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Association of Dyslipidaemia and Ischaemic Heart Disease in Type II Diabetes Mellitus Patients: A Prospective Study.

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ABSTRACT

Background: In developed countries, most dyslipidemias are hyperlipidemias; that is, an elevation of lipids in the blood. This is often due to diet and lifestyle. Prolonged elevation of insulin levels can also lead to dyslipidemia. The aim of present research is to study the array of dyslipidaemia and varied clinical display of ischaemic heart disease, its risk factors in type 2 diabetes mellitus patients. **Methods:** A total of 100 patients of age >30 years were conscripted over a period of one year. The study included patients diagnosed to have type 2 diabetes mellitus irrespective of symptoms suggestive of ischaemic heart disease. Results on measurements were presented on Mean ± SD and in number (%), respectively. Significance was assessed at 5% level of significance. Student's t-test and Chisquare/ Fisher exact test used to find the significance of study parameters on categorical scale between two or more groups. **Result:** Incidence of IHD was found to be 42% with a male predominance. Evaluation of risk factors has shown its strong association with IHD. Incidence of IHD was high when low HDL (P <0.001), increased TC, TG, LDL (P<0.001), which were statistically significant. However, BMI >25 had negatively significant association with IHD in type 2 diabetics. **Conclusion:** The current study points out that there exists an increased incidence of ischaemic heart disease in diabetics with few, but not all risk factors contributing to it. Early detection, optimal glycaemic control, reduction of risk factors and patients education can reduce the mortality and morbidity.

Keywords: Dyslipidaemia, Ischaemic Heart Disease, Type II Diabetes Mellitus.

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic disorders in which there are high blood sugar levels over a prolonged period. Symptoms of high blood sugar include frequent urination, increased thirst, and increased hunger. If left untreated, diabetes can cause many complications. Acute complications can include diabetic ketoacidosis, hyperosmolar hyperglycemic state, or death. Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, and damage to the eyes.[1]

Diabetes is due to either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced. There are three main types of diabetes mellitus: 1) Type 1 DM results from the pancreas's failure to produce enough insulin. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes". The cause is unknown. 2) Type 2 DM begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses a lack of insulin may also develop. This form was previously referred to as "non-insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". The most common cause is excessive body weight and not enough exercise. 3) Gestational diabetes is the third main form and occurs when pregnant women without a previous history of diabetes develop high blood sugar levels.[2-5]

Type 2 DM is characterized by insulin resistance, which may be combined with relatively reduced insulin secretion. The defective responsiveness of body tissues to insulin is believed to involve the insulin receptor. However, the specific defects are not known. Diabetes mellitus cases due to a known defect are classified separately. Type 2 DM is the most common type of diabetes mellitus. Type 2 DM is primarily due to lifestyle factors and genetics. A number of lifestyle factors are known to be important to the development of type 2 DM, including obesity (defined by a body mass index of greater than 30), lack of physical activity, poor diet, stress, and urbanization. Excess body fat is associated with 30% of cases in those of Chinese and

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Japanese descent, 60–80% of cases in those of European and African descent, and 100% of Pima Indians and Pacific Islanders. Even those who are not obese often have a high waist–hip ratio.[6-13]

Dyslipidemia is an abnormal amount of lipids (e.g. triglycerides, cholesterol and/or fat phospholipids) in the blood. In developed countries, most dyslipidemias are hyperlipidemias; that is, an elevation of lipids in the blood. This is often due to diet and lifestyle. Prolonged elevation of insulin levels can also lead to dyslipidemia. Likewise, increased levels of O-GlcNAc transferase (OGT) may cause dyslipidemia.[14,15]

Basic researchers classify dyslipidemias in two distinct ways: a) Presentation in the body (including the specific type of lipid that is increased) b) Underlying cause for the condition (genetic, or secondary to another condition). This classification can be problematic, because most conditions involve the intersection of genetics and lifestyle issues. However, there are a few well-defined genetic conditions that are usually easy to identify.[8,9]

Coronary artery disease (CAD), also known as ischemic heart disease (IHD), is a group of diseases that includes: stable angina, unstable angina, myocardial infarction, and sudden cardiac death. Risk factors include: high blood pressure, smoking, diabetes, lack of exercise, obesity, high blood cholesterol, poor diet, depression, and excessive alcohol. The underlying mechanism involves reduction of blood flow and oxygen due to atherosclerosis of the arteries of the heart.[16,17]

The aim of present research is to study the array of dyslipidaemia and varied clinical display of ischaemic heart disease, its risk factors in type 2 diabetes mellitus patients.

