ASSESSMENT OF BIOCHEMICAL PARAMETERS IN DIABETIC AND NON-DIABETIC ACUTE MYOCARDIAL INFARCTION PATIENTS

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Abstract

Background: The present study was designed to assess the level of altered lipid profile, lipoprotein sub fractions, oxidative stress and antioxidants in coronary artery disease with type-2 diabetes mellitus’s patients and non diabetic patients.

Methods: This case–control study included 300 subjects; out of which, 100 subjects were with normal blood glucose level and with normal ECG (Normal, N), 100 subjects were with normal blood glucose level and AMI (non-diabetic and AMI, N-AMI) and 100 subjects were with diabetes and AMI (Diabetic and AMI, D-AMI)

Results: D-AMI individuals had high level of total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), and low level of high density lipoprotein (HDL) in comparison to N-AMI individuals. The cardiac markers such as Troponin I, creatine phosphokinase (CPK), creatine kinase-MB (CK-MB), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), and C-reactive protein (CRP) levels were significantly increased in patients suffering from myocardial infarction with diabetes mellitus (DM) compared to patients of myocardial infarction without DM. The antioxidant superoxide dismutase (SOD) and glutathione (GSH) were lower in D-AMI patients than in N-AMI. However, levels of malondialdehyde (MDA) and catalase (CAT) were higher in D-AMI than in N-AMI controls.

Conclusion: Our study suggested that patients with D-AMI have elevated cardiac markers and reduced antioxidants levels as compared to N-AMI patient.

Keywords: Diabetes Mellitus, Acute Myocardial Infarction, Creatine Phosphokinase, Glutathione

Introduction:

Coronary artery diseases (CAD) and CAD with T2DM are the most frightening of the health prediction for the new millennium worldwide. According to world health report 2002, CVD will be the largest death causing disease in India. In India by 2020AD, 2.6 million Indian are predicted to die due to CAD, which constitutes 54.1 % of all CVD death. CAD, the most common form of heart disease is characterized by atherosclerosis and the development of fibro-fatty plaques, which is followed by the formation of occlusive thrombi and the precipitation of acute events that interrupts the blood flow. This condition leads to a disparity between oxygen supply and demand. If this imbalance is exceeds, it results in myocardial infarction (MI). Type 2 Diabetes Mellitus (T2DM) is a group of abnormal metabolic paradigms with the essential feature of hyperglycemia and is dubbed as the disease of “premature ageing”. Incidence of CAD with T2DM is rising all over the world at worrying rate, despite, comprehensive and coordinated effects of World Health Organization (WHO), International Diabetes Federation and Several Social Science Agencies. All efforts have failed till date to arrest this rising incidence. 6.6 % of the world population was affected by this disease in 2020 with an estimated 385 million carriers and the number may become almost double (552 million) by 2030. India is facing an even grimmer scenario. In 2000, the number of diabetic carriers was 31.7 million which rose to 68.7 million in 2020 and 12 million more patients are expected to get added in another 10 years. On the basis of affected population, both in terms of percentage and numbers India has significantly more patients than China and other neighboring countries and is often referred to as the diabetic capital of the world. The reasons for this lopsided proclivity are still poorly understood.

Metabolically, coronary artery disease (CAD) with T2DM is a hetrogenous multifactorial syndrome with environmental and pleotropic involvement in which the former are overwhelmingly significant factors. Indeed, hyperglycemia is an essential expression due to relative or absolute lack of insulin action or secretion. Pathway selective insulin resistance is a cardinal, if not essential feature. It is almost inevitably accompanied with hyperglycemic complexities such as altered lipid metabolism and raised oxidative status due to unfavorable
“Cellular Redox Homeostatic Box”. Several researchers have corroborated this condition by animal cell culture and in vitro studies and our recent animal studies also support that findings.5 Therefore, present study was design to assess the level of altered lipid profile, lipoprotein sub fractions, oxidative stress and antioxidants in CAD with T2DM patients and non diabetic patients.

Material and Methods

**Study design**- This case–control study included 300 subjects; out of which, 100 subjects were with normal blood glucose level and with normal ECG (Normal, N), 100 subjects were with normal blood glucose level and AMI (non-diabetic and AMI, N-AMI) and 100 subjects were with diabetes and AMI (Diabetic and AMI, D-AMI).

**Study area:** This study was conducted in the Department of Biochemistry, Shri Aurobindo Medical College and PG Institutes, Indore, Madhya Pradesh with due permission from the institutional ethical committee and review board and after taking written informed consent from the patients.

**Study period:** Data collection for study started from July 2016 to June 2017 or till the sample size is achieved (whichever is earlier). Then it took another two months to process and analyse data.

