ORIGINAL ARTICLE
Dyslipidemia in Type 2 Diabetes Mellitus

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ABSTRACT

Objective: To determine the correlation of plasma glucose levels with lipid profile in type 2 Diabetes Mellitus (T2DM).

Study Design: Case control study.

Place & Duration of study: This study was conducted in Army Medical College Rawalpindi from 11th November 2014 to 11th November 2015.

Materials & Methods: The number of participants comprised in the study was 120. The study population was divided into two groups A & B. 60 individuals were placed in each group. Group A comprised of Type 2 diabetics and group B were healthy controls with no major illness. The patients were recruited from the Military Hospital's medical wards and Endocrinology outpatient department. The participants' blood samples were analyzed for Fasting Plasma Glucose (FPG), glycosylated hemoglobin (HbA1c) and lipid profile (Total Cholesterol, Triglycerides, LDL-Cholesterol and HDL-Cholesterol).Body mass index (BMI) was calculated by measuring the height and weight of men & women based on body fat.

Data was analyzed using SPSS version 20.

Results: FPG was (11.23±3.65 in diabetics vs 4.35±0.68 in controls), HbA1c was (6.84±0.482 vs 5.31±0.487). Serum total cholesterol was (4.68±0.96 vs 3.99±1.01 p<0.001), triglycerides (TG) were (2.42±1.22 vs 1.56±0.87 p<0.001) and LDL-Cholesterol was (2.46±0.77 vs 2.17±0.72 p<0.05). These parameters were significantly raised then the controls. Whereas HDL-Cholesterol in the diabetics were relatively lower than the controls (1.04±0.224 vs 1.21±0.222 p<0.001). The diabetics Body mass index (BMI) was also significantly more than the controls (28.57±1.97 vs 24.46±2.32 p<0.001).

Conclusion: This study shows that serum FPG, HbA1c, Total Cholesterol, TG and LDL-Cholesterol are significantly increased in T2DM while HDL-Cholesterol levels are decreased significantly which might be the reason for high coronary heart diseases incidence in T2DM.

Key Words: Type2 Diabetes Mellitus,Dyslipidemia,Total Cholesterol,Triglycerides,LDL-Cholesterol and HDL-Cholesterol

Introduction

"Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia caused by defective insulin secretion, ineffective insulin function or both which leads to disturbance of carbohydrate, fat and protein metabolism."[1,2] There are two major types of diabetes mellitus, T1DM previously called insulin dependent diabetes mellitus (IDDM), occurs when insulin secretion is deficient and T2DM or non-insulin dependent diabetes mellitus (NIDDM), occurring because of insulin resistance with or without insulin relative deficiency.[3] "Chronic hyperglycemia causes structural and functional damage to blood vessels and tissues leading to complications such as diabetic neuropathy, nephropathy, retinopathy, hypertension, hyperlipidemia, cerebrovascular diseases and atherosclerotic coronary heart disease."[4,5]

Diabetes mellitus is a rapidly growing epidemic. 285 million people were suffering from diabetes in year 2010. This number is going to be 439 million worldwide in year 2030.[6] Similarly there is rise in coronary mortality in diabetic patients having dyslipidemia. Expected increase in deaths from 2000

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to 2030 would be 8-11 million worldwide and most of these patients would be diabetics.

Dyslipidemia association with atherosclerosis is well established. The progression of atherosclerosis in diabetes is mainly due to the associated hyperglycemia, obesity and insulin resistance.[7,9] Excess free fatty acids (FFA) liberation from adipose tissue occurs in T2DM due to insulin resistance.[10,12] To a large extent lipoproteins hepatic metabolism is controlled by insulin. It has implications on lipid profile and increased role in coronary heart disease development.[13,14]

Atherosclerosis starts as inflammation of the blood vessels and in the presence of T2DM the process speeds up. In T2DM atherosclerosis and high blood glucose levels are related to each other.[15] All proteins glycosylation, like collagen linking arterial wall matrix proteins and collagen linking are caused by persistently raised blood glucose levels leading to endothelial cells dysfunction which further contributes to atherosclerosis. In T2DM there is 95% prevalence of dyslipidemia.[16] A large number of studies have shown a significant reduction in T2DM related complications and mortality rate due to coronary heart diseases if a normal glycemic control is maintained. Studies have shown that Langerhans beta cells apoptosis is not the only damage that high blood sugar levels causes but also leads to increased accumulation of oxidized LDL in pancreatic islets and coronary arteries thus increasing the risks of development of coronary heart disease.[17] A triad of increased levels TGs, LDL-Cholesterol and decreased levels of HDL-Cholesterol in diabetic patients is called diabetic dyslipidemia. The abnormalities of lipids in DM is mainly due to insulin resistance that affects the enzymes and pathways in lipid metabolism.[6, 9, 18, 19]

