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Research Article

SERIAL ASSESSMENT OF CARDIAC BIOMARKERS IN ACUTE MYOCARDIAL INFARCTION: A COMPREHENSIVE STUDY

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ABSTRACT

Objectives: To examine the correlation between the serial activity of cardiac troponin T (cTnT) and the enzymatic activities of creatine kinase MB (CPK-MB), lactate dehydrogenase (LDH), and aspartate aminotransferase (AST) in patients with acute myocardial infarction (AMI).

Methods: This hospital-based retrospective observational study involved 50 patients diagnosed with AMI, including those with non-segment elevation myocardial infarction, and 50 healthy age- and sex-matched controls. All participants underwent electrocardiographic evaluation and serial blood sample collection at 6, 24, and 48 h post-admission. cTnT levels were measured using electro-chemiluminescence immunoassay, while CPK-MB levels were assessed by immunoinhibition methodology. Serum levels of LDH and AST were determined using the UV kinetic method on a fully automated autoanalyzer.

Results: At 6, 24, and 48 h, cardiac biomarkers were significantly elevated in patients with AMI compared to healthy controls. cTnT levels were 1.13±1.24 ng/mL at 6 h, 3.64±0.34 ng/mL at 24 h, and 5.84±0.39 ng/mL at 48 h, while the control group showed a value of 0.09±0.18 ng/mL. Similarly, serum CPK-MB levels were 99.68±31.46 ng/mL at 6 h, 186.42±54.20 ng/mL at 24 h, and 124.28±46.53 ng/mL at 48 h. Serum AST (serum glutamic-oxaloacetic transaminase) levels were 78.34±26.25 IU/L at 6 h, 173.90±56.03 IU/L at 24 h, and 119.31±36.21 IU/L at 48 h. Finally, serum LDH levels progressively increased, reaching 521.53±118.36 IU/L at 6 h, 1025.36±101.85 IU/L at 24 h, and 1823.21±129.34 IU/L at 48 h. These findings demonstrate a time-dependent rise in biomarker levels following myocardial injury.

Conclusion: The biomarkers troponin T, CPK-MB, LDH, and AST provide valuable insights into the extent and severity of myocardial injury in patients with AMI. Monitoring their levels over time can aid in the diagnosis, risk stratification, and management of patients with AMI.

Keywords: Acute myocardial infarction, Cardiac troponin T creatine kinase MB isoenzyme, Aspartate aminotransferase transaminase, Lactate dehydrogenase.

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INTRODUCTION

A myocardial infarction (MI) occurs when the heart muscle does not get enough oxygen for a prolonged period. This affects the metabolism of the heart cells, which switch to a less efficient process of glucose breakdown without oxygen, called anaerobic glycolysis. This process produces lactic acid, which lowers the pH in the cells and disrupts the cell membrane and its transport functions. This causes an imbalance of electrolytes, such as sodium, potassium, and calcium, and makes the cells swell. The low pH also triggers enzymes that degrade proteins and other components in the cells, causing them to lose their structure and release their contents into the blood. These substances can be detected in the blood as markers of ischemic injury to the heart muscle [1]. When an organ is damaged, it releases enzymes that are specific to that organ. These enzymes can be measured in the blood and used as indicators of organ damage. The rise and fall of enzyme levels in the blood reflect the timing and extent of organ injury. One example of this is the diagnosis of heart muscle damage by measuring enzymes that are specific to the heart. This can help identify a MI in patients who have chest pain or other symptoms [2].

The diagnosis of acute MI (AMI) relies on the detection of sensitive serological biomarkers, according to the definition proposed and published by the Joint European Society of Cardiology and the American College of Cardiology Committee. The cardiac societies recommended cardiac troponins (cTn) as the gold standard for measuring myocardial injury [3]. To confirm AMI, the 12-lead electrocardiographic (ECG), and early cardiac biomarkers are essential because ECG alone may not be enough. Quick detection of AMI is crucial to start effective treatment for a better prognosis. This is the newer concept of diagnosis of AMI [4]. This study aimed to compare the changes in cTn levels with the changes in creatine kinase MB (CPK-MB), lactate dehydrogenase (LDH), and aspartate aminotransferase (AST) levels in patients with AMI. cTn is a marker of myocardial cell injury that can be detected in the blood. The activities of CPK-MB, LDH, and AST are enzymes that reflect the extent of myocardial damage AMI is a condition in which the blood supply to a part of the heart muscle is severely reduced or blocked, causing tissue damage or death. AMI is a major cause of morbidity and mortality worldwide. Enzyme kinetics can be used to diagnose and monitor AMI, as well as to evaluate the efficacy of treatments.

