ASSOCIATION BETWEEN LIPID LEVELS AND DIABETES MELLITUS IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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Contribution
FJ conceived the idea and designed the study. Data collection and manuscript writing was done by FJ, MSQ, SB, ABC, and SI. All the authors contributed equally to the submitted manuscript.

ABSTRACT

Objective: This study was done to determine the association between lipid levels and diabetic Indices in confirm patients of myocardial infarction with versus without diabetes mellitus type II.

Methodology: Two hundred acute myocardial infarction having ST-segment elevation patients with diabetes mellitus type II and without diabetes mellitus type II were enrolled. Lipid levels and diabetic indices were measured, and the correlations among them were analyzed.

Results: Positive correlations were found between triglycerides and fasting blood sugar, low density lipoprotein and Insulin when compared among myocardial infarction patients. Comparison among myocardial infarction patients with diabetes mellitus type II and without diabetes mellitus type II, negative correlations were found between triglycerides and glycosylated hemoglobin (HbA1C), low density lipoprotein and glycosylated hemoglobin and Insulin.

Conclusion: Correlations between lipid levels and diabetic indices when compared were found to be Positive in myocardial infarction patients only and Negative when compared between myocardial infarction patients with diabetes mellitus type II and without diabetes mellitus type II.

Keywords: Myocardial infarction, Lipid profile, Diabetes Mellitus
INTRODUCTION

The presentation of acute myocardial infarction (AMI) is attributed to interruption in coronary artery blood supply on the basis of diseases related to coronary artery, which causes serious and persistent ischemia. The clinical features of AMI include persistent severe pain in back of chest, increased serum myocardial enzyme and electrocardiograph change, leading to the severe arrhythmia, shock, heart failure or even death. The admission rate and long-term mortality rate of patients in China, with AMI are 6% and 12%, respectively.

Coronary artery diseases risk factors include old age, high blood pressure, cigarette smoking, hyperlipidemia, diabetes mellitus, inflammatory reaction and others. Diabetes Mellitus Type II relates to dyslipidemia like decreased levels of HDL-cholesterol, increased levels of ox-LDL, and increased levels of triglycerides. If we compare pre-diabetic with non-diabetic’s the pre-diabetic’s have increased levels of TC, LDL-C, and TG and decreased levels of HDL-C which indicate an atherogenic pattern. In insulin resistance there is disturbance in the levels of f VLDL, LDL, and HDL. There is evidence in numerous studies; morbidity due to DMT2 is associated with cardiovascular diseases, due to dyslipidemia which causes change in the size or density of LDL.

Studies have shown that the factors which can predict CAD are increased levels of small dense LDL and it is not related to other risk factors of coronary disease diseases. The pathophysiology of dyslipidemia in diabetes mellitus type 2 leads to atherogenesis especially brought about TG’s rich lipoproteins, that is increased secretion of hepatic VLDL and lack in VLDL clearance. Intermediate-density lipoproteins (IDLs) which are rich in cholesterol are atherogenic in humans as well as in animal models.

Small dense LDL particles are produced as a result of clearance of large VLDL from plasma. Seven different LDL subspecies have been identified, with different metabolic behavior and pathological roles. Lipolysis releases through a series of steps involving breakdown of specific larger VLDL precursors into small dense LDL particles. Hepatic lipase further produces by the lipolytic action causing breakdown of phospholipids and TG’s into small dense LDL.

The major factor for reductions in HDL, insulin resistance and diabetes mellitus type 2 is due to rise in shifting of cholesterol from HDL to TG’s profile lipoproteins, with corresponding transfer of TG’s to LDL. Hepatic lipase rapidly catabolized and clear triglyceride-rich HDL particles from plasma. Surge of FFA from adipose tissue and uptake poor uptake by liver and skeletal muscles is attributed to insulin resistance and diabetes mellitus type II. Accumulation of FFA in the form of TG’s happens in heart, muscles, pancreas and liver due to insulin resistance. Hepatic lipase causes breakdown of phospholipids in LDL and HDL making smaller and denser LDL particles and a reduction in HDL.

An important property of HDL which makes it cardio protective is its anti-inflammatory and anti-oxidative properties and increased efflux of cellular cholesterol. Decreased HDL-Cholesterol and increased TG’s do often present together there by increasing the chances of CHD. Increased levels of insulin and TG’s are autonomously associated with low HDL levels. Small dense LDL have atherogenic potential which is due to the invasion in the sub endothelial space, susceptibility to oxidative modifications, binding to arterial wall proteoglycans is increased and reduced LDL receptor affinity.

A prospective study of 17 populations (meta-analysis) that probability of CAD is raised by each 1-mmol/l rise in triglyceride levels there is an increase in 32% for men and 76% for women. These data suggest that the insulin resistance and DMT2 are associated with dyslipidemia which in turns increases the risk of cardiovascular diseases. To see the association between dyslipidemia and DMT2 this study is carried out in which lipid levels and diabetic Indices in confirm patients of myocardial infarction with versus without diabetes mellitus type II were assessed.

