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DIABETIC DYSLIPIDEMIA: A TWO EDGED SWORD

Garima Charak[1], Tauseef Nabi[2*], Nadeema Rafiq[1]

[1]Department of Physiology, [2]Department of Medicine, MM Institute of Medical Sciences and Research, Mullana, Ambala, Haryana 133207, India.

ABSTRACT

Patients with type 2 diabetes have an increased prevalence of lipid abnormalities. A timely intervention to normalize circulating lipids could reduce the chances of cardiovascular complications. This aim was to evaluate the frequency and pattern of dyslipidemia and effect of age on alteration of lipid profile in male type 2 diabetes. A prospective study was conducted for investigation of the serum lipid profile viz the level of total cholesterol, Triglycerides, LDL cholesterol and HDL cholesterol and compare them with non obese non diabetic and normotensive control. The result revealed that serum total cholesterol, LDL cholesterol and triglycerides were significantly raised ($p<0.001$) where as the level of HDL cholesterol was significantly lower ($p<0.001$) in diabetic subjects as compared to control. The fasting blood sugar level of the diabetics was significantly higher ($P < 0.001$) than those of the controls. 21% diabetics in this study had hypercholesterolemia, 58% hypertriglyceridemia, 18% abnormal LDL levels and in 17% the HDL was less than 40 mg/dl. 63% of diabetic patients were dyslipidemic as compared with 12% of control patients. Of the dyslipidemic diabetic subjects (70%) were aged >50 years. Serum total cholesterol and LDL cholesterol were significantly raised ($P< 0.001$) where as the level of HDL cholesterol was significantly lower ($P< 0.0049$) in diabetic subjects aged more than 50 years as compared to diabetic subjects aged less than 50 years revealing increasing age is associated with severe and higher risk of dyslipidemia. The frequencies of high TC, high TG, and high LDL were higher in the diabetic group and thus indicating that diabetic patients are more prone to dyslipidemia which could cause cardiovascular disease. Thus lipid profile analysis must be made an integral part of type 2 DM patients' clinical reviews and treatment. Therefore early detection good glycaemic control can prevent development and progression of lipid-abnormalities among patients with diabetes mellitus.

Key Words:- Diabetes, cholesterol, triglycerides, HDL cholesterol and LDL cholesterol.

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic diseases characterized by increase blood glucose level resulting from defects in insulin secretion, insulin action, or both (American Diabetes Association, 2005). Diabetes mellitus is a hereditary, chronic and endocrine metabolic disorder which causes deaths worldwide (Faghilimnai S *et al*., 2006). Certain ethnic and racial groups of Africa and Asia have a greater risk of developing diabetes (Manu A *et al*., 2007). India, a developing Asian country with fast industrialization and a modern lifestyle is facing a grave problem in having the largest number of people with diabetes (King H *et al*., 1998; Fall CH, 2001). Which is estimated to reach 80 million by the year 2030 (Bjork S *et al*., 2003; Rao CR *et al*., 2010). It is close to becoming the diabetic capital of the world. The major risk factors for Type 2 Diabetes mellitus are obesity (>120% ideal body weight or a body mass index >30 kg/m^2) and a sedentary lifestyle (Van Dam RM, 2003).

Dyslipidemia is elevation of plasma cholesterol, triglycerides (TGs) or both or a low high density lipoprotein (HDL) level that contributes to the development of atherosclerosis. Hyperglycemia and

Corresponding Author

Tauseef Nabi
Email:- dr.tauseefnabi@gmail.com

atherosclerosis are related in type-2 diabetes (Devrajani BR *et al*., 2010). Persistent hyperglycemia causes glycosylation of all proteins, especially collagen cross linking and matrix proteins of arterial wall. This eventually causes endothelial cell dysfunction, contributing further to atherosclerosis. The prevalence of dyslipidemia in diabetes mellitus is 95% (Chattanda SP *et al*., 2008). Dyslipidemia is generally present at the time of diagnosis of type 2 diabetes and persists despite treatment of hyperglycemia.

Dyslipidemia is a well recognised and modifiable risk factor that should be identified early to institute aggressive cardiovascular preventive management (Keech A *et al*., 1984). The most typical lipoprotein pattern in diabetes, also known as diabetic dyslipidemia or atherogenic dyslipidemia consists of moderate elevation in triglyceride levels and small dense LDL particles and low HDL cholesterol values (Smith JM *et al*., 2013). Insulin impacts the liver apolipoprotein production which regulates the enzymatic activity of lipoprotein lipase and cholesterol ester transport protein. These could be the likely causes of dyslipidemia in Diabetes mellitus as reported by Goldberg (1996). Over and above this, insulin deficiency also reduces the activity of hepatic lipase and several other steps in the production of biologically active lipoprotein lipase may also be altered in DM (Tavangar K *et al*., 1992)