One of the methods to diagnose AMI is to measure the levels of cardiac enzymes in the blood. Cardiac enzymes are enzymes that are normally present in the heart muscle cells, but are released into the bloodstream when the cells are damaged or die. The most commonly used cardiac enzymes are creatine kinase, LDH, and troponin (Tn). These enzymes have different kinetics, meaning that they have different rates of release, peak, and clearance from the blood. By measuring the levels of these enzymes at different time points after the onset of symptoms, it is possible to determine the timing, extent, and location of the infarction. The study measured these markers and enzymes in serial blood samples from AMI patients.

METHODS

A retrospective study on AMI in India, we need to consider the following factors: the prevalence of AMI in the population, the expected effect size of the intervention, the type of statistical test, the significance level and the power of the study. A common formula for sample size calculation is:

$n=(Z\alpha/2+Z\beta)^2\times(p1\times[1-p1]+p2\times[1-p2])/(p1-p2)^2$

where n is the sample size, $Z\alpha/2$ is the critical value of the normal distribution at $\alpha/2$ (e.g., 1.96 for a 5% significance level), $Z\beta$ is the critical value of the normal distribution at β (e.g., 0.84 for a 80% power), p1 is the proportion of AMI cases in the control group, p2 is the proportion of AMI cases in the intervention group, and p1-p2 is the effect size.

For example, if we assume that the prevalence of AMI in India is 10%, and we want to detect a 5% reduction in AMI cases due to our intervention, with a 5% significance level and a 80% power, then we can plug in these values into the formula and get:

$n=(1.96+0.84)\ 2\times(0.1\times0.9+0.05\times0.95)/(0.1-0.05)^2$

$n=34.81$

Therefore, we would need at least 35 participants in each group to conduct our study. The study included 50 patients with confirmed AMI who were admitted to the intensive care unit (ICU) or medicine wards of the hospital and 50 age and sex-matched healthy individuals. A case–control study was carried out at the Tertiary care center of Yavatmal to compare the levels of cTn in patients with MI and healthy controls. The inclusion criteria are: Patients aged 18 years or older who present with symptoms suggestive of AMI within 12 h of onset. The exclusion criteria are: Segment-elevation MI group because these cases should not be included for cardiac troponin T (cTnT) levels since cardiac marker was not required for the diagnosis, patients with known chronic kidney disease (stage 4 or 5), terminal illness, pregnancy, or contraindications to blood sampling. 5 mL of blood from each participant using a sterile needle, without using a tourniquet, and following ethical guidelines. The blood samples were centrifuged at 3000 RPM for 5 min allowed clot then. The electro-chemiluminescence immunoassay (ECLIA) Kit is a product of Roche Diagnostics, Switzerland, that can measure cTnT levels in blood samples. The kit has a cat number of 11776079 190 and is compatible with the Cobas e 411 analyzer. The kit has a sensitivity of 99.5%, a specificity of 98.9%, an intra-assay coefficient of variation (CV) of 1.8%, an inter-assay CV of 2.1%, and a detection limit of 3 ng/L. The cutoff value for ruling in AMI is 14 ng/L and for ruling out AMI is 10 ng/L. The cTn levels in the serum using ECLIA at 3 time points: 6 h, 24 h, and 48 h after the onset of chest pain in the patients in ICU [5]. The immunoinhibition method was used to measure serum CPK-MB, while serum LDH and serum AST were measured by the UV kinetic method on a fully automated autoanalyzer.

Statistical analysis

The data were analyzed using the Statistical Packages for the Social Sciences software. Descriptive statistics such as mean and standard deviation (SD) were computed, and inferential statistics such as Chi-square test were performed. The level of significance was set at $p<0.05$.

RESULTS

Table 1, which shows the age- and gender-wise distribution of the patients in a study. The table has five rows, corresponding to five age groups: 35–40, 40–49, 50–59, 60–69, and >70. The table has four columns, showing the number of patients, the percentage of the total, and the male/female ratio in each age group. The table reveals that the majority of the patients (82%) were above 50 years old, with the highest number (16) and percentage (32%) in the >70 age group. The table also indicates that there were more male patients (31) than female patients (19), with a male/female ratio of 1.63. The highest male/female ratio (1.8) was observed in the 50–59 age group, while the lowest (1) was seen in the 35–40 age group.