MATERIALS AND METHODS

A total of 100 patients of age >30 years attending the diabetic clinic or admitted into medical wards, ICU of tertiary care centre were conscripted over a period of one year. The study included patients diagnosed to have type 2 diabetes mellitus irrespective of symptoms suggestive of ischaemic heart disease. Patients were informed about the study and written consent was taken. A clinical valuation was made for selection of patients with type 2 DM and those often exhibits the features like- develop diabetes after the age of 30 yrs. A) Usually obese (80% are obese, but elderly individuals may be lean), b) may not require insulin therapy initially, c) may have associated conditions such as insulin resistance, hypertension, cardiovascular disease, dyslipidaemia or polycystic ovarian syndrome.

Exclusion criteria

a) Type 1 diabetes mellitus,
b) Women with gestational diabetes mellitus,
c) Patients with pulmonary embolism, cor pulmonale, rheumatic heart disease and congenital heart disease,
d) Patients with acute pericarditis and acute myocarditis.

A baseline Electrocardiogram (ECG) was taken in all cases irrespective of clinical evidence of cardiac involvement. Patients with normal ECG pattern were further evaluated by Treadmill Testing (TMT or stress test) for subclinical cardiac involvement. A detail general and systemic examination was done for all the patients.

Criteria for selection of patients:

a) Diabetes Mellitus- As per WHO criteria, people with fasting glucose levels from 6.1 to 6.9 mmol/l (110 to 125 mg/dl) are considered to have impaired fasting glucose. People with plasma glucose at or above 7.8 mmol/l (140 mg/dl), but not over 11.1 mmol/l (200 mg/dl), two hours after a 75 g oral glucose load are considered to have impaired glucose tolerance. Of these two pre-diabetic states, the latter in particular is a major risk factor for progression to full-blown diabetes mellitus, as well as cardiovascular disease.

b) Ischaemic Heart Disease Angina- The patients with symptoms of angina with or without ECG changes. Asymptomatic patients with typical ECG changes for silent ischaemia were also included.

c) Acute Myocardial Infarction- (i) The patients with typical symptoms and signs of acute myocardial infarction with ECG changes. (ii) Asymptomatic patients with ECG changes suggestive of acute MI (silent MI). (iii) In patients with typical symptoms of acute MI, but whose ECG is unequivocal, the diagnosis of acute MI was made based on the levels of cardiac enzymes.

d) Latent Coronary Artery Disease (Stress Test)- Modified Bruce protocol was used for stress test as it can be used in old age patients and patients with decreased exercise capacity. Test was considered positive if following criterias were satisfied.

1. Horizontal or down slopping ST depression of 1 mm or greater at 80 ms from J point (1.5 mm if it is up sloping).
2. ST segment elevation of 1 mm or more than the control tracing in any lead except aVR.
3. In the presence of ST depression in the control tracing, additional depression of 1 mm more than the rest.
4. ST segment depression for greater than 5 mins during recovery period.
5. Abnormal blood pressure response.
6. Ventricular arrhythmias.

Stress Test was Terminated if-

1. Anginal pain is progressive.
2. Drop in systolic blood pressure below the resting value or non-raising systolic BP with continued exercise.
3. Frequent VPC's developing in pairs or with increasing frequency as exercise increases or when ventricular tachycardia or ventricular fibrillation develops.

4. Onset of second or third-degree heart block.
5. Marked ST segment depression (>3 mm).
6. ST segment elevation of 2 mm or more.
7. Patients are unable to continue because of dyspnoea, fatigue or dizziness.
8. Development of bundle-branch block that cannot be distinguished from ventricular tachycardia.

Congestive Cardiac Failure

1. The patients were selected with typical signs and symptoms like exertional breathlessness, easy fatigability and clinical signs of cardiomegaly, pulmonary oedema and tender hepatomegaly and raised JVP.
2. Patients with radiographic and/or electrocardiographic/echo evidence of cardiomegaly.

f) Arrhythmias- was based on ECG criteria.

g) Hypertension- As per the Seventh US Joint National Committee (JNC 7) criteria. The patients were categorised as hypersensitive if he is in stage I or stage II.