It may be present at the diagnosis of type 2 Diabetes mellitus and is a component of the metabolic syndrome and the determination of the serum lipid levels in people with diabetes is now considered as a standard of the diabetes care. The dyslipidemia is a major risk factor for coronary heart disease (CHD) (Krishna P *et al*., 2005). The cardiovascular disease (CVD) is a cause of morbidity and mortality in patients with diabetes mellitus because of disturbance in lipoproteins. Thus the management of diabetic dyslipidemia is a key approach in preventing CVD in individuals with Type 2 Diabetes Mellitus. This research aims to determine the influence of diabetes on lipid profile (dyslipidemia) of affected subjects. Early detection and treatment of hyperlipidemia in diabetes mellitus can prevent the progression of lipid abnormalities and minimize the risk for atherogenic cardiovascular disorder and cerebrovascular accident. Initial therapy for dyslipidemia include dietary changes, as well as lifestyle modifications (smoking cessation, blood pressure control, weight loss, increased physical activity) and lipid lowering drugs.

MATERIALS AND METHODS

For this study, a total of 120 non obese, non hypertensive male subjects aged 33-65 years with no other cardiovascular, renal or thyroid ailments reporting to OPD of Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana (Ambala) were included.

Control: 60 subjects (Males) having normal blood sugar and no other metabolic disease were selected as control.

Case: The remaining 60 subjects (Males) having high blood sugar levels were diagnosed as diabetics. Only patients with known diagnosis of Type 2 DM of recent onset were included (duration < 1 year).

Exclusion Criteria

Patients with known diagnosis of Type 2 DM for > 1 year
Patients with known diagnosis of Type 1 DM
Female subjects
Hypothyroidism
Chronic renal failure, Nephrotic syndrome
Familial hypercholesteremic syndromes.
Patients already on lipid lowering drugs.
Hypertension
Subjects using Alcohol and smoking
BMI more than 30 kg/m^2

After obtaining informed consent from patients, detailed history was taken followed by thorough physical examination and laboratory investigations as under –

About 5ml of venous blood sample was collected from patient/control after 8-12 hrs of fasting from antecubital vein and analysed for estimation of fasting blood glucose and lipid profile (TG, LDL, HDL and TOTAL CHOLESTEROL).

Estimation of serum glucose by Glucose oxidase-peroxidase method. Serum total cholesterol level was determined by enzymatic (CHOD-PAP) colorimeter method. Triglyceride by enzymatic (GPO-TRINDER) method. HDL-cholesterol was estimated using precipitant method. LDL-cholesterol by Friedewald formula.

LDL CHOLESTEROL = (Total cholesterol)-(HDL cholesterol)-(Triglyceride)/5

For serum lipid reference level, National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline was referred. According to NCEP-ATP III guidelines, hypercholesterolemia is defined as TC > 200 mg/dl, high LDL when value > 100 mg / dl, hypertriglyceridemia as TG > 150 mg/dl and low HDL when value < 40 mg/dl. Dyslipidemia was defined by presence of one or more than one abnormal serum lipid concentration (Menik HL *et al*., 2005).

All values were expressed as mean±S.E.Statistical analysis was carried out by using student's.t test

RESULTS

The mean age of the subjects was 50.0 ± 10.7 and 48.2 ± 9.2 years for the diabetic and the control groups respectively. All diabetic males show significant increase in serum cholesterol ($p<0.001$), triglyceride ($p<0.001$), LDL ($p<0.001$) and significantly lower HDL cholesterol ($p <0.001$) as compared to non-diabetic males. The fasting blood sugar level of the diabetics was significantly higher ($P < 0.001$) than those of the controls.

The result revealed that serum total cholesterol, LDL cholesterol and triglycerides were significantly raised where as the level of HDL cholesterol was significantly lower in diabetic subjects as compared to control. The present study also analyzed the prevalence rate of hypercholesterolemia, hypertriglyceridemia, high LDL and low HDL among type 2 diabetics. It was found that (13)21% diabetics in this study had hypercholesterolemia, (35)58% hypertriglyceridemia and (11)18% abnormal LDL levels. In (10)17% of type 2 diabetics, the HDL was less than 40 mg/dl. (38) 63% of diabetic patients were dyslipidemic as compared with (7)12% of control patients. Of the dyslipidemic diabetic subjects (70%) were aged >50 years. Serum total cholesterol and LDL cholesterol were significantly raised ($P< 0.001$) where as the level of HDL cholesterol was significantly lower ($P< 0.0049$) in diabetic subjects aged more than 50 years as compared to diabetic subjects aged less than 50 years revealing increasing age is associated with severe and higher risk of dyslipidemia.

