CLINICAL STUDY ON PREVALENCE AND PATTERN OF DYSLIPIDEMIA IN TYPE 2 DIABETES MELLITUS PATIENTS IN A TERTIARY TEACHING HOSPITAL OF NORTH EAST INDIA

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BACKGROUND
Diabetes mellitus (DM) is a common secondary cause of dyslipidaemia, particularly if glycaemic control is poor, and can be an important risk factor for atherosclerosis and coronary artery disease and that can be a major cause of morbidity and mortality in diabetic patients. Our aim was to determine the prevalence and pattern of dyslipidaemia in patients with type 2 DM in this region.

METHODS
This study was carried out among 200 type 2 diabetic patients attending the Diabetic Clinic and indoor medicine department, North Bengal Medical College and Hospital, Darjeeling. Patients suffering from other known cause of secondary dyslipidaemia were excluded. Each patient's lipid profile and HbA1c results were estimated. The lipid profile included total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C). Patients with one or more of the above parameters outside the targets recommended by the National Cholesterol Education Programme (NCEP) guidelines were considered to have dyslipidaemia.

RESULTS
Of these 200 type 2 DM patients studied, 110 were male and 90 were female. The most prevalent lipid parameter not at target was triglyceride >150, HDL (<40 in male, <50 in female an LDL-C of ≥130 mg/dl in nearly 80% of patients). The most common pattern of dyslipidaemia was hypertriglyceridaemia, low HDL and combined dyslipidaemia. No significant relationship was found between HbA1c and any of the lipid parameters.

CONCLUSIONS
The vast majority of the type 2 diabetic patients studied had dyslipidaemia. Dyslipidaemia as a metabolic abnormality is frequently associated with diabetes mellitus and is a strong clustering risk factor for coronary artery disease in diabetic subjects. Measures should aim at controlling dyslipidaemia and at reducing the burden of coronary artery disease.

KEYWORDS
Diabetes Mellitus, Dyslipidaemia, Hypertriglyceridaemia, HDL, Combined Dyslipidaemia, Lipid Targets.


BACKGROUND
Type 2 diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action or both.1 The International Diabetes Federation has estimated that the number of people with diabetes worldwide in 2015 was 415 million and this is projected to reach 642 million by 2040.2 The long term macro vascular complications of diabetes contribute to the high morbidity and mortality associated with the disease with as many as 80% dying from some form of cardiovascular disease (CVD).3 Major risk factors for CVD include age, gender, hypertension (HT) and DM. Other lifestyle behaviours’ such as tobacco smoking, excessive alcohol consumption, sedentary lifestyle and poor diet with resultant obesity further contribute to elevating one’s CVD risk. Diabetic patients often suffer from HT and also have abnormal lipoprotein metabolism.3,4 Dyslipidaemia is one of the major risk factors for CVD in DM. The common pattern of dyslipidaemia is hypertriglyceridaemia and reduced HDL cholesterol levels and an increased concentration of small dense low-density lipoprotein (LDL) particles. This peculiar combination of lipid abnormalities is known as diabetic dyslipidaemia. Type 2DM patients have higher chances of developing coronary artery disease and cerebrovascular disease as compared to nondiabetics. It is believed that associated dyslipidaemia significantly imparts a role to higher prevalence of macro vascular disease that must be aggressively managed.

Cardiovascular disease (CVD) is the leading cause of death worldwide, and mortality due to CVD is higher in low- and middle-income countries.5,6 Diabetes is basically a...
lifelong disease and has no cure, if not controlled it becomes gradually progressive disease, develops multiorgan complications. Persons with persistent uncontrolled diabetes drastically reduce the quality of life and shortens life expectancy. To avoid complications, one must also tightly control blood pressure and dyslipidaemia besides keeping blood sugar under control. Studies on diabetic dyslipidaemia particularly in this region are a few or large-scale representative studies are lacking in recent time to assess the magnitude the problem.