METHODOLOGY

This observational comparative study was carried out at National Institute of Cardiovascular Diseases, Karachi, Pakistan. Two hundred age and sex
matched subjects were included in the study. Group I included AMI patients without T2DM and Group II were AMI with Diabetes Mellitus, all the patients had undergone coronary angioplasty in the same institute, from June 2017 to December 2017.

The selections of patients were made on the diagnostic criteria of AMI that is ST-segment elevation and raised Troponin T levels. The exclusion criteria were as follows: acute metabolic complications like hypoglycemia, diabetic ketoacidosis, hyperglycemic states, inherited disorders or family history of dyslipidemia, Cerebrovascular accidents, deranged liver functions and acute infections. Submission of written informed consent was mandatory before the start of the study. Ethical committee of National Institute of Cardiovascular Diseases approved the study. (Reference No: ERC-11/2017).

Data including gender, age, hypertension, diabetes, smoking and body mass index (BMI) were collected. Venous blood around 10 ml was taken after 10-14 hrs of fasting; Serum collected after centrifugation for biochemical assays was stored at –80°C.

Different biochemical parameters which include: Glucose oxidase method by commercial kit by Merck was used to determine Fasting blood glucose levels. HbA1C was determined by automated kit on cobas integra provided by Roche. Serum Insulin levels were done by radioimmunoassay (RIA) from Merck. Serum Triglycerides, LDL and Cholesterol was done by enzymatic kit method obtained from Merck and Friedwald formula was used to calculate LDL-Cholesterol. Angiography performed on TOSHIBA Infinix 2000 by a consultant cardiologist.

Data were analyzed with SPSS ver.23, appropriate mean ± SD or frequency (%) were calculated. Diabetic and non-diabetic groups were compared by applying t-test. Pearson correlation coefficient was calculated to assess the relationship between continuous variables.

RESULTS

The age of patients was 40-65 years, with average age of 56±3 years. There were 131 males and 69 females. 100 MI with DMT2 patients and 100 MI without DMT2 patients were included in this study.

Table 1: Includes baseline and physical parameter of the two groups. Age, duration of diabetes and DBP were non-significant between the two groups. BMI and SBP were found to be significantly higher (P<0.001) in MI DMT2 patients, when compared with MI without DMT2 patients. Gender and smoking were non-significant among the two groups when Chi Square test was applied to them.

<table>
<thead>
<tr>
<th></th>
<th>Without T2DM</th>
<th>with T2DM</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>100</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>Gender (Male /Female)</td>
<td>68 / 32</td>
<td>63 / 37</td>
<td>0.457</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>55 ± 4</td>
<td>56 ± 3</td>
<td>0.079</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.55 ± 0.01</td>
<td>1.54 ± 0.01</td>
<td>0.201</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>68.22 ± 1.29</td>
<td>70.47 ± 2.49</td>
<td>0.001</td>
</tr>
<tr>
<td>Body Mass Index (BMI) (kg/m²)</td>
<td>27.57 ± 2.2</td>
<td>29.47 ± 4.71</td>
<td>0.001</td>
</tr>
<tr>
<td>Duration of Diabetes Mellitus (Years)</td>
<td>-</td>
<td>12 ± 3</td>
<td>-</td>
</tr>
<tr>
<td>Smoking</td>
<td>20</td>
<td>25</td>
<td>0.404</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>130 ± 5</td>
<td>129 ± 8</td>
<td>0.001</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>80 ± 4</td>
<td>81 ± 6</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Table 2: Includes the levels of fasting blood sugar and insulin which were found significantly higher (P<0.001) in MI DMT2 when compared with MI without DMT2 patients. Triglycerides, LDL and Cholesterol were non-significant in the two groups, while High density lipoprotein and Glycosylated hemoglobin were significantly lower (P<0.001) in MI patients in comparison to MI DMT2 patients.

<table>
<thead>
<tr>
<th></th>
<th>Without T2DM</th>
<th>with T2DM</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Blood Glucose (mg/dl)</td>
<td>105.7 ± 15</td>
<td>110.4 ± 14.8</td>
<td>0.001</td>
</tr>
<tr>
<td>Insulin (μIU/ml)</td>
<td>22.4 ± 6.5</td>
<td>30.1 ± 7.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>150 ± 30</td>
<td>160 ± 35</td>
<td>0.051</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dl)</td>
<td>100 ± 15</td>
<td>110 ± 20</td>
<td>0.013</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dl)</td>
<td>40 ± 5</td>
<td>35 ± 4</td>
<td>0.001</td>
</tr>
<tr>
<td>Glycosylated hemoglobin (%)</td>
<td>6.5 ± 1.2</td>
<td>7.2 ± 1.5</td>
<td>0.001</td>
</tr>
</tbody>
</table>

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Figure 1: The correlation between different parameters of MI patients shows Positive correlations between Triglycerides and Fasting blood sugar ($r = +0.29 <0.01$), Low density lipoproteins and Insulin ($r = +0.26 <0.01$).