Table 1. Comparison of lipid profile between Diabetic male and non diabetic Control male

	Diabetic male n=60	Control male n=60	*P - value*
Cholesterol (mg/dl)	214.46 ±31.75	167.33 ±16.19	0.0001
Triglycerides (mg/dl)	185.80 ±31.01	128.50 ±11.59	0.0001
LDL cholesterol (mg/dl)	138.03 ±28.53	100.63 ±14.69	0.0001
HDL cholesterol (mg/dl)	31.06 ±8.75	41.13 ±4.29	0.0001
Glucose (mg/dl)	193.52± 75.	90.60± 11.00	0.0001

Table 2. Comparison of lipid profile between Diabetic male on the basis of age

Diabetic	Age >50 years n=42	Age < 50 years n=18	*P - value*
Cholesterol (mg/dl)	244.40 ±21.75	210.45 ±14.10	0.0001
Triglycerides (mg/dl)	204.80 ±28.0	196.50 ±19.0	0.2562
LDL cholesterol (mg/dl)	143.03 ±26.50	112.63 ±22.70	0.0001
HDL cholesterol (mg/dl)	27.06 ±6.45	32.13 ±5.34	0.0049

DISCUSSION AND CONCLUSION

The present study comprised of a random sample of population, which has been selected on criteria based on non-obese, non-diabetic and normotensive volunteers as control. Patients with type 2 diabetes mellitus are usually dyslipidemic, even when under relatively good glycemic control. The high levels of insulin and insulin resistance associated with type 2 diabetes has multiple effects on fat metabolism: (1) a decrease in lipoprotein lipase (LPL) activity resulting in reduced catabolism of chylomicrons and very low density lipoprotein (VLDLs), (2) an increase in the release of free fatty acid from the adipose tissue, (3) an increase in fatty acid synthesis in the liver, and (4) an increase in hepatic VLDL production (Dan L *et al*., 2012). Patients with type 2 diabetes mellitus have several lipid abnormalities, including elevated plasma triglycerides (due to increased VLDL and lipoprotein remnants), elevated levels of smaller dense LDL, and decreased plasma levels of HDL (Haffner SM, 1998). A strong clustering risk for coronary artery disease has been observed in diabetic subjects.

All diabetic males show significant increase in serum cholesterol ($p>0.001$), triglyceride (($p>0.001$), LDL ($p>0.001$) and significantly lower HDL cholesterol ($p>0.001$) as compared to non-diabetic (control) males. These observed increase and decrease in serum lipid profile associated with diabetes mellitus are in agreement with findings of (Onwuliri *et al*., 2004; Uddin *et al*., 1995; Idogun *et al*., 2007 and Albrki *et al*., 2007).

38(63%) of diabetic patients were dyslipidemic as compared with 7(12%) of controls. According to the CDC, 97% of adults with diabetes have one or more lipid abnormalities while the prevalence of diabetic dyslipidemia varies from 25% to 60% in various studies (Hidron AI *et al*., 2008). The reason for difference in dyslipidemic may be due to difference in the dietary habits as now more patients are aware of their physical well-being and changing dietary habits. Increasing use of cooking oils in place of vanaspati ghee has also contributed to the change in lipid profile. Another reason is increasing literacy rate and life style modification by most of the people and possibly genetic variation.

Serum total cholesterol and LDL cholesterol were significantly raised (P< 0.001) where as the level of HDL cholesterol was significantly lower (P< 0.0049) in diabetic subjects aged more than 50 years as compared to diabetic subjects aged less than 50 years revealing increasing age is associated with severe and higher risk of dyslipidemia.

Of the type 2 diabetics dyslipidemic subjects (78%) were aged >50 years. It was found that 58% diabetics had hypertriglyceridemia, 21% had hypercholesterolemia, and 18% abnormal LDL levels. In 17% of type 2 diabetics, the HDL was less than 40 mg/dl. Thus hypertriglyceridemia was most common abnormality followed by hypercholesterolemia, high LDL and low HDL. Similar pattern was revealed was by Mumtaz et al in the study type 2 diabetes mellitus and lipid abnormalities in 2010 (Mumtaz Ali, 2001).

Type of dyslipidemia reported among diabetic population is numerous in different places of world indicating that dyslipidemia can be influenced by the interaction of genetic and environmental factors. Our study showed that 58% of the diabetic population had hypertriglyceridemia which is almost similar to prevalence rates of hypertriglyceridemia among type 2 diabetic Punjabi population (53%) (Carlos A *et al*., 2001) and (54%) in Mexican nationwide survey (Singh G *et al*., 2012).

In diabetes many factors affect blood lipid levels, this is because carbohydrates and lipid metabolism are interrelated to each other if there is any disorder in carbohydrate metabolism it also leads disorder in lipid metabolism so there is high concentration of cholesterol and triglyceride and due to this there is reduction in HDL cholesterol levels. Therefore early detection, good glycaemic control can prevent development and progression of lipid-abnormalities among patients with diabetes mellitus. Initial therapy for dyslipidemia include dietary changes, as well as lifestyle modifications (smoking cessation, blood pressure control, weight loss, increased physical activity) and lipid lowering drugs (Dan L *et al*., 2001).

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