Study of fasting serum lipid and lipoproteins profile in type-II diabetic patients attending NMCTH

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ABSTRACT
Dyslipidemia is one of the primary causes for cardiovascular disease (CVD) and development of myocardial infarction (MI) which often leads to coronary artery disease (CAD). The elevated level of total cholesterol (TC), triglycerides (TG), low-density lipoproteins-cholesterol (LDL-C), and lowered high-density lipoprotein-cholesterol (HDL-C) are the predictable risk factor for CAD with type-II diabetic patient. The present study was undertaken taken with an objective to frame out the lipid profile in type-II diabetic patients attending OPD (outpatient department) of Nepal Medical College Teaching Hospital (NMCTH) Jorpati, Kathmandu. Samples of 148 individuals with age varying from 30-73 were analyzed. Out of which 96 patients were diabetic and 52 were control group. The mean ±SD (mg/dl) levels of Cholesterol, TG and LDL-C were found significantly higher compared to non-diabetic, and these are statistically significant when compared with healthy control group. The study concludes that the study of accessing fasting lipid profile in type-II diabetic will be a tool of accessing risk for cardiovascular and other coronary artery complications.

Keywords: (Myocardial infarction, cardiovascular disease, coronary artery disease, Dyslipidemia, Type-II Diabetes.)

INTRODUCTION
Dyslipidaemia is a well recognized and modifiable risk factor for cardiovascular diseases which is currently a leading cause of morbidity and mortality worldwide.1 Adverse lipid and lipoprotein profile have been recognized as independent risk factor for atherosclerosis and coronary artery disease (CAD).2,3 Diabetes mellitus (DM) is a global health problem, especially among elderly. Diabetics are at high risk for dyslipidemia, cardiovascular disease (CVD), coronary heart disease (CHD) and mortality.4,5 Lipid disorder often leads to myocardial infarction and heart failure.6 Dyslipoproteinemia has been found to be a significant independent predictor of CHD in patients with Type-II diabetes and also linked to complications of DM.7,8 DM is a chronic metabolic disorder characterized by impaired metabolism of glucose, protein and fat, as well as the late development of vascular and neuropathic complications.9 DM consists of a group of disorders involving distinct pathogenic mechanisms in which hyperglycemia is the common denominator.10 DM is a global public health problem, especially among elderly. Diabetics are at high risk for dyslipidemia, cardiovascular disease (CVD), coronary heart disease (CHD) and mortality.4,11-13 It increases the risk of cardiac, cerebral and peripheral vascular disease two- to seven folds and as a major contributing factor to neonatal morbidity and mortality.10 DM and dyslipidemia constitute major independent and modifiable risk factors of CHD.14,15 In addition, DM enhances the effects of the other major cardiovascular risk factors; smoking, hypertension and hypercholesterolemia.5 Dyslipoproteinemia has been found to be a significant independent predictor of CHD in patients with Type-II Diabetic7 and also linked to complications of DM.8,16 In Basrah, Southern Iraq, changes in lipid and lipoprotein profile in several important medical diseases like CHD and thyroid dysfunction have been studied.17 The aim of our study was to determine the abnormal pattern of lipid and lipoprotein profile in patients with Type-II diabetes patients.

METHODS AND METHODOLOGY:
The study was carried out in Nepal medical college and teaching hospital (NMCTH) Jorpati Attarkhel, Kathmandu, Nepal. It was a hospital based descriptive study. Patients’ data, history and details were obtained along with the sample. A total sample of 96 Type-II diabetic patients out of which 36 male and 60 Female attending NMCTH was included in the study and their age ranged from 30-73. 52 (23 Males and 29 Females) age and sex matched healthy controls without diabetes were also included.
The controls are selected on the basis of including non obese, non diabetic and normotensive patients. Diabetes was defined as per American diabetes association. For serum lipids, a national cholesterol education programme –Adult treatment panel –III (NCEP-ATPIII) guideline was referred. The inclusion criteria are Age (30-73)years, Type-II diabetes mellitus, 12-14 hrs of fasting where as pregnancy, patients suffering from heart disease and patients who were unable to fast for 12 hrs were excluded from the criteria.

LDL-C= TC - (HDL-C+TG/5) and VLDL-C=TG/5 (provided that TG concentration is not exceeding 400 mg/dl). Quality control sera from bioMerieux, France were included in each assay batch for all analyses.