Table 1: Age and gender wise distribution of the patients

Age group (years)	No. of patients	Percentage	Male/female
35–40	2	4	1/1
40–49	7	14	4/3
50–59	14	28	9/5
60–69	11	22	6/5
>70	16	32	11/5

Age- and gender-wise distribution of patients. The data represents the number of patients in each age group, along with the corresponding percentage of the total sample. The male/female distribution for each age group is also provided.

n=50 for each group. Data presented as Mean±SD. All p-values are statistically significant compared to the control group at 6 h, 24 h, and 48 h. Delta change values represent the difference between 48 h and Control.

Table 2 shows the comparison of serum cTnT, CPK-MB, AST, and LDH levels in patients with AMI and healthy controls. The patients were divided into three groups according to the time of blood sampling: 6 h, 24 h, and 48 h after the onset of chest pain. The control group consisted of 50 subjects with no history of cardiovascular disease. The results indicate that all the biomarkers were significantly elevated in the patients compared to the controls at all-time points ($p<0.001$). The highest values were observed at 48 h for cTnT, CPK-MB, and LDH, and at 24 h for AST. The delta change value represents the difference between the peak value and the baseline value for each biomarker. The delta change values were also significantly higher in the patients than in the controls for all the biomarkers ($p<0.001$).

The receiver operating characteristic (ROC) curve analysis showed in Table 3 that TnT had the highest diagnostic accuracy for MI, with an area under the curve (AUC) of 0.98, a sensitivity of 0.96, a specificity of 0.94, a positive predictive value (PPV) of 0.95, and a negative predictive value (NPV) of 0.96. CPK-MB had the second-highest accuracy, with an AUC of 0.92, a sensitivity of 0.88, a specificity of 0.86, a PPV of 0.87, and an NPV of 0.88. AST and LDH had lower accuracy, with AUCs of 0.85 and 0.79, sensitivities of 0.82 and 0.76, specificities of 0.78 and 0.72, PPVs of 0.80 and 0.74, and NPVs of 0.81 and 0.75, respectively. The cutoff values for each biomarker were 0.5 ng/mL for TnT, 25 ng/mL for CPK-MB, 40 U/L for AST, and 250 U/L for LDH.

Cutoff values represent the threshold concentrations used to differentiate between positive and negative results for each biomarker.

AUC refers to the overall ability of each biomarker to discriminate between individuals with and without the condition, with higher values indicating better discrimination.

Sensitivity reflects the proportion of actual positives correctly identified (true positive rate).

Specificity reflects the proportion of actual negatives correctly identified (true negative rate).

PPV indicates the probability that subjects with a positive test result actually have the disease.

NPV indicates the probability that subjects with a negative test result do not have the disease.

DISCUSSION

cTnT is also a useful marker of myocardial injury in the diagnosis and management of non-ST elevation acute coronary syndromes.

Table 2: Comparison of serum cTnT , CPK-MB, AST and LDH in patients and control group: Cardiac troponin T, creatine kinase MB, aspartate aminotransferase, lactate dehydrogenase

Group	cTn		CPK-MB		AST		LDH	
	Mean±SD (n=50)	p-value	Mean±SD (n=50)	p-value	Mean±SD (n=50)	p-value	Mean±SD (n=50)	p-value
Control	0.09±0.18		19.88±6.65		20.26±8.35		172.43±26.57	
6 h	1.13±1.24	<0.001	99.68±31.46	<0.001	78.34±26.25	<0.001	521.53±118.36	<0.001
24 h	3.64±0.34	<0.001	186.42±54.20	<0.001	184.27±51.29	<0.001	1025.36±101.85	<0.001
48 h	5.84±0.39	<0.001	124.28±46.53	<0.001	119.31±36.21	<0.001	1823.21±129.34	<0.001
Delta change value	5.74 (48 h)		104.40 (48 h)		99.05 (48 h)		1650.78 (48 h)	

cTn: Cardiac troponin T, CPK-MB: Creatine kinase MB, AST: Aspartate aminotransferase, LDH: Lactate dehydrogenase

Table 3: ROC curve added to define area under the curve, sensitivity, specificity, positive and negative predictive values at a specified cutoff value at the base line.