Several studies have proposed that in diabetic dyslipidemia the lipid particles composition is more atherogenic than the other type of dyslipidemia.[9,20] WUL and Parhofer KG in their study showed that diabetes and increased cardiovascular risk of diabetic patients is linked mainly to the lipid changes. The increased concentration of FFA, alteration of insulin sensitive pathways and low grade inflammation being the pathophysiology, all these play an important role. The results being decreased catabolism and overproduction of intestinal and hepatic origin triglycerides rich lipoproteins. The observed changes in LDL and HDL are a sequence to this.[21] Marcello et al in their study explained that the lipoprotein abnormalities are mainly determined by increased production of very low density lipoproteins (VLDL) by the liver. The multiple mechanisms involved in this are increased FFA influx into the liver, reduction of inhibitory effects of insulin on VLDL production and enhanced de novo lipogenesis. All this leads to increased concentration of Apo-B-containing lipoproteins and abnormal function of HDL particle which may impair cholesterol removal from deposits. All these changes can lead to atherogenesis.[22]

Apart from link of diabetic dyslipidemia and atherosclerosis, uncontrolled T2DM is itself a high risk factor for atherosclerosis as Selvin et al in 2010 in their community based study done on more than 11,000 participants observed the tendency for increasing risk of stroke, heart diseases and cardiac deaths.[9,23] The current literature suggests to diagnose and treat dyslipidemia in type 2 diabetics at the earliest. It will help improve the quality of life and prevent the associated complications. The main objective of this study was to determine the correlation of plasma glucose levels with lipid profile in T2DM in our own population.

Material and Methods

This case control study was conducted in Army medical College Rawalpindi from 11th November 2014 – 11th November 2015. A total of 120 participants were included in the study. They were divided into group A & B. Group A included 60 diagnosed patients (30 males & 30 females) with T2DM. Individuals with thyroid, Liver, Kidney, Adrenal disorders were excluded from the study. Group B included 60 healthy persons (30 males & 30 females) free from any major illness.

Under aseptic conditions five ml of fasting venous sample of at least 8-12hs was obtained from left median cubital vein. The blood was centrifuged for 5 mins at 4000 rpm for serum separation. Selectra E, a fully automated chemistry analyzer was used for the FPG and lipid profile measurement. To estimate the levels of HbA1c levels Ion exchange method was used. Body mass index (BMI) was calculated by measuring the height and weight of men & women based on body fat.

Patient's selection was done from medical wards & Endocrinology Department of Military Hospital (MH) Rawalpindi using Non Probability convenient

sampling technique. Sample size was calculated using WHO calculator.

This parametric data was entered and analyzed using SPSS version 20 and results of the test were subject to appropriate statistical analysis. Quantitative data was compared using independent t-test. The data was statistically considered significant with P-value of < 0·05.

Results

120 individuals were selected for the study of which 60 were diabetics and 60 were healthy individuals who were gender & age matched. Comparison of biochemical profile of different analytes in diabetic patients (Group A) and healthy controls (Group B) are summarized in table I. FPG levels (mean ± SD) in group A was 11.23±3.65 as compared to group B 4.35±0.68, HbA1c was (6.84±0.482 group A vs 5.31±0.487 group B) and in the lipid profile, serum total cholesterol was (4.68±0.96 group A vs 3.99±1.01 group B p< 0.001), triglycerides (TG) were (2.42±1.22 group A vs 1.56±0.87 group B p< 0.001) and LDL cholesterol was (2.46±0.77 group A vs 2.17±0.72 group B p< 0.05). Whereas HDL cholesterol was (1.04±0.224 group A vs 1.21±0.222 group B p< 0.001). The BMI was raised significantly in group A than group B (28.57±1.97 vs 24.46±2.32 p< 0.001).

Table I. Comparison of Biochemical Characteristics between Cases and Controls

Variables (reference range)	Group A (Diabetic) n=60	Group B (Control) n=60	P-Value
BMI (kg/m^2) (18-24.9)	28.57±1.97	24.46±2.32	<0.001***
FBG (mmol/L) (3.3-5.6)	11.23±3.65	4.35±0.68	<0.001***
HbA1C (%) (4.0-6.0)	6.84±0.482	5.31±0.487	<0.001***
Total Cholesterol (mmol/L) (<5.2)	4.68±0.96	3.99±1.01	<0.001***
Triglycerides (mmol/L) (0.40-1.60)	2.42±1.22	1.56±0.87	<0.001***
LDL-Cholesterol (mmol/L) (<2.50)	2.46±0.77	2.17±0.72	<0.05*
HDL-Cholesterol (mmol/L) (>0.90)	1.04±0.224	1.21±0.222	<0.001***

Note: ***Significance at 0.001,
**Significance at 0.01 level, *Significance at 0.05 level