Venous blood sample after 10-14 hrs fasting were collected from the patients for the identification of glucose, cholesterol, Triglyceride, HDL cholesterol, and LDL cholesterol by using sterile disposable syringe. Sera were separated and either analyzed immediately or stored for later analysis within 2 days. FBS (fasting blood sugar) was estimated immediately, and was determined enzymatically using kit. The other parameters (TC, HDL-C, and TG) were determined using kits from bioMerieux, France. LDL-C and VLDL-C were estimated using Friedwiald equation.18

**RESULT**

A total of 96 diagnosed Type-II diabetes patients who attended in NMCTH, Attarkhel, Jorpati, Kathmandu Nepal and 52 healthy individuals as a control group were selected in this study. The average age of diabetic patients was 52±10.6 in ranging between 30-73 years. While the average age of normal healthy control 48±10.8 years. Among diabetic patients 36 patients were male representing 38% whereas 60 were female representing 62%. On the other hand, 23 individuals of control group were male representing 44% and 29 were female representing 56% (Table-1).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Diabetic cases (n=96)</th>
<th>Healthy control (n=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.0 ± 10.6</td>
<td>48.6 ± 10.8</td>
</tr>
<tr>
<td>Male/Female</td>
<td>36/60</td>
<td>23/29</td>
</tr>
<tr>
<td>BMI(kg/m²)</td>
<td>26.0 ± 5.2</td>
<td>25.9 ± 5.7</td>
</tr>
<tr>
<td>Fasting blood sugar (mg/dl)</td>
<td>144.3 ± 59.6</td>
<td>86.3 ±12.6</td>
</tr>
<tr>
<td>Postprandial blood sugar mg/dl</td>
<td>219.0 ± 93.4</td>
<td>115.3 ± 11.6</td>
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</table>

The levels of fasting lipid profile among Type-II diabetic patients and healthy participants were estimated. All diabetic subjects have significantly higher cholesterol level (176.3±34.6 Vs 165.8±27.4; P= >0.05) Triglyceride (176.2 ±77.4 Vs 126.3 ± 48.8; P= <0.05) and LDL cholesterol (101.9 ± 31.4 Vs 89.0 ± 24.2; P = <0.05) and significantly lower HDL cholesterol (38.7±12.1 vs 51.0±11.5; P=<= 0.05) as compared to non diabetic control group. The P value of total cholesterol >0.05 indicates that there was significant between Type-II diabetic patients and healthy control group. Similarly, the P value of triglyceride <0.05 HDL cholesterol <0.05 and LDL cholesterol <0.05 indicates there was not significantly difference between them (Table-2).

The fasting and non fasting lipid profile levels in diabetic patients and non-diabetic healthy control were also compared, where total cholesterol, TG, HDL-C in postprandial state were marginally increased compared to fasting state in both Type-II diabetes and non-diabetic control group people (Fig. 1).

**DISCUSSION**

DM is the most common endocrine disease, and is associated with vascular changes resulting in accelerated atherosclerosis.19 This association exists in patients with Type-II diabetes in whom plasma insulin levels may be low, normal or even high and is accompanied by changes in plasma lipids and lipoproteins regardless the mode of treatment.20 Type-II diabetes and the metabolic syndrome are both becoming more prevalent, and both

<table>
<thead>
<tr>
<th>S. No</th>
<th>Lipid profile parameters (mg/dl)</th>
<th>Diabetic patients Mean ± SD</th>
<th>Healthy control Mean ± SD</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Fasting total cholesterol TC</td>
<td>176.4 ± 34.6</td>
<td>165.8 ± 27.4</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>2.</td>
<td>Fasting Triglyceride</td>
<td>176.2 ± 77.4</td>
<td>126.3 ± 48.8</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>3.</td>
<td>Fasting HDL</td>
<td>38.7 ± 12.1</td>
<td>51.0 ± 11.5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>4.</td>
<td>Fasting LDL</td>
<td>101.9 ± 31.4</td>
<td>89.0 ± 24.2</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
increase the risk of CVD. Many patients are prone to atherogenic dyslipidemia, the so-called “atherogenic lipid triad” involving high serum TG-levels, low serum HDL-C levels, and a preponderance of small, dense, LDL-C particles. All of the processes involved in atherogenesis can be exacerbated by insulin resistance or the metabolic syndrome.\(^\text{21}\) One of the end points of atherosclerosis is CHD,\(^\text{22}\) which remains the leading cause of morbidity and mortality in developed and developing countries.\(^\text{23,24}\) Several novel risk factors for atherosclerosis have recently been proposed, with lipid parameters among these factors. They are suggested as potential criteria for improved detection of subclinical atherosclerosis.\(^\text{25}\) The cholesterol that accumulates in atherosclerotic lesions originates primarily in plasma lipoproteins, mainly LDL.

