesity prevalence has increased at a faster rate in patients with T1DM compared to the general population [12].

The lipid profile of obese and non-obese T1DM patients has been described in many previous studies and compared with control subjects. Some previous studies demonstrated that the levels of TC, TG, and LDL-C increased and the level of HDL-C decreased in obese and non-obese T2DM patients as compared to control subjects [13-14]. However, another study demonstrated that the levels of TC, TG, LDL-C, and VLDL-C and in obese and non-obese T2DM patients as compare to control subjects [15]. The prevalence of dyslipidemia in patients with diabetes was observed high in Henan province, China [16]. The aim of the present study was to observe the variations in lipid profiles of obese and non-obese T1DM patients compared to control subjects in our local population.

MATERIALS AND METHODS

The present study was based on 30 obese T1DM patients, 20 control subjects, and 70 non-obese T1DM patients, 26 control subjects having the age of 25 to 60 years. Blood samples were taken in the fasting state of each of the T1DM patients from services hospital Lahore Pakistan and control subjects from the different areas of Lahore. The patients of a diagnosed case of T1DM were taken for study. According to WHO Report 2012 [17], BMI was calculated as kg/m^2 using the information of height and weight at the time of blood sample collection. The subjects having a BMI $\geq$ of 30 kg/m^2 were considered obese and the subjects having a BMI $\leq$ of 30 kg/m^2 were considered as non-obese. The venipuncture method was used to draw the blood of diabetics and healthy subjects. Blood samples were allowed to clot for 20-25 minutes and then for the separation of serum, they were centrifuged at 4000 rotations per minute. Serum was separated out from the top of the clotted blood and then used. Glucose is determined by enzymatic reaction (glucose oxidase and peroxidase = GOD-POD) [18]. Serum total cholesterol was determined by an enzymatic (CHOD-PAP) colorimetric method [19]. Triglycerides were determined by an enzymatic (GPO-PAP) method [20]. HDL-Cholesterol was estimated by a precipitant method [21]. LDL-Cholesterol was estimated by using Friedewald formula [LDL-Cholesterol = Total Cholesterol – (HDL cholesterol + Triglycerides/5)] [22]. To get the value of VLDL-C, if triglycerides are less than 100 then it was divided by factor 5. And if serum triglycerides value is greater than 100 then it was multiplied by 0.16 to get the value of VLDL-C in blood serum. Mean ± S.D of serum samples of obese and non-obese T1DM patients and their control subjects were calculated. Statistical analysis of the data was carried out by employing

the Student't' test. The 'P' value less than 0.05 was considered significant

RESULTS

The study included 30 obese T1DM patients, 20 control subjects, and 70 non-obese T1DM patients, 26 control subjects. The age ranges from 25 to 60 years for T1DM patients and control subjects.

Table 1. Comparison of lipid levels of obese T1DM patients and Control subjects.

Lipids	Obese T1DM	Control	P-value
Cholesterol	178.40 ± 9.07	177.85 ± 4.49	> 0.05
Triglyceride	208.86 ± 22.29	161.05 ± 12.47	> 0.05
HDL-C	42.00 ± 2.26	42.41 ± 1.60	> 0.05
LDL-C	98.58 ± 6.29	110.60 ± 5.08	> 0.05
VLDL-C	41.77 ± 4.59	32.21 ± 1.95	> 0.05
Total Lipid	630.61 ± 68.23	560.16 ± 41.16	> 0.05

Table 2. Comparison of lipid levels of non-obese T1DM patients and Control subjects.

Lipids	Non-obese T1DM	Control	P-value
Cholesterol	181.07 ± 10.13	178.07 ± 17.70	> 0.05
Triglyceride	165.87 ± 32.03	157.69 ± 9.60	> 0.05
HDL-C	40.80 ± 0.87	43.14 ± 0.97	> 0.05
LDL-C	103.97 ± 4.41	105.19 ± 11.95	> 0.05
VLDL-C	33.18 ± 2.75	31.90 ± 1.91	> 0.05
Total Lipid	586.66 ± 18.19	567.63 ± 22.27	> 0.05

Table 1 shows the mean values with standard error of various lipid fractions of obese T1DM patients and controls subjects. Mean total cholesterol levels in obese T1DM patients were higher as compared to control subjects (178.40 vs. 177.85 mg/dl, P > 0.05). Mean TGs levels in obese T1DM patients were higher as compared to control subjects (208.86 vs. 161.05 mg/dl, P > 0.05). Mean HDL-C levels in obese T1DM patients were lower as compared to control subjects (42.0 vs. 42.41 mg/dl, P > 0.05). Mean LDL-C levels in obese T1DM patients were higher as compared to control subjects (167.53 vs. 110.6 mg/dl, P < 0.01). Mean VLDL-C levels in obese T1DM patients were higher as compared to control subjects (41.77 vs. 32.21 mg/dl, P > 0.05). Mean total lipid levels in obese T1DM patients were higher as compared to control subjects (630.61 vs. 560.16 mg/dl, P > 0.05).

Table 2 shows the mean values with standard error of various lipid fractions of non-obese T1DM patients and control subjects. Mean total cholesterol levels in non-obese T1DM patients were higher as compared to control subjects (181.07 vs. 178.07 mg/dl, P > 0.05). Mean TGs levels in non-obese T1DM patients were higher as compared to control subjects (165.87 vs. 157.69 mg/dl, P > 0.05). Mean HDL-C levels in non-obese T1DM were lower as compared to control subjects (40.80 vs. 43.14 mg/dl, P > 0.05). Mean LDL-C levels in non-obese T1DM patients were lower as compared to control subjects (103.97 vs. 105.19 mg/dl, P > 0.05). Mean VLDL-C levels in non-obese T1DM patients were higher as compared to control subjects (33.18 vs. 31.9 mg/dl, P > 0.05). Mean total lipid levels in non-obese T1DM patients were higher as compared to control subjects (586.66 vs. 567.63 mg/dl, P > 0.05).

