STUDY OF PANEL OF DIAGNOSTIC CARDIAC MARKERS FOR ACUTE MYOCARDIAL INFARCTION

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INTRODUCTION

Myocardial infarction (MI) may be described as the death of the heart muscles. Coronary artery disease (CAD) leads to blood flow obstruction to the heart, and the results form a spectrum of diseases, acute coronary syndrome and a consequence of which leads to decrease in the blood flow to the heart [1].

CAD is one of the main causes of death and disability in developed countries [2]. Although the mortality for this condition has gradually declined over the past decades in western countries, it still causes about one-third of all deaths in people older than 35 years [3]. The diagnosis of acute MI (AMI) established by the World Health Organization, requires at least two of the following criteria: A history of chest pain, evolutionary changes on the electrocardiogram (ECG), and elevation of serial cardiac enzymes. If ECG fails to demonstrate an AMI, the cardiac markers must be used [4].

Various cardiac markers-creatine kinase (CK); lactate dehydrogenase (LDH); Cardiac Troponin-I and Troponin-T (TnT); myoglobin; cholesterol; triglycerides; low-density lipoprotein; high-density lipoprotein, C-reactive protein (CRP), and aspartate aminotransferase (AST) have been proposed till date [4]. The assessment of the myocardial injury varies dramatically with the detection of AST, LDH, creatine kinase (CK), CK isoenzymes (CKMB), and troponin (T) which add prognostic information regarding acute short-term or chronic long-term risk and the severity of the injury [5].

Each individual marker carries significance in different scenarios. Serum LDH is a known pathologic marker for myocardial ischemia [6], but it can be falsely elevated with strenuous physical activity. CK-MB rises in the serum at 4-9 h after the onset of chest pain, peaks at 24 h and returns to baseline values at 48-72 h. CK-MB has an advantage over troponins because of the early clearance that helps to detect reinfarction [7]. Anoop CRP is an acute phase protein that rises with an inflammatory stimulus. CRP is increased in patients with unstable angina; however, owing to the lack of sensitivity and specificity, it cannot be employed as a diagnostic marker alone. As a prognostic indicator, high CRP levels have also been linked to poor outcome [8].

Thus, this study was conducted to assess the most sensitive cardiac marker out of all these three cardiac markers for the early diagnosis of AMI.

MATERIALS AND METHODS

A cross-sectional study was conducted in the department of biochemistry in a tertiary care hospital. A total of 172 patients were included in this study, divided into two groups. Group I (Cases) - consisted of 100 patients with non-diabetic MI and 72 apparently healthy controls with no history of diabetes and/or MI. Informed consent was obtained from patients.

Information extraction forms were utilized to collect data from patient care units of the Santosh Medical College Hospital and RC Ghaziabad. This study, divided into two groups. Group I (Cases) - consisted of 100 patients with non-diabetic MI and 72 apparently healthy controls with no history of diabetes and/or MI. Informed consent was obtained from patients.

All patients >35 years (males and females) of confirmed non-diabetic MI based on ECG findings and cardiac enzymes (TnT/CPK-MB) were included in the study. Patients with diabetes mellitus having MI, recent history of surgery and trauma within the preceding 2 months, renal insufficiency [serum creatinine >1.5 mg/dl], patients with cerebrovascular accidents or previous history of cerebrovascular accidents, patients having evidence of infections, inflammatory disease, malignancy, patient taking drugs such as Vitamin B-complex or folic

RESULTS:

The mean age of the cases was 62.15±7.75 years and in the controls was 61.49±8.35 years (p=0.592). The mean value of CK-MB, LDH, and CRP in the TnT positive group was 111.94±29.59 IU/L, 564.43±110.99 IU/L, and 15.69±4.04 mg/L, whereas in the TnT negative group was 16.36±3.77 IU/L, 223.68±36.23 IU/L, and 6.08±2.02 mg/L, respectively (p<0.0001). CK-MB was deranged in 100% of TnT positive group, and in only 2.78% in TnT negative group (p=0.0001). LDH was deranged in 100% TnT positive group, and in 16.67% in TnT negative group (p<0.0001). CRP was deranged in 4% TnT positive group, and in 0% in TnT negative group (p=0.141).

CONCLUSION:

This study indicated that CK-MB and LDH are sensitive cardiac markers for the diagnosis of MI.

