A STUDY OF HEPATIC TRANSAMINASE ENZYMES PATTERN IN ACUTE MYOCARDIAL INFARCTION

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Abstract

Background: Acute myocardial infarction (AMI) is an international burden brought on by ischemia, which causes myocardial necrosis and an imbalance in perfusion. The liver receives about 25% of the total cardiac output, making it susceptible to hemodynamic disturbances. Even though the ratio of serum alanine transaminase (ALT) to aspartate transaminase (AST) is a commonly used marker of liver diseases, patients with acute coronary syndromes (ACS) frequently have elevated levels of these enzymes. This is typically due to myocardial injury, but it can also be caused by low cardiac output and arterial hypoperfusion. Their importance is frequently underdiagnosed and understudied, and there aren't many studies done on them. Hence, this study aims to determine the pattern of hepatic transaminase enzymes (AST and ALT) in patients presenting with acute myocardial infarction and no prior history of any kind of liver disease.

Materials and Methods: This hospital based cross-sectional study enrolled 137 patients above 18 years of age, admitted to Intensive Coronary Care Unit (ICCU), Medicine ICU and Medicine wards with diagnosed Myocardial Infarction(MI), according to WHO and joint ESC/ACCF/AHA/WHF guidelines, at RIMS hospital, Imphal from January 2021 to October 2022. Electrocardiography, echocardiography, CK-MB/Troponin-I and liver function test were done along with serial monitoring of ALT and AST was done on day 1, day 3 and day 5. A p value <0.05 was considered significant.

Result: A total of 137 MI patients were enrolled in our study with the mean age of 56.79±11.57 years and majority males (51.8%). Majority (59.9%) patients had STEMI and the most common presenting symptom was chest pain (95.6%). In both STEMI and NSTEMI group, majority had positive result for CKMB (87.8% and 94.5%) and Troponin I (93.9% and 96.4%). Regional wall motion abnormality (RWMA) was present on echocardiogram in 65.9% STEMI and 25.5% NSTEMI patients. While decreased left ventricular ejection fraction (LVEF) was found in 64.6% of STEMI and 25.5% of the NSTEMI patients. Majority of the patients in both STEMI and NSTEMI had normal values for total bilirubin, alkaline phosphatase level, gamma-glutamyl transferase level, total protein and albumin levels.

Conclusion: The present study showed that the majority of patients (59.9%) had STEMI and troponin I was positive in 93.9% patients of them. There was no statistical significance of both STEMI and NSTEMI with cardiac biomarkers (CKMB, Troponin I), blood pressure and heart failure but had significance with RWMA and reduced LVEF (p value <0.001). Mean values of Alkaline phosphatase (ALP), albumin, AST, ALT, AST/ALT ratio were higher for STEMI patients at Day 1, 3 and 5, however the statistical significance was observed between the two groups (p value <0.05) only for AST. Hence, hepatic transaminases can be used as useful tool to predict mortality of MI patients.
INTRODUCTION

Acute myocardial infarction (AMI) is a pathology brought on by ischemia, which leads to myocardium necrosis and produces a perfusion imbalance as a result of both coronary artery disease (CAD) and ischemic heart disease (IHD). It is exhibited when an atherosclerotic plaque bursts and a growing thrombus completely or partially obstructs the coronary artery, limiting blood flow to the heart.[1-3] Across the globe, AMI is a leading cause of both mortality and morbidity.[4] Cardiovascular diseases (CVD) and AMI cause 17.5 million deaths annually.[5] Every year, about 10% of people with chest discomfort who are admitted to emergency rooms are found to have had a heart attack; of these, almost half of the deaths happen before the patient ever gets to the hospital.[6,7] Therefore, prompt detection of myocardial ischemia is essential for the successful treatment of AMI patients.[8]

The importance of liver transaminases (alanine transaminase (ALT) and aspartate aminotransferase (AST)) in independently predicting cardiac-related morbidity and mortality has garnered considerable attention, according to recent studies.[9,10] and are linked to a higher rate of death from heart-related causes.[11,12] Hepatic dysfunction is widespread in heart disease, according to a number of prospective epidemiological investigations.[13,14] Hepatocytes are the primary source of ALT, a commonly used specific serum marker of liver illness. The primary source of AST is the liver, but it also comes from other organs like the heart, red blood cells, and muscle, making it an unreliable indicator of liver function.[9,10,15] In 1954, the first description of the use of liver transaminases, specifically AST, in myocardial damage and necrosis was published.[8] The most significant biomarker linked to myocardial infarction (MI) is still AST.[16-18] It has been demonstrated that the volume of the infarcted myocardium is correlated with the height to which the AST rises.[19]

