Prevalence of dyslipidemia in patients with type 2 diabetes mellitus: a hospital based study in Kishanganj, India

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ABSTRACT

Background: A major risk factor for cardiovascular disease in type 2 diabetes mellitus (T2DM) is dyslipidemia characterized by high plasma triglyceride (TG), low HDL and increased LDL. Early detection of dyslipidemia in T2DM helps in the management and prevention of cardiovascular disease. The present study is based on the detection of anomalous lipid profile in T2DM patients.

Methods: A total of 35 T2DM patients with fasting blood glucose (FBG) > 110 mg/dL, and 32 subjects with FBG (70-110 mg/dL) were considered as controls. Serum samples were assayed for determination of the levels of total Cholesterol (TC), HDL, LDL, TG, and VLDL. Variables were compared between T2DM subjects and controls, with statistical significance at p < 0.05.

Results: The prevalence of dyslipidemia was 12 (34.29%) and 9 (25.71%) with abnormal lipids levels of TC and TG respectively whereas 11 (31.43%), 12 (34.29), and 9 (25.71%) were found with lipoprotein abnormalities of HDL, LDL and VLDL respectively in T2DM subjects either singly or in combination. The serum parameters TC, TG, HDL, LDL, and VLDL were significantly correlated with FBG levels in both diabetic and non-diabetic subjects. The variables were also significantly associated among each other in T2DM patients.

Conclusion: The present study provides evidence to suggest that lipid variables are associated with each other in T2DM patients among the population of Kishanganj, India.

Keywords: Lipid profile, Type 2 diabetes mellitus, Dyslipidemia

INTRODUCTION

The constellation of abnormalities caused by insulin deficiency due to dysregulation of insulin release from the B cells, along with insulin resistance in peripheral tissues such as skeletal muscle, brain, and liver is called Type 2 diabetes mellitus (T2DM).1 The prevalence of T2DM worldwide has increased dramatically in recent decades and is expected to increase to 300 million by the year 2025.2 The lipid changes accompanying diabetes mellitus are attributed to increased free fatty acid flux supplementary to insulin resistance and aggravated by increased inflammatory adipokines.3 This affects the key enzymes and the pathways of lipid metabolism including apoprotein synthesis, lipoprotein lipase regulation, action of cholesteryl ester, transfer proteins and hepatic and peripheral actions of insulin.4

The distinctive pattern of diabetic dyslipidemia is characterized by the atherogenic triad of high plasma triglyceride (TG) concentration, low HDL cholesterol concentration and increased concentration of small dense LDL cholesterol particles.5 This form of lipoprotein is existent even before the commencement of diabetes that are proposed to be more atherogenic implying that even normal lipid concentrations might be more atherogenic in diabetic than in non-diabetic subjects.6 An early detection of dyslipidemia in T2DM can help in the management of the therapeutic array.
METHODS

The present investigation was a cross-sectional study involving patients presenting with fasting plasma glucose (FBG) > 110 mg/dL having associated symptoms of DM along with dyslipidemia assessed on the basis of elevated TC, TG, or both, or a low HDL, attending the Department of Biochemistry, MGM Medical College and LSK Hospital, Kishanganj, India, for the diagnosis of blood sugars and lipid profile, after prescription and medication from OPD and IPD of the MGM Medical College and LSK Hospital, Kishanganj, India, between September-April 2014, were selected for the present study. The patients reported with other ailments and metabolic disorders and with the history of using medications affecting glucose metabolism were excluded from the study. The information regarding their age and gender was also collected. Clearance from the Institutional Ethical Committee was obtained prior to the study. Healthy non-diabetic subjects with FBG (70-110 mg/dL) without any co-morbidity were selected as controls.

Serum analysis

The diagnostic kits for glucose, TC and TG, were procured from Merck Specialities Pvt. Ltd, (Mumbai, India) and HDL was procured from Chemelex, S.A., (Canovelles, Barcelona) and stored at 2-8°C. Blood sample was collected for estimation of fasting blood glucose (FBG) and for investigation of serum lipid profile including TC, TG, HDL, LDL, and VLDL levels, after 10 hours overnight fast. The concentration of TC in the serum sample was measured using cholesterol oxidase - peroxidase method, TG by glycerol phosphate oxidase-peroxidase method, HDL by cholesterol oxidase-peroxidase method, and LDL calculation by Freidewald Formulae. The concentration of glucose was determined by glucose oxidase and peroxidase method. The biochemical estimations were carried out using fully-automated enzymatic analyser, Selectra Pro S (Elitech Clinical Systems, USA).