KEYWORDS: Myocardial, Troponin, Dehydrogenase.

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acid, hormone replacement therapy, and those who were not willing to participate were excluded from the study. The initial evaluation of patients with MI consisted of history, physical examination, ECG changes, and laboratory investigation (Troponin T). The blood samples were collected from all the cases and controls and were immediately analyzed for biochemical parameters.

Under all aseptic precautions, about 5 ml of venous blood samples were collected by clean venepuncture in a sterile plain and ethylenediaminetetraacetic acid vial. Blood samples were allowed to coagulate after which they were centrifuged at 3000 rpm for 5 min to obtain serum. The separated clear serum was transferred into sterile bottles and used for the enzyme assay. When not used immediately, they were kept at −20°C and later used within 5 days.

Measurement of Troponin T was done qualitatively by rapid test kit method manufactured by Roche Diagnostics International Ltd., CH-6343 Rotkreuz, Switzerland. Measurement of creatine kinase-myocardial band (CK-MB) and LDH was done following a method that has been carried out in accordance with the International Federation of Clinical Chemistry (IFCC) protocol. The commercial kit produced by TransAsia Biomedical Ltd., (H.P.) was used. Measurement of CRP was done by endpoint method. The commercial kit produced by Erba Lachema s.r.o., was used.

Statistical analysis

Categorical variables were presented in number and percentage (%), and continuous variables were presented as mean ± standard deviation and median. Normality of data was tested by the Kolmogorov-Smirnov test. If normality was rejected, then the nonparametric test was used.

Statistical tests were applied as follows:
1. Quantitative variables were compared using the independent t-test/Mann-Whitney test (when the data sets were not normally distributed) between the two groups
2. Qualitative variables were correlated using the Chi-Square test/Fisher's exact test
3. Spearman rank correlation coefficient was used to measure the association of various parameters with each other
4. Univariate logistic regression was used to evaluate significant risk factors for Troponin T positive.

A value of p<0.05 was considered as statistically significant.

Data were entered into MS Excel spreadsheet and analysis was performed using the Statistical Package for Social Sciences version 21.0.

RESULTS

In the present study, a total of 100 Troponin T positive cases and 72 Troponin T negative as controls were examined. Troponin T positive group had 39% of patients within the age group of 61-70, 36% between 51 and 60, 18% were >70 years, and 7% were ≤50 years. In Troponin T negative group, 40.28% were between 61 and 70 years, 33.33% were between 51 and 60 years, 16.67% were >70 years of age, and 9.72% were ≤50 years (Table 1 and Fig. 1). The mean age in the cases were 62.15±7.75 years and in the controls was 61.49±8.35 years. There was not any statistical difference between the two groups (p=0.592). It has been shown in Table 1a.

In the present study, Troponin T positive group had 29% of females and 71% of males, whereas the control group had 29.17% of females and 70.83% of males. It has been shown in Table 2 and Fig. 2.

The mean value of CK-MB, LDH, and CRP in the Troponin T positive group was 111.94±29.59 IU/L, 564.43±110.99 IU/L and 15.69±4.04 mg/L, whereas in the Troponin T negative group it was 16.36±3.77 IU/L, 223.68±36.23 IU/L, and 6.08±2.02 mg/L, respectively (p<0.0001) (Table 3).

In the present study, CK MB was deranged in 100% Troponin T positive group, and in only 2.78% in Troponin T negative group. The difference was statistically significant (p<0.0001) as shown in Table 4.

LDH was deranged in 100% Troponin T positive group, and in only 16.67% in Troponin T negative group. The difference was statistically significant (p<0.0001) as shown in Table 5.

CRP was deranged in only 4% Troponin T positive group, and in 0% in Troponin T negative group. It was normal in the rest of the patients. The difference was not statistically significant (p=0.141) as shown in Table 6.