The liver has a high rate of perfusion and metabolic activity, and acute circulatory changes—like cardiogenic shock after an AMI—have a direct impact on hepatic blood flow.[20-22] Hepatic blood flow is reduced by around 10% for every 10 mmHg drop in arterial pressure.[23,24] Hepatocellular dysfunction and an increase in AST/ALT are the outcomes of compensatory mechanisms in the liver that are triggered by circulatory failure. These mechanisms increase oxygen extraction from the blood to 95%.[25]

The present study showed that AST level peaked near day one following presentation and ALT levels peaked between day one and six.[26] Raise in transaminase level is transient and later reverts to normal over a period of four to seven days. Both AST and ALT correlated well CK-MB area under the curve, with AST more strongly correlated and reflect the severity and clinical significance of infarcts as well. AST and ALT are independent predictors of all-cause 30-day mortality.[27] Liver enzyme elevations occur with ST-segment elevation myocardial infarction (STEMI); however, their significance in the modern era is not well-defined.[26]

There has been increasing incidence of MI in the state of Manipur and very less study has been conducted on pattern of hepatic enzymes in patients with AMI in Manipur. Hence, this study was designed to determine the pattern of hepatic transaminase enzymes (AST and ALT) in patients presenting with AMI.

MATERIALS AND METHODS

This hospital based cross-sectional study enrolled 137 patients admitted to Intensive Coronary Care Unit (ICCU), Medicine ICU and Medicine wards with diagnosed Myocardial Infarction, according to WHO and joint ESC/ACCF/AHA/WHF guidelines, at RIMS hospital, Imphal for a period of 22 months from January 2021 to October 2022.

Inclusion Criteria
Included all patients diagnosed with acute myocardial infarction above 18 years of age.

Exclusion Criteria
Included those with known case of liver disease, those on hepatotoxic drugs and not giving consent for the study.

Sample size: Taking the proportion of AST elevation among MI patients as 85.6% in a study done by Lofthus DM et al[28], the sample size was calculated using the formula:

\[ n = \frac{4 \cdot P \cdot (1-P)}{L^2} \]

Where, \( n = \) sample size, \( P = 85.6\% \); \( L = \) Absolute Allowable error = 6%. Therefore, calculated sample size \( (n) = 136.96 \approx 137 \)

Study procedure: Data was collected in pre-designed proforma after written informed consent and included demographic data such as age, sex, occupation, chief complaints, socioeconomic history, general physical examination, examination of cardiovascular system as per WHO and ESC/ACCF/AHA/WHF guidelines. Investigations like electrocardiography, CK-MB/Troponin-I, echocardiography, liver function test were done along with serial monitoring of ALT and AST was done on day 1, day 3 and day 5.

Operational Definitions

Myocardial Infarction: Acute Myocardial Infarction (AMI) is defined according to WHO and joint ESC/ACCF/AHA/WHF guidelines based on cardiac biomarkers level of CK-MB or Troponin-I plus one of the following criteria: ischemic symptoms, ST segment elevation or depression, T wave changes, pathological Q wave or presumed new left bundle branch block (LBBB) on electrocardiogram.[27]

Serum Cardiac markers: CK-MB was measured with Semi Auto analyzer, Troponin I with rapid test kit. Electrocardiography was done using 12 – Lead
Electrocardiogram while echocardiography: was done using 2D Echocardiogram using SONOACE X8. The study measured IFCC (UV method) as described by Wrobleswki F and Ladue JS18 using RANDOX Rx IMOLA Auto analyzer (Manufactured 2007, United Kingdom). They are a group of enzymes that catalyses the inter conversion of the amino acids and alpha oxoacids by the transfer of amino groups. Aminotransferase measurements are used in diagnosis and treatment of certain liver diseases (eg viral hepatitis and cirrhosis) and heart diseases. Elevated levels in serum aminotransferases can indicate myocardial infarction, hepatic diseases, muscular dystrophy and organ damage. Normal values of ALT was 5 to 30 IU and AST was 5 to 40 IU.