Figure 2: Negative correlations were found between different parameters of MI DMT2 patients, and patients of MI without DMT2, those are Triglycerides and HbA1C ($r = -0.20 <0.05$), Low density lipoproteins and HbA1C ($r = -0.25 <0.05$), HbA1C and Insulin ($r = -0.27 <0.01$).
Table 2: Biochemical Parameter of patients in relation to Blood Glucose and Blood lipid Levels

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Myocardial Infarction Without T2DM</th>
<th>Myocardial Infarction with T2DM</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>100</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>Fasting Blood Glucose (mg/dl)</td>
<td>80 ± 4</td>
<td>132 ± 16</td>
<td>0.001</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>5 ± 0.70</td>
<td>7 ± 0.81</td>
<td>0.001</td>
</tr>
<tr>
<td>Fasting Insulin (µIU/mL)</td>
<td>11 ± 2</td>
<td>19 ± 4</td>
<td>0.001</td>
</tr>
<tr>
<td>Serum Triglycerides (mg/dl)</td>
<td>190 ± 25</td>
<td>185 ± 26</td>
<td>0.172</td>
</tr>
<tr>
<td>Serum Total Cholesterol (mg/dl)</td>
<td>204 ± 22</td>
<td>196 ± 24</td>
<td>0.013</td>
</tr>
<tr>
<td>Serum LDL Cholesterol (mg/dl)</td>
<td>147 ± 30</td>
<td>144 ± 37</td>
<td>0.557</td>
</tr>
<tr>
<td>Serum HDL Cholesterol (mg/dl)</td>
<td>24 ± 5</td>
<td>27 ± 7</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Cardiovascular diseases which are, one of the leading causes of death throughout the world have convinced us to focus on the detailed research to be done over the years, to make us understand the importance how severe can the damage be and the mortality caused by it and leads us to find out ways to control its effects and prevent it. Diabetic dyslipidemia is attributed to insulin resistance. Alterations in VLDL metabolism leading to plasma lipid and lipoprotein abnormalities increase the probability of atherosclerosis leading to CHD in DM T2 patients. Many therapeutic methods can be implemented to improve dyslipidemia like physical activity, weight loss, and use of fibrates, nicotinic acid, statins and TZDs and these treatments contributed to reduce small dense LDL particles which in turns showed promising effects in reduction of coronary artery disease progression. In 1957 Blorck et al., was the first one to report that after acute myocardial infarction lipid levels were modified.22 Another study showed reduction of 47% in TC, 39% in LDL-C and 11% in HDL-C and rise of 50% in TG in serum.23 After 24-48 hours of AMI, the changes appear, reach their peaks in 4-7 days, and then subside after some months. Severity of infarction, tissue necrosis their extent and duration before the event take place can be assessed by the change in lipid levels.24 It is unclear that the lipid levels can be changed by therapeutic interventions including percutaneous coronary interventions and thrombolytic treatment. The protocol which should be followed in acute coronary syndrome patients admitted in hospitals that their lipid levels must be checked within 24 hrs and then rhythmically till a steady healthy state is reached. A minimal change is seen in first 24 hrs which is followed by phasic changes. The first measurement of lipid levels can be a quite dependable source for selection of the lipid lowering therapy. If the results are within physiological range even than lipid-lowering therapy must be initiated in first few days even if the levels of TC, LDL, and HDL are decreasing periodically after MI.25

Our study focused on the lipid levels and diabetes mellitus in two groups one with MI without DMT2 and the other MI with DMT2. The lipid levels were compared between the two groups' it was found that triglycerides, LDL and were non-significant among them. HDL levels were remarkably lower (P< 0.001) in patients of MI without DMT2 when compared with patients of MI with DMT2.

HDL increases the chances of deposition of cholesterol in vessels which in turn enhances the chances of formation of atherosclerosis in arteries especially of heart which leads to coronary artery diseases.

The diabetic indices fasting blood sugar and insulin levels were statistically significantly (P<0.001) in MI DMT2 patients when compared with MI patients without DMT2. Triglycerides, LDL and Cholesterol were found non-significant in the two groups, while HDL and Glycosylated hemoglobin were lower significantly (P<0.001) in Myocardial Infarction patients in comparison to Myocardial Infarction with diabetes mellitus type II patients.

The correlation between different parameters of Myocardial Infarction patients shows Positive correlations between Triglycerides and Fasting blood sugar (r = + 0.29 <0.01), Low density lipoproteins and Insulin (r = + 0.26 <0.01). Negative correlations were found between different parameters of MI with DMT2 patients and MI without...
DMT2 patients, those are Triglycerides and HbA1C (r = - 0.20 <0.05), Low density lipoproteins and HbA1C (r = - 0.25 <0.05), HbA1C and Insulin (r = - 0.27 <0.01).

CONCLUSION

There was a Positive correlation between Triglycerides and Fasting blood sugar. Low density lipoproteins and Insulin in Myocardial Infarction with diabetes mellitus type II patients. While Negative correlations were found between Triglycerides and HbA1C, Low density lipoproteins and HbA1C, HbA1C and Insulin in Myocardial patients without diabetes.

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