DISCUSSION

The ongoing battle to reduce the incidence of cardiovascular disease has led to the discovery of numerous clinical markers. In this study, TnT was taken as a standard positive marker for AMI and all correlations of the cardiac biomarkers were done on the basis of the groups defined

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Troponin-T negative (n=72), n (%)</th>
<th>Troponin-T positive (n=100), n (%)</th>
<th>Total, n (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤50</td>
<td>7 (9.72)</td>
<td>7 (7.00)</td>
<td>14 (8.14)</td>
<td>0.913</td>
</tr>
<tr>
<td>51-60</td>
<td>24 (33.33)</td>
<td>36 (36.00)</td>
<td>60 (34.88)</td>
<td></td>
</tr>
<tr>
<td>61-70</td>
<td>29 (40.28)</td>
<td>39 (39.00)</td>
<td>68 (39.53)</td>
<td></td>
</tr>
<tr>
<td>&gt;70</td>
<td>12 (16.67)</td>
<td>18 (18.00)</td>
<td>30 (17.44)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Age distribution
showed a significant difference between hsCRP values of 61.49±8.35 and 15.69±4.04. The difference was statistically significant (p<0.0001).

In the present study, the mean values of CRP in the Troponin T positive group were 564.43±110.99 and the Troponin T negative group was 223.68±36.23. The difference was statistically significant (p<0.0001). Shah et al. [13] showed a significant difference between the LDH values of STEMI and NSTEMI patients. The difference was statistically significant (p=0.047), thereby confirming the relevance of LDH as a cardiac marker.

Inflammation plays a major role in the pathogenesis of atherosclerosis. The chronic inflammatory process develops to an acute clinical event by the induction of plaque rupture and therefore, causes acute coronary syndromes [13].

In the present study, the mean values of CRP in the Troponin T positive group were 564.43±110.99 and the Troponin T negative group was 56.500–68. The difference was statistically significant (p=0.002). Aseri et al. [13] showed a significant difference between the LDH values of STEMI and NSTEMI patients. The difference was statistically significant (p=0.047) in the Troponin T positive group, and in only 16.67% in the Troponin T negative group. The difference was statistically significant (p<0.0001).

Serum LDH is a known pathologic marker for a diversity of diseases, including myocardial ischemia. Its activity rises in serum within 12–24 h after AMI reaches to peak level after 48–72 h after AMI and reverts to normal in 10–14 days. That's why considered as a late marker [6].

In the present study, LDH was deranged in 100% Troponin T positive group, and in only 16.67% in the Troponin T negative group. The difference was statistically significant (p<0.0001).

Although both cardiac and skeletal muscles contain Tropon T like other cardiac markers, the amino acid sequence of the protein in the two types of muscles differs, thus making it possible to raise antisera against cardiac-specific Tropon T and detect it more efficiently. The high specificity and sensitivity of cardiac Tropon T in diagnosing and monitoring AMI, the undetectable values of cardiac troponin T in healthy individuals, has made its measurement a powerful tool in the diagnosis of AMI [9].

CK-MB is one of the most important myocardial markers, and it is an established marker in confirmation of AMI. In AMI, the plasma concentration of CK-MB increases within 4–9 h of onset of chest pain, the peak is attained within 9–30 h and return to baseline levels after 48–72 h [7].

In the present study, the mean value of CK-MB in the Troponin T positive group was 16.36±3.77 IU/l. The difference was statistically significant (p<0.0001). Shah and Haridas [9] showed that CK-MB values were better than CK as the mean values of CK-MB after 6 h of chest pain was 98.8±7.72 and was 85.±41.9 among controls in Troponin T negative patients which corroborated with the present study. Aseri et al. [13] showed a significant difference between CK-MB values of STEMI and NSTEMI patients (p=0.034), thereby confirming the relevance of CK-MB as a cardiac marker. Shah [14] also assessed various cardiac markers in 50 AMI cases and 20 controls. Mean values of Total CPK were 148±279.1 in control and 648±806.7 in MI cases. CPK-MB was 20.9±9.58 in control and 89.4±18.07 in MI cases. The difference was statistically significant (p=0.002), and it was comparable to our study.
CONCLUSION

CK-MB and LDH are found to be sensitive cardiac markers for the diagnosis of MI and thus, a panel of markers can be used for the specific diagnosis and follow-up of AMI cases.

AUTHOR CONTRIBUTIONS

1st Author- Guarantor, Data acquisition, from inception till end of study
2nd Author- Concept and Design of study, Clinical study, final approval of the version
3rd Author- Concept and Design of study, Clinical study, final approval of the version
4th Author- Concept and Design of study, Clinical study, final approval of the version.

CONFLICTS OF INTEREST

All authors have none to declare.

REFERENCES