Statistical analysis

The data obtained was evaluated for significance between the diabetic and non-diabetic groups by student’s t test. Pearson’s correlation coefficients and regression equation were determined between the FBG and serum lipid parameters. Variables were considered statistically significant at p ≤ 0.05.

RESULTS

A total number of 35 T2DM patients (27 males and 8 females) in the age range of 32-76 years, having fasting plasma glucose (FBG) >110 mg/dL, with associated symptoms of DM, were obtained. A total of 32 (16 males and 16 females) healthy non-diabetic subjects without any co-morbidities showed FBG in the range 70-110 mg/dL. The mean ± standard error of mean, SEM (range) age of all T2DM subjects was 51.31 ± 1.78 years (32–76 years) with mean ± SEM age (range) for male and female subjects was 51.15 ± 2.02 years (32–76 years) and 51.88 ± 3.97 years (35-68 years), respectively (p > 0.05).

The mean ± SEM FBG (range) for male and female subjects was 214.27 ± 18.84 mg/dL (125-480 mg/dL) and 168.85 ± 10.99 mg/dL (127-213 mg/dL) respectively with insignificant difference between the two groups (p>0.05) (Table 1). Similarly, there was insignificant difference (p>0.05) between males and females with respect to the serum lipid variables; for example, the mean ± SEM TC (range) were 186 ± 12.22 mg/dL (49-324 mg/dL) and 170.75 ± 16.76 mg/dL (104-223 mg/dL) respectively in the two groups while the mean ± SEM TG (range) were 101.52 ± 8.55 mg/dL (38-172 mg/dL), 107.38 ± 15.03 mg/dL (60-165 mg/dL) in males and females respectively. The mean ± SEM (range) FBS, TC, TG, HDL, LDL, VLDL of all T2DM subjects were 204.64 ± 23.02 mg/dL (125-480 mg/dL), 182.51±10.12 mg/dL (49-324 mg/dL), 102.85 ± 7.34 mg/dL (38-172 mg/dL), 45.97 ± 2.05 mg/dL (25.9-77.9 mg/dL), 113.08 ± 10.39 mg/dL (15.1-228 mg/dL), 20.60 ± 1.69 mg/dL (7.7-34.5 mg/dL) respectively. Among the T2DM patients, the number (percentage) of subjects having elevated lipid parameters such as TC, TG, HDL, LDL, VLDL were 12 (34.29 %), 9 (25.71 %), 11 (31.43 %), 12 (34.29 %), 9 (25.71 %) respectively; the normal values of FPG, TC, TG, HDL, LDL, VLDL being 70-110 mg/dL, <200 mg/dL, <150 mg/dL, >40 mg/dL, <140 mg/dL, <30 mg/dL respectively (Table 1).

Association of blood sugar levels with lipid parameters in diabetic and non-diabetic patients is expressed in terms of regression equation and correlation coefficient between the variables (Table 2). The lipid parameters HDL, LDL, and VLDL except TG are significantly (p <0.0001) negatively correlated to FBG in diabetic patients. TC is found to be insignificantly negatively correlated with FBG in diabetic patients. In non-diabetic patients FBG is significantly (p <0.0001) correlated to TC, TG, HDL, VLDL (except FBG vs LDL with p <0.01) with TG and VLDL showing negative association with FBG (Table 2). The maximum association (r = 0.54) was seen between FBG and LDL in non-diabetic patients. The association between FBG and lipid parameters in T2DM patients is depicted graphically which shows positive association between FBG vs TG, FBG vs VLDL, FBG vs TC, FBG vs HDL, FBG vs LDL (Figure 1). The HDL was negatively correlated (p <0.0001) with FBG in diabetic patients expressed by the regression equation HDL = -
0.0029 FBG + 45.924 with correlation coefficient of 0.02. The relationship between the concentration of FBG and serum lipid variables in diabetic and non-diabetic subjects indicates a significant difference (<0.0001) in the FPG levels and insignificant difference in the lipid variables (p>0.05) between the two groups (Figure 2).