Several studies reported high levels of TC and LDL-C among diabetic patients,\(^\text{25,27}\) a finding also observed in the present study. However, other studies couldn’t report similar finding.\(^\text{28}\) Furthermore; it has been found that loss of affinity for the Apo B receptors of the glycated LDL-C may contribute to the increased plasma TC level in diabetic patients.\(^\text{29}\) Type-II diabetes patients showed a low serum HDL-C level in comparison to controls. HDL turnover in patients with Type-II diabetes appears to be accelerated resulting in low serum HDL-C level. Also, the higher insulin level in such patients may lower HDL-C concentration.\(^\text{29}\) Low HDL-C levels are common in Type-II diabetes patients, and this finding seems to be related to the increased mortality and morbidity in CHD.\(^\text{30}\) The transport of cholesterol is reduced when HDL is glycated and the transfer activity of cholesteryl ester is increased.\(^\text{31}\) In addition, low HDL-C level is frequently encountered in association with increased TG level, and both disorders may be metabolically related.\(^\text{32}\) Management of DM leads to favorable changes in HDL-C concentrations.\(^\text{32}\) The present study revealed an increased serum LDL-C level in patients with Type-II diabetes compared to control subjects. This is in agreement with the observation of others.\(^\text{34}\) However, other studies found non-elevated LDL-C level among diabetic patients.\(^\text{35}\) Several changes in LDL particles have been noted in Type-II diabetes including non-enzymatic glycation\(^\text{36}\) and oxidation\(^\text{37}\) of LDL. Such LDL particles would be more susceptible for uptake by macrophage scavenger receptors leading to foam cell formation. Thereby, increasing the risk of atherosclerosis.\(^\text{38}\) Moreover, diabetics have small, dense and glycated LDL particles\(^\text{39}\) which are strongly associated with CHD.\(^\text{40,41}\) Lowering of low-density lipoprotein cholesterol with statins is obviously effective in the prevention and treatment of CHD.\(^\text{8,40,42}\)

Treatment of high LDL-C levels should be initiated early during diabetic management to reach target levels and to minimize the cardiovascular risk and CHD risk.\(^\text{34}\) Hypertriglyceridaemia is the most frequently recognized type of dyslipidaemia among Type-II diabetes patients, and usually associated with an increased risk of CHD.\(^\text{43}\) It has been proposed that increased plasma insulin levels promote VLDL synthesis resulting in elevated plasma TG levels, whereas, increased elimination of lipids and apolipoproteins from VLDL particles results in the increased production of intermediate density lipoprotein (IDL) and LDL.\(^\text{44}\) Beneficial changes in TG levels occurs with the optimal management of diabetes.\(^\text{34}\) Increased serum VLDL-C has been found among diabetic patients.\(^\text{45}\) Glycated LDL and VLDL levels are markedly elevated in diabetics than in normal subjects. However, only glycated VLDL was markedly increased in diabetic patients with atherosclerosis than in those without evident atherosclerotic disease.\(^\text{38}\) Moreover, proposed that glycation of VLDL may be the reason behind the development of atherosclerosis in diabetic patients. Achievement of good metabolic control using different antidiabetic agents including exogenous insulin has been found to be associated with improvement of atherogenic lipid profile.\(^\text{44,46,47}\) In addition, several lipid lowering drugs have been shown to be effective in improving atherogenic lipid profile.\(^\text{58-51}\) Combination lipid lowering therapy is more effective than statin monotherapy.\(^\text{52}\) Control of diabetes results in reduction of not only morbidity and mortality, but also the economic burden of the disease.\(^\text{53}\) Deterioration of the glycaemic control aggravates lipid and lipoprotein abnormalities\(^\text{13}\), and thus, accelerate the atherosclerotic process. Thus, identifying patients with dyslipidaemia provide an opportunity to reduce the incidence of CHD.\(^\text{54}\)

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