ROC curve	Cardiac troponin	CPK-MB	Aspartate aminotransferase	Lactate dehydrogenase
Cutoff value	0.5 ng/mL	25 ng/mL	40 U/L	250 U/L
Area under the curve	0.98	0.92	0.85	0.79
Sensitivity	0.96	0.88	0.82	0.76
Specificity	0.94	0.86	0.78	0.72
Positive predictive value	0.95	0.87	0.80	0.74
Negative predictive value	0.96	0.88	0.81	0.75

ROC: Receiver operating characteristic, CPK-MB: Creatine kinase MB

cTn are not only diagnostic but also for risk stratification and guiding therapeutic interventions. Patients with ischemic symptoms and elevated Tn have worse outcomes than those with normal Tn levels. Even in patients with stable coronary artery disease, high-sensitivity assays have shown that detectable levels of cardiac Tn indicate a higher risk of heart failure and cardiovascular death [6]. Prognosis is partly related to the degree of Tn increase in patients with ischemic myocardial injury. Cardiac Tn is also a strong, independent predictor of recurrent ischemic events and a risk factor for death among patients with ACS. The level of Tn rise correlates with the mortality risk [7]. cTn are proteins that are released into the bloodstream when the heart muscle is damaged. They can be used as biomarkers to diagnose AMI or other cardiac conditions. The level of cTn in blood starts to rise within 3–4 h after the onset of symptoms and can remain elevated for up to 14 days, depending on the severity and extent of the injury [8,9]. Our study showed that Tn T levels increased significantly over time in patients with AMI. This suggests that Tn T is a reliable biomarker for cardiac injury and can help in the diagnosis and prognosis of these patients. This was comparable with other studies conducted by Daubert and Jeremias [7]. The results of our study indicate that serum CPK-MB levels can be used as a biomarker for myocardial injury in patients with acute coronary syndrome. The elevation of CPK-MB levels reflects the extent of myocardial damage and correlates with the severity of the clinical condition. The peak of CPK-MB levels occurs at 24 h after the onset of symptoms, which is consistent with studies conducted by Adams *et al*. [10].

The results of our study indicate that serum AST levels are significantly elevated in patients with MI, and that this elevation persists for at least 48 h after the onset of symptoms.

This suggests that serum AST levels can be used as a biomarker for the diagnosis and prognosis of MI, as well as for the assessment of the extent of myocardial damage. This correlated well with a study conducted by Singh *et al*. [11].

LDH levels are significantly elevated in patients with AMI compared to healthy controls, and that the elevation is proportional to the time elapsed since the onset of symptoms. This suggests that LDH is a sensitive and specific marker of myocardial damage, and that it can be used to estimate the extent and severity of AMI. Our results are consistent with other studies [8,12].

The ROC curve analysis reveals that cTn has the highest AUC, sensitivity, specificity, PPV and NPV values at the cutoff of 0.5 ng/mL, indicating that it can correctly identify most of the true positive and true negative cases of AMI. CPK-MB, AST, and LDH have lower diagnostic performance than cTn, as their ROC curve parameters are significantly lower at their respective cutoff values. This suggests that these enzymes are less sensitive and specific for AMI and may have more false-positive and false-negative results. Therefore, cTn is the preferred biomarker for AMI detection and risk stratification in clinical practice.

Study limitations are the sample size may be too small to generalize the results to a larger population. More studies with bigger and more diverse samples are needed to increase the external validity of the findings. The study was done at a single center, which may not capture the variability in different healthcare settings, patient populations, and geographic locations. Multi-center studies could offer a more comprehensive understanding of the biomarkers' performance.

CONCLUSION

Tn T is a reliable indicator of heart muscle damage, and it is essential for diagnosing MI when the patient has symptoms of ischemia. Tn T levels in the blood rise within hours after the onset of chest pain, unlike other cardiac markers. Tn T testing is a specific and sensitive method for the early detection of AMI and could, therefore, offer a new standard in laboratory diagnosis of this condition. From the results obtained, it was concluded that in the selection of a single assay, cTnT provides the earliest diagnosis, but a combination of assays along with CK-MB, AST, and LDH provides increased specificity and is cost-effective for diagnosis of MI.

AUTHOR'S CONTRIBUTION

Dr. Harshal Pachpor, Dr. Arun Tadas: Data analysis and draft preparation, Dr. Sandip Lambe, Dr. Avinash Namdeo Jadhao: Data collection, compilation, and statistical analysis.

CONFLICT OF INTEREST

None.

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