Table 1: Fasting blood sugar and serum lipid levels in diabetic patients.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal level (mg/dL)</th>
<th>Total (n=35) Mean ± SEM (Range)</th>
<th>Male (n=27) Mean ± SEM (Range)</th>
<th>Female (n=8) Mean ± SEM (Range)</th>
<th>p value</th>
<th>Abnormal in n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBG</td>
<td>70-110</td>
<td>204.64 ± 23.02 (125-480)</td>
<td>214.27 ± 18.84 (125-480)</td>
<td>168.85 ± 10.99 (127-213)</td>
<td>&gt; 0.05</td>
<td>35 (100)</td>
</tr>
<tr>
<td>TC</td>
<td>&lt;200</td>
<td>182.51 ± 10.12 (49-324)</td>
<td>186 ± 12.22 (49-324)</td>
<td>170.75 ± 16.76 (104-223)</td>
<td>&gt; 0.1</td>
<td>12 (34.29)</td>
</tr>
<tr>
<td>TG</td>
<td>&lt;150</td>
<td>102.85 ± 7.34 (38-172)</td>
<td>101.52 ± 8.55 (38-172)</td>
<td>107.38 ± 15.03 (60-165)</td>
<td>&gt; 0.1</td>
<td>9 (25.71)</td>
</tr>
<tr>
<td>HDL</td>
<td>&gt;40</td>
<td>45.97 ± 2.05 (25.9-77.9)</td>
<td>46.5 ± 2.30 (25.9-77.9)</td>
<td>44.16 ± 4.73 (31.5-67.9)</td>
<td>&gt; 0.1</td>
<td>11 (31.43)</td>
</tr>
<tr>
<td>LDL</td>
<td>&lt;140</td>
<td>113.08 ± 10.39 (151.2-228)</td>
<td>115.4 ± 10.58 (151.2-228)</td>
<td>105.23 ± 12.87 (52.8-153.2)</td>
<td>&gt; 0.1</td>
<td>12 (34.29)</td>
</tr>
<tr>
<td>VLDL</td>
<td>&lt;30</td>
<td>20.60 ± 1.69 (7.7-34.5)</td>
<td>20.34 ± 1.70 (7.7-34.5)</td>
<td>21.48 ± 3.00 (12-33)</td>
<td>&gt; 0.1</td>
<td>9 (25.71)</td>
</tr>
</tbody>
</table>

FBG = Fasting blood glucose; TC = Total cholesterol; TG = Triglyceride; HDL = High density lipoprotein cholesterol; LDL = Low density lipoprotein cholesterol; VLDL = Very low density lipoprotein cholesterol; SEM = Standard error of mean

Table 2: Association of blood sugar levels with lipid parameters in diabetic and non-diabetic patients.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Regression equation</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic (n=35)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>^FBG vs TC</td>
<td>TC= -0.052 FBG +189.03</td>
<td>0.08</td>
</tr>
<tr>
<td>^FBG vs TG</td>
<td>TG=0.0155 FBG + 98.342</td>
<td>0.03</td>
</tr>
<tr>
<td>FBG vs HDL</td>
<td>HDL = -0.0029 FBG +45.924</td>
<td>0.02</td>
</tr>
<tr>
<td>FBG vs LDL</td>
<td>LDL = -0.0479 FBG +119.48</td>
<td>0.09</td>
</tr>
<tr>
<td>FBG vs VLDL</td>
<td>VLDL=0.0033 FBG +19.664</td>
<td>0.03</td>
</tr>
<tr>
<td>Non-diabetic (n=32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FBG vs TC</td>
<td>TC = 1.747 FBG + 26.73</td>
<td>0.26</td>
</tr>
<tr>
<td>FBG vs TG</td>
<td>TG = -0.6847 FBG + 173.88</td>
<td>0.15</td>
</tr>
<tr>
<td>FBG vs HDL</td>
<td>HDL = 0.3505 FBG +15.243</td>
<td>0.31</td>
</tr>
<tr>
<td>^FBG vs LDL</td>
<td>LDL = 1.5026 FBG +22.052</td>
<td>0.54</td>
</tr>
<tr>
<td>^FBG vs VLDL</td>
<td>VLDL = -0.1325 FBG +34.544</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Significant at p <0.0001; ^Significant at p <0.01; * Insignificant p >0.1; FBG = Fasting blood glucose; TC = Total cholesterol; TG = Triglyceride; HDL = High density lipoprotein cholesterol; LDL = Low density lipoprotein cholesterol; VLDL = Very low density lipoprotein cholesterol; SEM = Standard error of mean; r = correlation coefficient