**Abbreviations:**

- DM=Diabetes Mellitus
- TC= Total Cholesterol
- TG= Triglyceridermia
- LDL-C = Low density lipoprotein cholesterol
- HDL-C =High density lipoprotein cholesterol
- HT=Hypertension
- HbA1c = Glycosylated haemoglobin
- Pt = Patient
- CVD= Cardiovascular disease
- NBMC= North Bengal Medical College

**Definitions**

- Dyslipidaemia
  - National Cholesterol Education Programme (NCEP) guidelines were used for definition of dyslipidaemia as follows:
  - Hypercholesterolemia
    - Serum cholesterol levels >200 mg/dl (>5.2 mmol/l). Type 2DM patients have higher chances of developing coronary artery disease and cerebrovascular disease as compared to nondiabetics. It is believed that associated dyslipidaemia significantly imparts a role to higher prevalence of macro vascular disease that must be aggressively managed.
  - Hypertriglyceridermia
    - Serum triglyceride levels >150 mg/dl (>1.7 mmol/l). Low HDL cholesterol = HDL cholesterol levels, <40 mg/dl (1.04 mmol/l) for men and, <50 mg/dl (1.3 mmol/l) for women.
  - High LDL cholesterol
    - LDL cholesterol levels >130 mg/dl (>3.4 mmol/l).
  - Isolated Hypercholesterolemia
    - Serum cholesterol >200 mg/dl and and triglycerides <150 mg/dl.
  - Isolated Hypertriglyceridermia
    - Serum triglycerides >150 mg/dl and cholesterol <200 mg/dl. Isolated low HDL-C- HDL-C <40 mg/dl (1.04 mmol/l) for men and, <50 mg/dl (1.3 mmol/l) for women. Without hypertriglyceridermia or hypercholesterolemia.
  - Dyslipidaemia was classified into mixed dyslipidaemia (three abnormal parameters: high TG, low HDL-C as well as raised LDL-C), combined dyslipidaemia (any two abnormal parameters) and isolated (single parameter) dyslipidaemia (TC, TG, HDL-C or LDL-C).
- Diabetes
  - Individuals diagnosed by a physician and on antidiabetic medications (self-reported) and/or those who had fasting CBG >126 mg/dl (>7 mmol/L) and/or 2-hr post-glucose CBG value> 200 mg/dl (>11.1 mmol/L or HbA1c >6.5%).

**Aims and Objectives**

1. To study the prevalence and pattern of dyslipidaemia in patients with type 2 DM. (2) To determine the relationship (if any) between HbA1c and the lipid profile in type 2 diabetic patients.

**METHODS**

**Study Participants**

All T2DM patients were selected from diabetic clinic and indoor medicine department at North Bengal Medical College & Hospital, Darjeeling. Study included a total of 200 patients with 110 males and 90 females. Patients’ clinic files, the following clinical data were recorded: gender, age, sex, duration of DM, smoking status, height, weight (BMI), concomitant HT and medication pertaining to the management of their HT, DM and dyslipidaemia.

**Inclusion Criteria**

From February 2017 and January 2018.

**Exclusion Criteria**

1) Patient who are on dyslipidaemia drugs. 2) Pt's age below 20 yrs. above 80 yrs. 3) Type 1 diabetes mellitus, 4) Gestational diabetes, 5) Steroid induced diabetes or chronic pancreatitis as a secondary cause of DM. 6) Patients suffering from other causes of secondary dyslipidaemia such as overt hypothyroidism.