Normal	<120	<80
Prehypertension	120-139	80-89
Stage I	140-159	90-99
Stage II	>160	>100

Results on measurements were presented on Mean ± SD and in number (%), respectively. Significance was assessed at 5% level of significance. Student's t-test (two tailed, independent) has been used to find the significance of study parameters (on continuous scale between two groupsintergroup analysis) on metric parameters, Chisquare/ Fisher exact test used to find the significance of study parameters on categorical scale between two or more groups. Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver. 2.11.1 were used for the analysis of the data.

RESULTS

There were a total of 100 subjects, 64% were males and 36% were females. The mean age of patients was 56.2 years; maximum number of patients (74%) in the study group was in the age group of 41-60 years [Figure 1]. The mean BMI in males was 23.77 and in females was 22.1 kg/m2, respectively [Figure 2]. Difference in both the parameters was statistically insignificant (p<0.05).

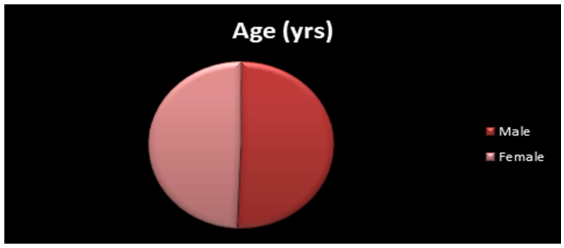

Figure 1: Demographic age of patients.

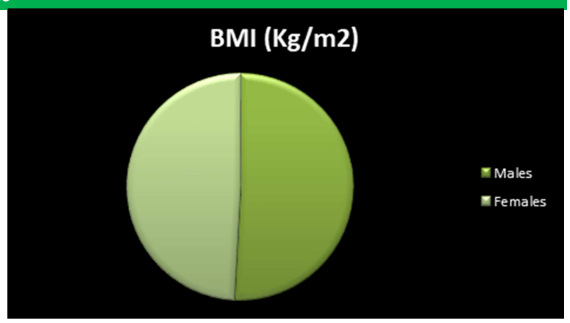

Figure 2: Comparison of BMI in both genders.

The mean fasting blood sugar and postprandial blood sugar in the study group was 190.2 mg% and 262.6 mg%, respectively [Figure 3]. Difference in blood sugar levels was statistically insignificant (p<0.05).

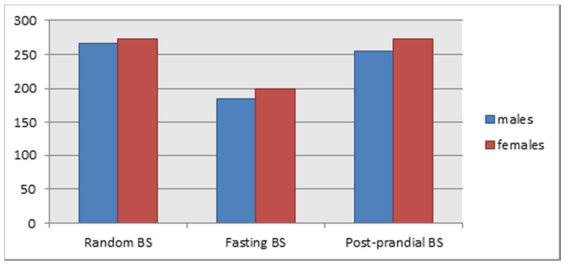

Figure 3: Graphical comparison blood sugar in Male and Female.

The mean total cholesterol, LDL cholesterol HDL cholesterol, triglyceride level and non-HDL cholesterol in the present study was 208.1 mg%, 117.5 mg%, 40.2 mg% and 163.4 mg%, 168 mg%, respectively, [Figure 4]. Mean total cholesterol, LDL cholesterol and triglycerides were higher in patients with CAD and HDL cholesterol was lower in patients with CAD when compared with patients without CAD, which was statistically significant. Therefore, the above mentioned factors were risk factors for CAD in patients with type 2 diabetes mellitus.

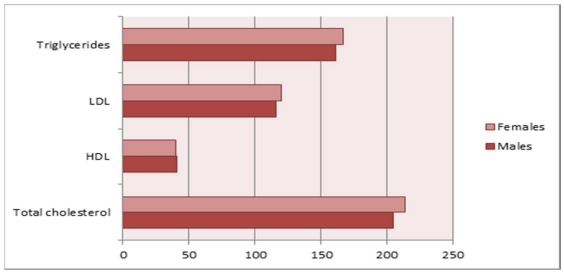

Figure 4: Graphical comparison lipid profile in Male and Female.

Table 1: Mean Lipid Parameters Patients with and without CAD.