The association between lipid parameters in diabetic patients expressed in terms of regression equation and correlation coefficient between the variables exhibits that TC is correlated to TG, HDL, LDL, VLDL with high significance (p <0.0001), TG is correlated to HDL and VLDL with high significance (p <0.0001), HDL is correlated to LDL and VLDL with high significance (p <0.0001), and LDL is correlated to VLDL with high significance (p <0.0001) while the association between TG and LDL is insignificant (p >0.1) (Table 3). The highest correlation is between TG and VLDL (r = 0.99) followed by TC vs LDL (r = 0.96) while TC vs VLDL and LDL vs VLDL, both were correlated with r = 0.72. The lowest correlation was between HDL vs VLDL (r = 0.16) and TG vs HDL (r = 0.15). Different patterns of dyslipidemia was present among the diabetic patients (Table 4); only 1 female patient, aged 45 years out of 35 T2DM had dyslipidemic pattern of elevated lipid and lipoprotein variables except HDL, whose serum concentrations of FBG, TC, TG, HDL, LDL, and VLDL...
were 174 mg/dL, 218 mg/dL, 155 mg/dL, 33.8 mg/dL, 153.2 mg/dL, and 31 mg/dL respectively. A 5.71% of the dyslipidemic showed only hypertriglyceridemia. Fredrickson phenotype IIa characterized by elevated TC and LDL is present in 8.57% of the diabetic patients in this study whereas phenotypes IIb and IV comprising the pattern TC+TG+LDL+VLDL and TG+VLDL respectively is found in 20% and 5.71% of the diabetic patients (Table 4).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Regression equation</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC vs TG</td>
<td>TG=0.5171 TC + 8.4779</td>
<td>0.71</td>
</tr>
<tr>
<td>TC vs HDL</td>
<td>HDL=0.1092 TC+ 26.04</td>
<td>0.54</td>
</tr>
<tr>
<td>TC vs LDL</td>
<td>LDL= 0.814 TC - 35.489</td>
<td>0.96</td>
</tr>
<tr>
<td>TC vs VLDL</td>
<td>VLDL=0.1036 TC + 1.683</td>
<td>0.72</td>
</tr>
<tr>
<td>TG vs HDL</td>
<td>HDL=0.0428 TG + 41.562</td>
<td>0.15</td>
</tr>
<tr>
<td>TG vs LDL</td>
<td>LDL= 0.836 TG + 27.093</td>
<td>0.71</td>
</tr>
<tr>
<td>TG vs VLDL</td>
<td>VLDL= 0.1994 TG + 0.0866</td>
<td>0.99</td>
</tr>
<tr>
<td>HDL vs LDL</td>
<td>LDL= 1.9561 HDL + 23.162</td>
<td>0.46</td>
</tr>
<tr>
<td>HDL vs VLDL</td>
<td>VLDL= 0.1139 HDL + 15.361</td>
<td>0.16</td>
</tr>
<tr>
<td>LDL vs VLDL</td>
<td>VLDL= 0.1214 HDL + 6.8713</td>
<td>0.72</td>
</tr>
</tbody>
</table>

Table 3: Association between lipid parameters in diabetic patients.

DISCUSSION

Patients with T2DM have a higher mortality rate than the general population attributed mainly to cardiovascular disease (CVD) caused by dyslipidemia. Dyslipidemia is elevation of TC, TG, or both, or a low HDL and diagnosed by measuring plasma levels of TC, TG, and lipoproteins. In the present study, the results show that the concentrations of TC, TG, LDL, VLDL were elevated in 34.3%, 25.7%, 34.3%, 25.7% respectively while the HDL were lowered in 31.4% among the T2DM patients; hypercholesterolemia and hypertriglyceridemia was present in 34.3% and 25.7% diabetic patients respectively. Abnormal HDL in 67 (50.4%) whilst
abnormal TC, HDL and LDL in 23 (17.3%) were reported in 133 dyslipidaemic diabetic patients. In the present study there were 24 (68.57%) diabetic adults who had one or more lipid abnormalities. According to the report of CDC, 97% of diabetic adults showed one or more lipid abnormalities while the prevalence of diabetic dyslipidemia varied from 25% to 60% in NHSN study. Another study reported 65(74%) hyperlipidemias among T2DM patients and the pattern of lipid abnormalities observed was high triglyceride in 22 (31%) patients, high LDL in 14 (19%), low HDL in 08 (11%), high cholesterol in 10 (14%) and combined hyperlipidemia in 18 (25%) diabetic patients indicative of diabetic patients to be more prone to develop hyperlipidemia. This variation in prevalence may be attributed to the anthropometric differences as well as to the variation in genetic disposition of the individuals.