**Blood Sample Collection**

A fasting venous blood sample was collected, and lipids were measured. The samples were assayed for total cholesterol, Triglycerides and HDL cholesterol. LDL cholesterol. Total cholesterol (Esterase oxidase-peroxidase-aminopyrine method), serum triglycerides (glycerol phosphate oxidase-peroxidase-aminopyrine method), and high-density lipoprotein cholesterol (direct method polyethylene-glycol-pre-treated enzymes) were measured using the Beckman Coulter AU 2700/480 Auto-analysers (Beckman AU (Olympus), Ireland). Low and very low-density lipoproteins were calculated from Freidewald’s formula. All biochemical assays were carried out by the same team of laboratory technicians using the same method, throughout the study period. The samples were assayed for total cholesterol, triglycerides and HDL & LDL cholesterol.

**Statistical Analysis**

After collecting all data entry was done in Microsoft Excel. Data were organized and expressed as by applying principle of descriptive statistics. Categorical data was analysed using...
chi-square test and continuous variable analysed using Student t test and ANOVA where applicable. Appropriate statistical software was used for analysis.

Ethics Statement
Ethics committee approval of the Institution NBMC, was obtained prior to study commencement. Written informed consent was taken from all willing person. Anonymity and confidentiality was ensured.

RESULTS
Among the sample group of 200 diabetic patients, 110 were males and 90 females. The mean age of the sample was 52.89 years (SD=12.52). Prevalence of dyslipidaemia in our study population was 72% (144 pt among 200) of patients, among them 84 and 60 patients were males and females respectively. Over 52.77% of subjects in the age range of 35–50 years (male 38.19% & female 14.58%) had abnormalities in one of the lipid parameters with a male preponderance. Between 51 to 65 yrs. incidence was 39.58% (male 27.27%, female 11.8%).The youngest age group (20–24 years) and age between 65 to 80 yrs. also has dyslipidaemia (5.5%). (Table 1). Factors associated with dyslipidaemia included male gender, obesity, sedentary lifestyle, diabetes, dysglycaemia and hypertension.

The most prevalent lipid abnormality in our study was (Table 2); hypercholesterolemia was found in 23.6% (n= 34), hypertriglyceridemia in 66.66% (n= 96), low HDL-C in 50% (n=72) and high LDL-C in 29.2% (n= 42) of the cases. Hypertriglyceridemia (47.2% & 19.4% of male & female respectively), high LDL-C (20.83% & 19.4% male & female respectively) was more common in male but low HDL-C was more common in female cases. (23.6% & 26.38% of male & female respectively), (Table 3). Different types of dyslipidaemia according to age group shown in Table 3. Mean lipid profile value in diabetic patient were TC=220.48 ± 19.986; TG=208.12 ± 20.24; HDL-C= 34.60 ± 4.60; LDL-C=142.07 ± 15.75. (Table 4). The most common pattern of dyslipidaemia was a combined dyslipidaemia (any two abnormal lipid parameters) in a total of 46 of the 144 patients (31.94%). The most common pattern of combined dyslipidaemia was low HDL-C levels (<40 mg/dl in male 8.50 mg/dl in female)+ elevated TG (≥150 mg/dl) in 16.66%; elevated cholesterol + elevated TG in 6.95% of cases; elevated LDL-C levels (≥ 130/dl) + elevated TG (≥ 150 mg/dl) in 2.77%; elevated LDL-C levels (≥ 130/dl) + decreased HDL-C in 2.77% of cases. When we evaluated mixed pattern combined dyslipidaemia (three abnormal parameters) our result was about 16.66% of the adult population had mixed dyslipidaemia: high TC + high TG + raised LDL-C (8.33%), high TG + low HDL-C + raised LDL-C (2.77%); high TC + high TG + low HDL-C + raised LDL-C (4.16%) of cases. (Table 5).

HbA1C
The mean HbA1C in this study was 8.25% (SD 2.4); range 5.2–11%. The majority of the patients, 130 out of 200 (65%), had poor glycaemic control with an HbA1C of ≥7%. Only 70 patients (35%) had a target HbA1C of <7%. The majority of patients 114 (87.69%) among 130 patients had HbA1C levels >8%.Of these 130 patients with an HbA1C of ≥7 dyslipidaemia was seen in 46% and 70 patients with an HbA1C of <7%, 54% had dyslipidaemia outside the recommended levels.