Ultrasound whole abdomen: was done using SAMSUNG Medison Co Ltd, Model no HS 70A, (Manufactured South Korea).

Statistical analysis:IBM SPSS Version 21.0 for Windows, Armonk NY: IBM Corp. was used for statistical analysis and summarized using frequencies & proportions for variables like gender, religion, occupation, etc. Mean and Standard deviation was used to present continuous data such as age, abdominal circumference etc. Chi squared test was used to test the difference between independent variables like gender, age group, Type of MI with dependent variable i.e AST and ALT at day 1, 3 and 5. A p – value <0.05 was considered significant.

Approval of Research Ethics Board and Informed Consent: The study was approved by Research Ethics Board Regional Institute of Medical Sciences, Imphal (REB No: A/206/REB – Comm (SP)/RIMS/2015/706/48/2020).

RESULTS

In this study, a total of 137 diagnosed AMI patients were recruited. The baseline characteristics of the study subjects were given in table no I. The age of the respondents ranged from 31 to 84 years, with mean age of 56.79±11.57 years and majority males (51.8%). Majority (59.9%) of the patients had STEMI and the common presenting symptom was chest pain (95.6%), followed by shortness of breath (31.4%), palpitation (21.9%), pain abdomen (13.9%), nausea (7.3%) while two (1.5%) patients came with vomiting and one patient presented with syncope. Comparison of variables among STEMI and NSTEMI groups and their statistical significance was given in table II. CKMB was positive in 87.8% of STEMI and 94.5% NSTEMI patients while troponin I was positive in 62.2% STEMI and 76.4% NSTEMI. Regional wall motion abnormality (RWMA) was present on echocardiogram in 65.9% STEMI and 25.5% NSTEMI patients. While decreased left ventricular ejection fraction (LVEF) was found in 64.6% of STEMI and 25.5% of the NSTEMI patients. Majority of patients both STEMI and NSTEMI had normal systolic blood pressure (BP) (62.2% and 76.4% respectively) and normal diastolic blood pressure (73.2% and 85.5% respectively). There was no statistical significance between these two groups with cardiac biomarkers (CKMB, troponin I), BP, s/o heart failure (pedal edema, raised JVP and inspiratory crackles) (p value >0.05), however significant for RWMA and reduced LVEF (p value <0.001). Association table of type of MI with Liver function was shown in table III. Majority of the patients in both STEMI and NSTEMI had normal values for total bilirubin, alkaline phophatase level, gamma-glutamyl transferase level, total protein and albumin levels. There was no significant difference seen between the two groups and liver function tests (p value >0.05). Mean level of liver function parameters in different types of MI was shown in table IV and association of MI with AST/ALT ratio given in table V. The mean levels of ALP and albumin were higher in NSTEMI patients but no statistical significance was observed between the two groups (p value >0.05). Mean level of ALT at Day 1 was higher in NSTEMI patients as compared to STEMI patients, but mean level at day 3 and day 5 were higher for STEMI Patients. No statistical significance was observed between the two groups for ALT at Day 1,3 and 5 (p value >0.05). Mean level of AST and AST/ALT ratio at day 1,3 and 5 were consistently high for STEMI patients and statistical significance was observed between the two groups (p value <0.05) only for AST.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Study patients (N = 137), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td></td>
</tr>
<tr>
<td>Upto 65</td>
<td>110(80.3%)</td>
</tr>
<tr>
<td>&gt;65</td>
<td>27(19.7%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>71(51.8%)</td>
</tr>
<tr>
<td>female</td>
<td>66 (48.2%)</td>
</tr>
<tr>
<td>Religion</td>
<td></td>
</tr>
<tr>
<td>Hindu</td>
<td>70(51.1%)</td>
</tr>
<tr>
<td>Christain</td>
<td>57(41.6%)</td>
</tr>
<tr>
<td>Muslim</td>
<td>10(7.3%)</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
</tr>
<tr>
<td>Govt employee</td>
<td>64(46.7%)</td>
</tr>
<tr>
<td>Housewife</td>
<td>34(24.8%)</td>
</tr>
<tr>
<td>Variables</td>
<td>STEMI (%)</td>
</tr>
<tr>
<td>----------------------------</td>
<td>-----------</td>
</tr>
<tr>
<td>Retired</td>
<td>23(16.8%)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>74(53.3%)</td>
</tr>
<tr>
<td>Address Urban</td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>131(95.6%)</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
</tr>
<tr>
<td>Chest pain</td>
<td>43(31.4%)</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>30(21.9%)</td>
</tr>
<tr>
<td>Palpitations</td>
<td>2(1.5%)</td>
</tr>
<tr>
<td>Pain abdomen</td>
<td>73(53.3%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>131(95.6%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2(1.5%)</td>
</tr>
<tr>
<td>History of alcohol intake</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>131(95.6%)</td>
</tr>
<tr>
<td>Absent</td>
<td>1(0.7%)</td>
</tr>
<tr>
<td>Types of MI</td>
<td></td>
</tr>
<tr>
<td>STEMI</td>
<td>82(59.9%)</td>
</tr>
<tr>
<td>NSTEMI</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Comparison of variables among STEMI and NSTEMI groups (N= 137).