The mean TC, TG, HDL, LDL and VLDL in female patients were 202.2 ± 5.9 mg/dl, 168.3 ± 8.2 mg/dl, 44.9 ± 1.3 mg/dl, 123.6 ± 5.2 mg/dl and 33.7 ± 1.7 mg/dl respectively, while the mean values for TC, TG, HDL, LDL and VLDL in male patients were 182.5 ± 4.8 mg/dl, 128.1 ± 10.8 mg/dl, 40.8 ± 1.2 mg/dl, 105.4 ± 4.8 mg/dl and 36.2 ± 2.2 respectively. All the lipid and lipoprotein parameters except HDL were insignificantly higher in females with T2DM compared with males (p > 0.05) and T2DM females had significantly higher serum TC (7.42 ± 1.63 mmol/L) than non-T2DM males (5.76±1.57 mmol/L; p < 0.05) indicating prevalence of dyslipidemia in T2DM female population with greater TC compared to the males. In another study TG levels were higher in diabetic females compared to males whereas TC and LDL levels were higher among diabetic males. Firdous et al. reported that the effect of diabetes mellitus on dyslipidemia was more antagonistic with attenuating effect on protective mechanism against CVD in woman compared to men. However in our study, there was an insignificant difference between the FBG and all the serum lipid parameters in diabetic males and females which is in agreement with the findings of Vinter-Repalust et al. This gender indifference could be attributed to the absence of the distinct pattern of diabetic dyslipidemia characterized by the atherogenic triad of high TG, low HDL and high LDL in males and females. According to Fredrickson phenotypes, dyslipidemias is classified by patterns of elevation in lipids and lipoproteins. The most common form of abnormal lipid in T2DM in the current study is TC and LDL being 34.29 % each (Table 1). Fredrickson phenotype IIa is characterized by elevated TC and LDL which corresponds to 8.57 % of the diabetic patients in this study whereas phenotypes IIb and IV comprises the pattern TC+TG+LDL+VLDL and TG+VLDL respectively consisting of 20 % and 5 % of the diabetic patients. A 5.71 % of the dyslipidemias showed only hypertriglyceridemia. Hypertriglyceridemia is considered an independent risk factor for CVD in diabetics; the two mechanisms for hypertriglyceridemia is attributed to production of VLDL in higher amounts and to the removal defect of circulating triglycerides. Reduced HDL was present in maximum number comprising 25.71 % of the diabetic patients (Table 4).Packard et al. reported reduced HDL as a powerful risk factor for early CVD.

There was an insignificant difference in the serum lipid variables here between the diabetic and non-diabetic groups. LDL concentrations in T2DM are generally similar to those found in the general population and LDL cholesterol are considered to be very atherogenic since they undergo oxidative modification that are subjected to increased uptake by the arterial wall. The lipoproteins such as remnant lipoproteins, LDL, lipoprotein(a) and abnormalities such as hypo-alpha lipoproteinemia are proposed to be atherogenic in T2DM even if they are apparently normolipidemic advocating strict control of plasma lipid levels of T2DM patients compared to the non-diabetic subjects to prevent the risk of CVD.

FBG = Fasting blood glucose; TC = Total cholesterol; TG = Triglyceride; HDL = High density lipoprotein cholesterol; LDL = Low density lipoprotein cholesterol; VLDL = Very low density lipoprotein cholesterol

Figure 1: FBG and serum lipid variables in diabetic subjects.

Figure 2: FBG and lip profile in diabetic and non-diabetic patients.

TC = Total cholesterol; TG = Triglyceride; HDL = High density lipoprotein cholesterol; LDL = Low density lipoprotein cholesterol; VLDL = Very low density lipoprotein cholesterol

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The lipid parameters in diabetic patients showed a highly significant correlation between each other except between TG and LDL (Table 3). TG is correlated to HDL and VLDL, HDL is correlated to LDL and VLDL, and LDL is correlated to VLDL with high significance (p <0.0001). A positive correlation of TC with TG, LDL and VLDL; negative correlation of TG with HDL; negative correlation of HDL with LDL and VLDL was reported. Plasma VLDL levels correlate with increased density and decreased size of LDL which in turn are inversely related to plasma levels of HDL. LDL arise through lipolysis of VLDL which after triglyceride supplementation by cholesteryl ester transfer protein, along with hepatic lipase mediated hydrolysis of triglyceride and phospholipids leads to increased production of LDL.

The prevalence and severity of dyslipidaemia was statistically associated with diabetes control with significant difference (p <0.001) between the two. An early identification of dyslipidaemia as a well-known amenable risk factor of CVD is important for the implementation of therapy for its effective prevention and management. Thus achievement of proper treatment and strict control of diabetes is imperative in dyslipidaemia towards prevention and treatment of complications of CVD. Enumeration of the prevalence of dyslipidaemia in population and its association with diabetes can avert future atherogenic cardiovascular and cerebrovascular disease through proper management of diabetic dyslipidaemia at the earliest possible.

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