Diabetes was diagnosed by analyzing the level of glycated hemoglobin (HbA1c > 6.5%). Diagnosed cases of diabetic and non-diabetic AMI patients were included after obtaining a written consent from their caretakers to take part in the study. Questionnaires were duly filled in with bio-data of the patients, detailed medical history, blood pressure, electrocardiography (ECG), complete blood count (CBC) along with available additional information.

**Inclusion criteria**- Subjects of all ages and both genders with the history of AMI were included. AMI diagnosis was based on a history of chest pain, ECG changes, and elevated cardiac enzymes. Diabetic and non-diabetic AMI patients were included in this study. The control subjects were selected on basis of being normotensive and with normal ECG.

**Exclusion criteria**- Subjects who have the history of smoking, obesity, or any other disease were excluded from this study.

**Data collection**- Collection of blood samples and separation of serum were done from cubital vein from all subjects and instantly transferred from hospital to laboratory in an icebox. Blood samples were centrifuged at 2000g for 10 min at 4 °C. Serum was aspirated, aliquoted, and stored at -20 °C for analysis.

**Evaluation of cardiovascular parameters**- Serum levels of TC, TG, and HDL were measured spectrophotometrically using commercial assay kits. LDL was calculated by using Friedewald formula.

**Analysis of cardiac markers**- Levels of various cardiac enzymes including troponin-I (TnI), CPK, CK-MB, LDH, AST, and CRP were assessed using commercial kits.

**Estimation of oxidative stress**- Oxidative stress was measured by analyzing the serum level of MDA, CAT, SOD, and GSH using commercial kits.

**Statistical analysis**- Statistical analysis was performed using Epi-info software. At first one-way ANOVA was used to compare quantitative variables between three groups and then Bonferroni post hoc test was used to confirm where the differences occurred between groups. All data were presented as mean±standard deviation (SD). P < 0.05 was considered statistically significant.

### Results

#### Table 1: General demographic characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>N-AMI</th>
<th>D-AMI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male : female</td>
<td>62:38</td>
<td>65:35</td>
<td>64:36</td>
<td>0.789</td>
</tr>
<tr>
<td>Age in yrs</td>
<td>65.23±12.35</td>
<td>65.18±13.14</td>
<td>64.54±11.28</td>
<td>0.369</td>
</tr>
<tr>
<td>Hb1Ac (%)</td>
<td>4.09±1.24</td>
<td>4.18±1.11</td>
<td>8.53±2.69</td>
<td>0.001</td>
</tr>
<tr>
<td>SBP in mm of Hg</td>
<td>124.12±4.56</td>
<td>136.23±8.69</td>
<td>161.23±15.23</td>
<td>0.001</td>
</tr>
<tr>
<td>DBP in mm of Hg</td>
<td>81.25±6.98</td>
<td>84.12±7.10</td>
<td>96.12±12.54</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Mean age and sex were comparable in all groups. Systolic blood pressure (SBP) and diastolic pressure (DBP) were high in D-AMI and N-AMI compared with normal group. Fasting blood glucose (FBG) and HbA1c levels were significantly high in D-AMI group (p < 0.001) compared with N-AMI and normal group.

#### Table 2: Bio-chemical parameters

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>N-AMI</th>
<th>D-AMI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol in mg/dl</td>
<td>182.46±13.26</td>
<td>236.54±11.14</td>
<td>272.36±16.24</td>
<td>0.001</td>
</tr>
<tr>
<td>Triglyceride in mg/dl</td>
<td>150.32±29.14</td>
<td>230.12±24.01</td>
<td>304.65±20.13</td>
<td>0.001</td>
</tr>
<tr>
<td>LDL in mg/dl</td>
<td>139.12±12.34</td>
<td>247.21±19.56</td>
<td>291.36±22.31</td>
<td>0.001</td>
</tr>
<tr>
<td>HDL in mg/dl</td>
<td>40.12±6.21</td>
<td>31.24±3.26</td>
<td>26.12±7.14</td>
<td>0.001</td>
</tr>
<tr>
<td>CRP in mg/L</td>
<td>1.23±0.48</td>
<td>4.41±0.64</td>
<td>7.81±0.31</td>
<td>0.001</td>
</tr>
<tr>
<td>Tro-I in ng/ml</td>
<td>0.98±0.48</td>
<td>1.82±0.18</td>
<td>3.33±0.24</td>
<td>0.001</td>
</tr>
<tr>
<td>CPK in IU/L</td>
<td>130.12±6.21</td>
<td>340.12±10.23</td>
<td>1076±36.24</td>
<td>0.001</td>
</tr>
</tbody>
</table>
D-AMI group showed significant increase in TC (272.3±616.24 mg/dL), TG (304.56±20.13 mg/dL), LDL (291.7±22.4 mg/dL) levels compared to that of N-AMI group for TC (236.54±11.14 mg/dL), TG (230.12±24.01 mg/dL), LDL (247.21±19.56 mg/dL) and N group for TC (182.46±13.26 mg/dL), TG (150.32±29.14 mg/dL), LDL (139.12±12.34 mg/dL), respectively. Whereas, D-AMI group showed significantly lower level of HDL (26.12±7.14 mg/dL) in comparison to N-AMI group (31.24±3.26 mg/dL) and N group (40.12±6.21 mg/dL), respectively.