Table 3: Association table of type of MI with Liver function (N=137).

Table 4: Mean level of liver function parameters in different types of MI (N=137).
study by Djakpo DK et al, the patients had NSTEMI which is consistent with majority (59.9%) of the had STEMI while 40.1% of In concordance with various literatures, pain to be the most common symptom and these syncope. Yildirim A et al with vomiting and one patient presented with Breath (31.4%), Palpitations (21.9%), Pain abdomen (13.9%), Nausea (7.3%). Two (1.5%) patients came with an increased mean age and male preponderance. Majority (95.6%) of the patients enrolled. The age of the respondents ranged from 31 to 84 years, with mean age of 56.79±11.57 years in this study, a total of 137 AMI patients were enrolled. The age of the respondents ranged from 31 to 84 years, with mean age of 56.79±11.57 years and majority males (51.8%) which was similar to the study by Madan S and Ambrosy AP et al with an increased mean age and male preponderance. Majority (95.6%) of the patients presented with Chest pain, followed by Shortness of Breath (31.4%), Palpitations (21.9%), Pain abdomen (13.9%), Nausea (7.3%). Two (1.5%) patients came with vomiting and one patient presented with syncope. Yildirim A et al also reported chest pain to be the most common symptom and these symptoms are characteristic of AMI and supported by various literatures.

In concordance with literatures, we observed that majority (59.9%) of the had STEMI while 40.1% of the patients had NSTEMI which is consistent with study by Djakpo DK et al (63.3% STEMI and 36.7% NSTEMI).In the present study, majority of both STEMI and NSTEMI patients (62.2% and 76.4% respectively) had normal systolic and diastolic blood pressure, although no statistical significance was seen between the two groups (p value >0.05). On the contrary, a study reported majority (60%) of their patients to have high blood pressure. On examination of the patients, almost one-third of both STEMI and NSTEMI patients (61% and 65.5% respectively) had no edema on examination, 6 patients having STEMI had raised JVP while only 2 patients with NSTEMI had raised JVP on examination. 9 patients diagnosed as STEMI had respiratory crackles while only 2 patients with NSTEMI had respiratory crackles on examination. On echocardiogram, RWMA present in 65.9% of the STEMI and 25.5% of the NSTEMI. Decreased LVEF was noticed in 64.6% STEMI and 25.5% NSTEMI patients, which is at par with published literature.

In both STEMI and NSTEMI patients, majority of the patients had normal values for total bilirubin, ALP, GGT level, total protein and albumin levels. No significant difference was seen between the two groups. An Indian study found association between raised GGT and adverse cardiovascular outcome, although GGT levels can be elevated in all pathological conditions which speeds the process of inflammation, thus limiting its specificity. Mean level of ALP and albumin were higher in NSTEMI patients but no statistical significance was observed between the two groups (p value >0.05). This finding is in line with existing literature. In the present study, the mean level of ALT at Day 1 was higher in NSTEMI patients as compared to STEMI patients, but mean level at day 3 and day 5 were higher for STEMI patients, although no statistical significance was observed between the two groups. We also observed that the mean level of AST at day 1, 3 and 5 were consistently and significantly higher for STEMI patients. Generally, STEMI patients results from total coronary artery blockage whereas NSTEMI patients had less coronary artery blockage. We observed that the AST/ALT ratio (De Ritis ratio) measured at day 1,3 and 5 in our study were significantly high for STEMI patients as compared to NSTEMI patients (p value >0.05). Therefore, the elevated De-Ritis ratio might also be associated with total occlusion, thereby increasing the risk of mortality. De-Ritis