<table>
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<th>Age Group</th>
<th>No. (total=144)</th>
<th>Male</th>
<th>Female</th>
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<tr>
<td>20-35</td>
<td>3</td>
<td>2</td>
<td>1</td>
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<tr>
<td>36-50</td>
<td>76(52.77%)</td>
<td>55(38.19%)</td>
<td>21(14.58%)</td>
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<td>51-65</td>
<td>57(39.58%)</td>
<td>40(27.27%)</td>
<td>17(11.8%)</td>
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<th>Variables Numbers</th>
<th>Prevalence (%=, %)</th>
<th>Male (%=, %)</th>
<th>Female (%=, %)</th>
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<tr>
<td>Total cholesterol &gt;200 mg/dl</td>
<td>34(23.6%)</td>
<td>18(12.5%)</td>
<td>16(11.1%)</td>
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<tr>
<td>Triglyceride &gt;150 mg/dl</td>
<td>90(66.6%)</td>
<td>68(47.2%)</td>
<td>28(19.4%)</td>
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<tr>
<td>HDL-C &lt;40 mg/dl</td>
<td>72(50%)</td>
<td>34(23.6%)</td>
<td>38(26.38%)</td>
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<td>LDL-C &gt;130 mg/dl</td>
<td>4(2.79%)</td>
<td>3(2.08%)</td>
<td>1(0.71%)</td>
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<th>Parameters</th>
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<tr>
<td>TC</td>
<td>220.48 ± 19.986</td>
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<tr>
<td>TG</td>
<td>208.12 ± 20.24</td>
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<td>HDL-C</td>
<td>34.60 ± 4.60</td>
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<tr>
<td>LDL-C</td>
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<th>Type</th>
<th>Total</th>
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<tr>
<td>Combined</td>
<td>46(31.94%)</td>
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<tr>
<td>mixed</td>
<td>24(16.66%)</td>
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<table>
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<tr>
<th>Table 1. Age Group Variation</th>
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<tr>
<td>Table 2. Prevalence Rate of Different Types of Dyslipidaemia</td>
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<td>Table 3. Mean Lipid Profile Value in Diabetic Patient</td>
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<td>Table 4. Breakdown of The Pattern of Dyslipidaemia</td>
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DISCUSSION
The aim of the present study was to focus on the prevalence and pattern of dyslipidaemia in diabetic patients in a tertiary medical care centre in north east zone of India. The relation between diabetes mellitus and serum lipid profile had been much discussed during the past decades. Dyslipidaemia as a metabolic abnormality is frequently associated with diabetes mellitus. Several authors reported a positive improvement in lipid profile with fair glycaemic control. In uncontrolled diabetic patients, it has been reported that the activity of lipoprotein lipase and hence clearance of VLDL-C in the circulation is diminished due to insulin resistance. Earlier studies also indicated a strong clustering risk factor for coronary artery disease in diabetic subjects. Cardiovascular risk factors in T2 DM are the common causes of morbidity and mortality in patients with diabetes. Similarly, our results reveal high prevalence of hypercholesterolemia, hypertriglyceridemia and high LDL-C levels & low HDL which are well known risk factors for cardiovascular diseases among patients. In a developing nation such as India, limited information is available about.

the prevalence of dyslipidaemia and hypertension in T2DM patients & studies in this area are also limited. The reasons for the high prevalence of dyslipidaemia in the cohort could be multifactorial. It may be partly attributed to the current trend toward urbanization and adoption of a western diet and lifestyle, which results in a higher incidence of type2 DM with related metabolic abnormalities. In our study more than 70% of patients with type 2 diabetes mellitus had one or more types of dyslipidaemia. Our results reveal high prevalence hypercholesterolemia (29.17%), hypertriglyceridemia (66.66%) and high LDL-C (29.17%) & low level of HDL (50%), which are well known risk factors for cardiovascular diseases. One striking finding was low HDL-C level more common in female but hypertriglyceridaemia in male patient.