Table II. Comparison of Biochemical Characteristics between Cases and Controls in Females

Variables	Group A (Diabetic) n=30	Group B (Control) n=30	P-Value
BMI (kg/m^2)	28.68±1.90	24.84±1.91	<0.001***
FBG (mmol/L)	11.77±3.97	4.44±0.68	<0.001***
HbA1C (%)	6.91±0.58	5.41±0.45	<0.001***
Total Cholesterol (mmol/L)	4.89±0.98	4.31±0.84	<0.001***
Triglycerides (mmol/L)	2.58±1.07	1.72±1.06	<0.001***
LDL-Cholesterol (mmol/L)	2.47±0.92	2.42±0.64	0.84 NS
HDL-Cholesterol (mmol/L)	1.07±0.20	1.24±0.18	<0.001***

Note: ***Significance at 0.001,
**Significance at 0.01 level, *Significance at 0.05 level

Table II. Shows significant increase in levels of BMI, FBG, HbA1C, total cholesterol and TG in the diabetic females as compared to controls while HDL cholesterol was significantly lower in the diabetic group. In females LDL cholesterol showed no significance may be due the small sample size

Table III. Comparison Of Biochemical Characteristics between Cases and Controls In Males

Variables	Group A (Diabetic) n=30	Group B (Control) n=30	P-Value
BMI (kg/m^2)	28.46±2.08	24.08±2.64	<0.001***
FBG (mmol/L)	10.69±3.28	4.25±0.68	<0.001***
HbA1C (%)	6.76±0.34	5.22±0.51	<0.001***
Total Cholesterol (mmol/L)	4.47±0.90	3.67±1.08	<0.01**
Triglycerides (mmol/L)	2.27±1.36	1.40±0.62	<0.01**
LDL-Cholesterol (mmol/L)	2.45±0.63	1.82±0.72	0.001***
HDL-Cholesterol (mmol/L)	1.02±0.24	1.19±0.25	<0.01**

Note: ***Significance at 0.001,
**Significance at 0.01 level, *Significance at 0.05 level

Table III. Shows significant increase in levels of BMI, FBG, HbA1C, Total cholesterol, TG and LDL cholesterol in diabetic males as compared to controls while HDL cholesterol was lower in the diabetic males.

Discussion

Diabetes mellitus is a commonest systemic metabolic disorder. Prevalence of diabetes in Pakistan is very high ranging from 7.6-11% in its different regions. It is expected that number of diabetic patients may increase from 5.2 million in 2000 to 13.9 million by the year 2030. Cardiovascular disease is a major cause of morbidity and mortality in both men and women with T2DM. In patients with T2DM, risk factors like dyslipidemia and hypertension plays a major role in inducing cardiovascular disease and control of these factors is of paramount importance.

The main observation of this study is increased serum Total Cholesterol (p<0.001) & LDL Cholesterol (p<0.05) in diabetic patients. This is in agreement with study carried out by V.Siva Prabodh et al in 2012 which also showed that the frequencies of Total Cholesterol, Triglyceride and LDL-Cholesterol are higher in the diabetic group(p<0.001). [23] However mean serum Total Cholesterol and mean serum LDL Cholesterol was not as high in our study group as compared to study carried out by Narisimhaswamy KN in 2014. [24] This is probably because of limited sample size of our study. The other observation of our study is increased serum Triglyceride levels in our patients (p=<0.001) as compared to the control population. This is in accordance with the prior study done by V.Siva Prabodh et al in 2012 & Narisimhaswamy KN in 2014. Another important observation of our study is decreased serum HDL Cholesterol levels in diabetic patients (p=<0.001) as compared to healthy controls. This is in correspondence with results obtained by Deepa Singh et al. in 2015 showing that HDL-Cholesterol was significantly lower in diabetic patients (p< 0.005). [25] This study also compared the BMI of the T2DM patient's vs healthy controls. BMI is significantly raised in T2DM patients (p<0.001). Similar results were also shown by Dr Ratna et al in 2015 quoting that obesity leads to insulin resistance which in turn causes T2DM and both together leads to dyslipidemia. [26] Hypercholesterolemia and hypertriglyceridemia are the lipid abnormalities that occur in T2DM, which is the major cause of cardiovascular diseases. Blood glucose levels and lipid profile monitoring should be done routinely. Life style modifications including weight reduction, regular exercise and use of lipid lowering drugs are recommended in these patients.

Limitations of our study was small sample size. Future work with larger sample size and of longer duration is recommended.

Conclusion

Based on the findings of current study it is concluded that serum total cholesterol, triglycerides and LDL cholesterol levels are significantly raised in T2DM whereas serum HDL cholesterol levels are significantly decreased which might be the reason for high coronary disease incidence in T2DM.

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