DISCUSSION

The present study was conducted to observe the complete lipid profile (serum total cholesterol, triglycerides, HDL-C, LDL-C, VLDL-C, and total lipid) in obese and non-obese type 1 diabetes mellitus (T1DM) patients and their comparison with control subjects.

Our results indicated that fasting serum levels of total cholesterol, triglycerides, VLDL-C, and total lipid were significantly higher and levels of LDL-C and HDL-C were significantly lower in obese T1DM patients as compared to control subjects. Our results also indicated that fasting serum levels of total cholesterol, triglycerides, VLDL-C, and total lipid were non-significantly higher and levels of LDL-C and HDL-C were non-significantly lower in non-obese T2DM patients as compared to control subjects. These results are comparable with some previous studies which described higher levels of total cholesterol, triglycerides, VLDL-C, and total lipid and lower levels of LDL-C and HDL-C in obese and non-obese T1DM patients as compared to control subjects [13, 23-27].

The increase of blood cholesterol in T1DM patients is through an increase of free fatty acids in the blood. The excess of fatty acid in the blood associated with insulin deficiency also promotes conversion by the liver of some of the fatty acids into phospholipids and cholesterol. In the absence of insulin, all the effects of insulin that cause storage of fat are reversed. The most important fact is that hormone sensitive-lipase in the fat cell becomes strongly activated. This activation causes hydrolysis of stored triglycerides, releasing large quantities of fatty acids and glycerol into the circulating blood. Consequently, the level of free fatty acids begins to rise within minutes [2].

Lipoprotein lipase is involved in the breakdown of triglycerides into three fatty acids and one glycerol molecule. Diabetes has an additional indirect effect on lipoprotein metabolism by decreasing lipoprotein lipase, which is an important factor in the metabolism of cholesterol and triglycerides [28].

VLDL-C from patients with T1DM is frequently enriched in esterified cholesterol at the expense of triglycerides leading to an increased VLDL-C cholesterol/triglyceride ratio [29-30]. It has been suggested that this compositional change may be due to increased cholesteryl ester transfer between lipoproteins [30]. These changes increase the VLDL-C production in the liver. Both of these processes will prevent the degradation of newly synthesized apoB and lead to increased lipoprotein production. VLDL-C, like chylomicrons, requires LPL to begin its plasma catabolism, leading to the production of LDL-C or the return of partially degraded lipoprotein to the liver [31].

In the absence of insulin two products of fat metabolism phospholipids and cholesterol along with excess triglycerides formed in the liver, are then discharged into the blood in the lipoproteins. Occasionally the plasma lipoproteins increase as much as threefold in the absence of insulin, in T1DM patients giving a total concentration of plasma lipids of several percent rather than the normal 0.6 percent [2].

LDL-C is decreased during T1DM ketoacidosis
. The drop in plasma LDL-C levels is the direct consequence of the reduced triglyceride-rich lipoprotein catabolism that, in turn, is due to the reduced LPL activity [32]. LPL is the major enzyme responsible conversion of lipoprotein triglyceride into free fatty acids. This protein has an unusual intercellular for transport; LPL is synthesized primarily by adipocytes and myocytes but must be transferred to the luminal side of capillary endothelial cells, where it can interact with circulating triglyceride-rich lipoproteins such as VLDL-C and chylomicrons [33]. Humans with T1DM have been reported to have reduced LPL activity measured in post heparin blood [34]; the enzyme is released from the capillary walls and into the circulation by heparin. Several steps in the production of biologically active LPL may be altered in T1DM patients, including its cellular production [35] and possibly its transport to an association with endothelial cells [36].

The increase of VLDL-C caused a decrease of HDL-C due to poor availability of phospholipids remnants from VLDL-C which causes a decrease in HDL-C formation. HDL-C particles from patients with T1DM are often enriched in triglycerides [37-38]. This modification has been attributed to increased cholesteryl ester transfer between lipoproteins [30]. In HDL-C particles from patients with T1DM, the sphingomyelin/lecithin ratio within the peripheral layer is augmented, which may increase HDL-C rigidity [39]. These alterations are not totally reversed after the achievement of optimal glycemic control [38]. Apol-I within HDL-C is glycated in T1DM patients, which may impair the HDL-mediated reverse cholesterol pathway. Indeed, it has been shown that HDL-C particles containing glycated apo A-I were less effective to promote cholesterol efflux from the cells [40]. In addition to their role in the reverse cholesterol pathway, HDL-C has anti-oxidative, anti-inflammatory, anti-thrombotic, and vasorelaxant properties, potentially anti-atherogenic [41]. Some of these properties have been shown to be reduced in T1DM patients. Indeed, a significant reduction of the activity of paraoxonase, an antioxidative enzyme associated with HDL-C, is observed in patients with T1DM. As a consequence, HDL-C from patients with T1DM protects less efficiently erythrocyte membranes and LDL-C particles against oxidative damage than HDL-C from normal individuals [42-43].

CONCLUSION:

T1DM patients are prone to develop hyperlipidemia which can predispose patients to develop atherosclerosis and other complications of cardiovascular diseases. Control of glucose levels in these patients can prevent the development and progression of lipid abnormalities in T1DM patients like raised serum cholesterol, triglyceride, VLDL-C, total lipids, and low LDL-C, HDL-C.

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