<table>
<thead>
<tr>
<th>Variables</th>
<th>AST/ALT Ratio Day 1</th>
<th>AST/ALT Ratio Day 3</th>
<th>AST/ALT Ratio Day 5</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST/ALT Ratio Day 1</td>
<td>2.88±2.26</td>
<td>2.17±1.71</td>
<td>1.97±1.07</td>
<td>0.003</td>
</tr>
<tr>
<td>AST/ALT Ratio Day 3</td>
<td>1.77±1.76</td>
<td>1.45±1.22</td>
<td>1.55±1.20</td>
<td>0.003</td>
</tr>
<tr>
<td>AST/ALT Ratio Day 5</td>
<td>0.044</td>
<td>0.008</td>
<td>0.035</td>
<td></td>
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</tbody>
</table>

*Independent samples t-test

DISCUSSION

Ischemia and myocardial tissue necrosis are whole mark of MI. MI mostly present as acute condition secondary to atherosclerotic coronary artery diseases. Clinical presentation of MI may range from a mild chest pain to life-threatening symptoms or sudden death.[27]

Liver involvement has been mostly described and investigated in patients with chronic heart failure.[21,29] Liver enzyme alterations are usually classified as relating predominantly,[23] to liver cell necrosis (signified by transaminase elevations) or predominantly to cholestasis (signified by elevated alkaline phosphatase level).[30,31] Prior studies on hepatic abnormalities in MI have reported various patterns, ranging from predominantly hepatocellular to cholestatic.[23,32,33] Serum aspartate transaminase (AST) is found in liver, and heart muscle ALT is found in liver. The ratio of AST to ALT is commonly used to assess liver cell injury.[34] In AMI, ALT and AST levels are often elevated.[35] The prognostic importance of observed abnormalities in biochemical markers of hepatic function has varied widely between published studies.[7] Hence, this study was designed to determine the pattern of hepatic transaminase enzymes (AST and ALT) in patients presenting with AMI.

In this study, a total of 137 AMI patients were enrolled. The age of the respondents ranged from 31 to 84 years, with mean age of 56.79±11.57 years and majority males (51.8%) which was similar to the study by Madan S and Ambrosy AP et al with an increased mean age and male preponderance. Majority (95.6%) of the patients presented with Chest pain, followed by Shortness of Breath (31.4%), Palpitations (21.9%), Pain abdomen (13.9%), Nausea (7.3%). Two (1.5%) patients came with vomiting and one patient presented with syncope. Yildirim A et al also reported chest pain to be the most common symptom and these symptoms are characteristic of AMI and supported by various literatures.[39]

In concordance with literatures,[40] we observed that majority (59.9%) of the had STEMI while 40.1% of the patients had NSTEMI which is consistent with study by Djakpo DK et al.[41] (63.3% STEMI and 36.7% NSTEMI). In the present study, majority of
ratio is considered strong predictor for mortality in AMI. These findings were consistent with the studies done by Lofthus DM et al[26] Djakpo DK et al.[41]Gao M et al[45] and Steiningr M et al.[46] Few researchers found potential mechanisms for association between elevated AST levels and mortality in patients with AMI. Lifer is a high metabolic activity so any change in liver perfusion in MI directly or indirectly affects hepatic blood flow and parenchymal function. It leads to increase ALT and AST. In acute right ventricular dysfunction caused by liver congestion can also cause increased Liver transaminases. Venous congestion, decreased hepatocytes capacity to extract oxygen, and reperfusion injury were the main principle.[47] In STEMI and congestive heart failure, abnormality in forward perfusion(reduced) and backward congestion secondary to low cardiac output leads to hypoxic liver injury. [47,48] Ischemic myocardial tissue and its necrosis can lead to increased AST.[47]

The strength of the study was employing representative sample of patients, hence the study result can be generalized to similar patients. 

**Limitations:** One of the major limitations of the present study was that the investigation was a single center-based analysis and there was no follow-up done in this study. Reporting the time intervals between the onset of symptoms and hospital admission could not be done. Coronary angiography was not included in this present study.

**CONCLUSION**

In acute myocardial infarction, liver enzymes – AST,ALT are often elevated, especially in STEMI patients.To conclude, as liver function tests, including AST and ALT are routinely available in clinical practice, it can be easily used for risk assessment in order to ensure a personalized treatment approach and the treating physician can initiate secondary prevention measure.

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