A study among Asian Indian immigrants in the United States (n = 1038), reported a prevalence of hypercholesterolemia of 43.5%, hypertriglyceridemia of 42.3%, low HDL-C of 26.4% and high LDL-C of 41.4%. Similar rates were reported among Jordanian adults (n = 1121), with a prevalence of 48.8% of hypercholesterolemia 43.6% of hypertriglyceridemia, 40.1% of low HDL-C and 40.7% of high LDL-C. In a study conducted in Turkey, the authors reported that the prevalence of high TC, high triglycerides, low HDL-C and high LDL-C were 37.5%, 30.4%, 21.1% and 44.5% respectively. A study among rural adults in Pakistan (n = 1658), reported the prevalence of hypercholesterolemia, hypertriglyceridemia, low HDL-C and high LDL-C as 30.6%, 29.4%, 79.6% and 41.2% respectively. ICW INDIAB study by Shashank R. Joshi et al. showed 13.9% had hypercholesterolemia, 29.5% had hypertriglyceridemia, 73.2% had low HDL-C, 11.8% had high LDL-C levels and 79% had abnormalities in one of the lipid parameters. HDL-C was the most common lipid abnormality in all the four regions studied and 44.9% had isolated low HDL cholesterol in their study. Our study also had high prevalence of low HDL-C (50%). This study thus also confirms the findings of several earlier studies that Indians have high prevalence of low HDL cholesterol. Low HDL-C was positively associated with sedentary lifestyle, diabetes, female gender, generalized and abdominal obesity. This appears to be part of the Asian Indian phenotype. Which includes increased plasma insulin levels, insulin resistance, increased waist circumference, excess visceral fat and low adiponectin levels.

The most common pattern of combined dyslipidaemia (31.94%) in our study was low HDL-C levels + elevated TG in 16.66%; elevated cholesterol + elevated TG in 6.95% of cases; elevated LDL-C levels + elevated TG in 2.77%; elevated LDL-C + decreased HDL-C in 2.77% of cases. In our study about 16.66% of the adult population had mixed dyslipidaemia; among them high TC + high TG + raised LDL-C (8.33%); high TG + low HDL-C + raised LDL-C (2.77%); high TC+ high TG+ low HDL-C + raised LDL-C (4.16%); of cases; ICW INDIAB study by Shashank R. Joshi 1, et al. showed combined dyslipidemia in males was low HDL-C levels (≤ 1 mmol/l) and elevated LDL-C levels (≥ 1.8 mmol/l) (23.25%) and in females was an elevated TG (≥ 1.7 mmol/l) in combination with an elevated LDL-C level (19.29%) and About 7.7% (n =158) of the adult population had three lipid abnormalities (hypercholesterolemia + hypertriglyceridemia + low HDL-C) and 4.8% (n= 99) of the population had all four lipid abnormalities (hypercholesterolemia + hypertriglyceridemia + low HDL-C + high LDL-C). Only 21.1% (n= 431) had no lipid abnormality.

Limitations
A few limitations of our study are the small sample size, short period of study, regional differences, religion, diet pattern etc. those are also may be the cause of minor difference in results with other studies in different areas.

CONCLUSIONS
Dyslipidaemia is a strong cardiovascular disease risk factor (CVD) and is commonly associated with type 2 diabetes. Both compounded the risk of accelerated atherosclerosis, micro and macrovascular complications. The depressing scenario in our country is that a large no of patients is not subjected to periodic lipid profile estimation. Therefore, it is of utmost importance and requires an integrated approach to maintain euglycemia along with special emphasis on dyslipidaemia management in diabetes patient to reduce CVD risk and diabetes related morbidity and mortality.

REFERENCES