Parameters	Coronary artery disease		p value
	Absent	Present	
Total cholesterol (mg/dl)	196±2.1	229±4.0	<0.05*
LDL(mg/dl)	114±5.1	119±7.4	<0.05*
HDL(mg/dl)	44±1.8	39±8.2	<0.05*
Triglycerides(mg/dl)	146±2.5	189±1.7	<0.05*

<0.05*- Significant

The mean total cholesterol, LDL cholesterol and triglyceride and HDL-cholesterol levels were 229mg%, 119mg%, 189mg%, 39mg%, respectively in CAD patients [Table 1]. The mean HDL-cholesterol in females was less than in males. The mean total cholesterol and triglyceride levels were higher in females when compared to males.

DISCUSSION

Limitation of blood flow to the heart causes ischemia (cell starvation secondary to a lack of oxygen) of the myocardial cells. Myocardial cells may die from lack of oxygen and this is called a myocardial infarction. It leads to heart muscle damage, heart muscle death and later myocardial scarring without heart muscle regrowth. Chronic high-grade stenosis of the coronary arteries can induce transient ischemia which leads to the induction of a ventricular arrhythmia, which may terminate into ventricular fibrillation leading to death.[5,9,14]

Typically, coronary artery disease occurs when part of the smooth, elastic lining inside a coronary artery (the arteries that supply blood to the heart muscle) develops atherosclerosis. With atherosclerosis, the artery's lining becomes hardened, stiffened, and swollen with calcium deposits, fatty deposits, and abnormal inflammatory cells – to form a plaque. Deposits of calcium phosphates (hydroxyapatites) in the muscular layer of the blood vessels appear to play not only a significant role in stiffening arteries but also for the induction of an early phase of coronary arteriosclerosis.[3,9]

Hundred patients of diabetes mellitus were studied in our series, among which 60 were males and 40 were females (ratio of male:female was 1.5:1). The mean age of patients was 56.11 ± 10.89 years (males 56.47 ± 11.66 years and female 55.68 ± 9.75 years). The mean duration of diabetes mellitus was 8.66 years, (8.95 years in males and 8.23 years in females). In the present study, it was observed that type 2 diabetic patients had poor glycaemic control, which was reflected by higher values of fasting and post prandial blood sugar.

Gupta et al have reported in their study a prevalence of 36.3% of latent coronary artery disease. Among 25 patients of myocardial infarction,[12] 10 patients were males and 15 patients were females. Females out-numbered the males in this study, which correlates with the study of Partamian et al.[13] 13 out of 25 patients had evidence of anterior/anterolateral infraction (52%). 5 patients (20%) had evidence of inferior wall myocardial infarction. 2 patients had evidence of inferior wall myocardial infarction with right ventricular extension. 5 patients had subendocardial infarction (20%). Out of the 25 patients with myocardial infarction, 9 patients (36%) presented with atypical manifestations/silent infarction, which was detected by serial electrocardiographic recording. Our study correlates with study of Morgolis et al.[14] Other authors have estimated the occurrence of unrecognised myocardial infarction between 0-60%. The immediate mortality (within 1 week) in the present study among the 25 patients with myocardial infarction was 36%. 9 patients died within 1 week of admission; out of them, 5 died within 24 hours of admission. Partamian et al,[13] have reported immediate mortality among their patients to be 38% correlating with the present study.

The mean total cholesterol, LDL cholesterol and triglyceride and HDL-cholesterol, non-HDL cholesterol levels were 208.08 mg%, 117.88 mg%, 163.65 mg%, 40.67 mg%, and 168.06, respectively. The mean HDL-cholesterol in females was less than in males. The mean total cholesterol and triglyceride levels were higher in females when compared to males. Our study correlates with the Walia et al study.[11]

CONCLUSION

This study concludes that there is a high incidence of coronary artery disease with coronary risk factors in patients with diabetes mellitus. Early detection and treatment of hypertension can reduce the risk of cardiac complications. Diabetic dyslipidaemia also has strong association with it. Hypercholesterolaemia, high LDL cholesterol, hypertriglyceridaemia and low HDL cholesterol are all significant predictors of coronary artery disease in diabetes mellitus. All patients with type 2 diabetes mellitus should be screened for latent coronary artery disease as it has a prognostic implication.

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