D-AMI patients had significantly higher level of CRP (7.81±0.31 mg/L) as compared to N-AMI (4.41±0.64 mg/L) patients.

Trop-I level was also found significantly high in D-AMI patient (3.33±0.24 ng/mL) than N-AMI group (1.82±0.18 ng/mL).

The data demonstrated significant elevations of CPK (1076±36.24 IU/L) and CK-MB (241.23±16.24 IU/L) in D-AMI patients compared to N-AMI for CPK and CK-MB (340.12±10.23 IU/L), (107.12±9.23 IU/L).

Level of LDH was found to be elevated in serum of D-AMI (1001.35±112.1 IU/L) compared to N-AMI (612.23±102.3 IU/L). Similar to LDH, D-AMI patients showed significant elevations of AST (102.34±6.31 IU/L) compared to those of N-AMI patients (61.23±9.10 IU/L).

Oxidative stress induced in AMI was measured by evaluating levels of MDA, SOD, GSH, and CAT. There was an increase in MDA level (0.09±0.00) and CAT activity (0.50±0.1) in D-AMI group compared to N-AMI group for MDA (0.05±0.0) and CAT (0.90±0.0). Compared with N-AMI group, SOD activity (0.07±0.0) and GSH level (0.07±0.0) were decreased in D-AMI group for SOD (0.05±0.0) and GSH (0.05±0.0), respectively.

**Discussion**

AMI is initiated by myocardial ischemia due to enhanced production of ROS, impaired activation of pro-inflammatory reactions, impaired functioning of antioxidants, and increased lipid peroxidation. All these events elicit the activation of plaque, coronary blockage and ultimately heart attack. The large segment of population suffer from AMI.

There are numerous risk factors associated with the development of AMI, such as diabetes, dyslipidemia, hypertension, smoking, obesity, advancing age, etc. Bartels et al. reported that diabetes increases the risk of CVD in diabetic subjects compared with non-diabetic subjects. The present study, found the effect of hypertension, diabetes, and dyslipidemia in D-AMI patients. Type 2 diabetes was found to alter lipids and lipoproteins utilization and induce atherogenic dyslipidemia.

Our results show significantly higher levels of TC, TG, and LDL however; low level of HDL in D-AMI patients and this suggests an important role of atherogenic dyslipidemia in the development of AMI in diabetic subjects. Atherogenic dyslipidemia favors the oxidative modification of proteins along with lipids specially LDL and thus induces a local and systemic inflammatory responses. These inflammatory responses trigger myocardial tissue injury which is detected by measuring the CRP level. Indeed, CRP is systemic inflammation marker and gives prognostic information of cardiovascular events such as atherosclerosis and CAD. In this study, increased CRP was found in D-AMI patients compared to N-AMI.

Heart contractility is evaluated by measuring the myocardial tissue specific protein Trop I, involved in cardiac contractility. Previous studies indicated that Trop I is highly sensitive and specific marker of myocardial damage and therefore used as a diagnostic marker for AMI. In this study, significantly raised level of Trop I was found in D-AMI patients compared to N-AMI patients indicating that cardiac muscle cell death increases in diabetic subjects.

CPK and CK-MB are two important indicators of myocardial necrosis and a significant elevation of CPK and CK-MB was documented in D-AMI group in this study. We also found statistically significant difference in LDH and AST values between D-AMI and N-AMI groups, the two markers being advocated for diagnosis of infarct previously.

Hyperlipidemia and hyperglycemia-induced oxidative stress has been regarded as contributors to progression of AMI. The oxidative stress results in disturbance between free radicals and antioxidant defense mechanism. SOD, one of the important defense enzymes catalyzes the dismutation of superoxide radicals into either oxygen (O2) or hydrogen peroxide (H2O2). Glutathione peroxidase (GPX) or CAT catalyzes the reduction of H2O2 into H2O. CAT catalyzes this reduction independently without any cofactor, whereas GPX relies on reduced glutathione (GSH). GSH also inhibits lipid peroxidation. Previous reports showed that
lipid peroxidation increased in AMI patients 21 and this increased lipid peroxidation is a consequence of hyperglycemia-induced oxidative stress.

Conclusion

Our study suggested that patients with D-AMI have elevated cardiac markers and reduced antioxidants levels as compared to N-AMI patient. These results will be productive for clinicians in management of MI patients with DM.

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References