ROLE OF SERUM CARDIAC MARKERS IN DIAGNOSIS OF ACUTE CHEST PAIN

Dr ritu saxena[1*]

[1*]Associate professor , department of pathology , IQ city foundation , Durgapur

*Corresponding Author : Dr ritu Saxena

[1*]Associate professor , department of pathology , IQ city foundation , Durgapur

Abstract :
Introduction: Acute myocardial infarction (AMI) continues to be a major health problem in industrialized and developing countries like India despite progressive research in diagnostic and management over last three decades.AMI has typically been diagnosed on the basis of triad of clinical syndromes of chest pain, electrocardiogram (ECG) changes and elevated serum enzyme activity.Due to high cardiac specificity of ckmb,cTnI, these biomarkers have become the recommended biomarkers for the diagnosis of myocardial injury.
Aims: To study changes in serum cardiac markers and determine the sensitivity and specificity of Highly sensitive Troponin I, CK-MB and LDH.
Material and Methods: It was undertaken from November-2015 to December-2016 during which 200 patients were studied. All the patients having complaint of acute chest pain admitted in the emergency wards are included. Serum level of cardiac Troponin I was determined by using vidashigh sensitive troponin i (human cardiac specific) enzyme immunoassay kit, CK-MB was determined by the vitros 250 fully automated biochemistry analyser,serum level of LDH was determined by ldh-(p-l) reagent kit (kinatic procedure).
Result: In present study, out of 200 patients who admitted for complaining of acute chest pain, 110 patients actually diagnosed to have acute myocardial infarction. Sensitivity and specificity of hsTroponin I for diagnosis of acute myocardial infarction was 100%. CK-MB was 89.1% and 88.8% andLDH was 65.4% and 60% respectively.
Conclusion: Among the cardiac markers studied hsTroponin I is the most specific and sensitive for diagnosis of acute myocardial infarction. As CK-MB levels become normal within 2-3 days, it is helpful in diagnosis of reinfarction.

Key words:hsTroponin I, MyocardialInfarction, CK-MB, LDH

Introduction :
Coronary heart disease (CHD) is a major public health problem in developed countries and it is becoming more common worldwide. Acute coronary syndromes (ACSs) are attacks in which blood flow in coronary arteries is abruptly reduced or stopped, usually due to fissuring or rupture of atherosclerotic plaques and subsequent thrombosis, leading to myocardial ischemia. If this process leads to myocardial cell necrosis, the result is a myocardial infarction (MI)[1].
The early (30 days) mortality rate from AMI is approximately 30 percent, with more than half of these deaths occurring before individual reaches the hospital[2].Accurate identification of the cause of chest pain is a challenge to the emergency physician because a significant proportion of patients with acute coronary syndrome (ACS) present atypically [3].

In 1979, in addition to symptoms and ECG changes, WHO recognized officially the use of biomarkers in the diagnosis of acute MI, by demonstration of typical rising and falling pattern [4].In the middle of 1980s, mass assay of CK-MB instead of catalytic activity was developed [5]. CK-MB was the marker of choice (gold standard) in the diagnosis of acute MI in 1980s[6]. Assays for cardiac troponins were developed in the late 1980s and early 1990s[7].

Accuracy of ECG diagnosis of AMI is not more than 80 percent and it is often found that in cases of early AMI the ECG could be normal. So the enzyme estimation has become of immense utility in early diagnosis. For specific diagnosis, combination of several enzymes is used.Due to high cardiac specificity of cTnT and cTnI, these biomarkers have become the recommended biomarkers for the diagnosis of acute myocardial injury [8]. High sensitive cardiac troponin T (hs-cTnT) is a modification of 4th generation cTnT69[9].

In present study, we collected samples of 200 patients admitted with the complain of acute chest pain and measured the following markers, Highly sensitive Troponin I (HS-TROP I), CK-MB and LDH.

Material and method :

Study Design: This is a prospective study of 200 cases.

Study setting: The study was carried out in tertiary care centre. All the patients having complaint of acute chest pain admitted in the emergency wards are included.

Time Period: The study was from November-2015 to December-2016

Inclusion criteria

1. Age >18 yrs
2. Patients having complain of acute chest pain

The diagnosis was based upon the ECG findings, complains, other relevant clinical findings and serum cardiac markers. Serum estimation of Highly sensitive Troponin I, CK-MB, and LDH was done. Blood samples were collected in plain bulb, at the time of admission and serum were separated by centrifugation.

Method Used: The serum level of cardiac Troponin I was determined by using VIDAS HIGH SENSITIVE troponin i (human cardiac specific) enzyme immunoassay kit.The reference range for hs Troponin I with this kit is <19 ng/l. The measurement range ofHigh sensitivity Troponin I with this kit is from 4.9 to 40,000 ng/l.

The serum level of cardiac CK-MB was determined by the VITROS 250 fully automated biochemistry analyser registered trademark of ORTHO CLINICAL DIAGNOSIS.The reference range for CK-MB with this kit is17-51 U/L. The measurement range of CK-MB with this kit is 2.7 - 300 U/L.

The serum level of LDH was determined by LDH-(P-L) REAGENT KIT (KINATIC PROCEDURE). The reference range for LDH with this kit is 230 – 460 U/L. The measurement range for LDH with this kit is 8-2000 U/L.

Results

This study involves the changes in serum cardiac markers (hs-Troponin I, CK-MB, LDH) in patients admitting for the chest pain in emergency department.

Table-1: Demographic profile of the patients

Age group (yrs)	Number of Male patients	Number of Female patients	Total number of patients
21-30	04	04	08
31-40	12	00	12
41-50	28	04	32
51-60	56	20	76
61-70	28	08	36
71-80	18	08	26
81-90	06	04	10
Total	**152**	**48**	**200**

In present study, out of 200 patients admitted for acute chest pain 20 patients were in age group of 20 to 40 years, 144 patients were in age group of 40 to 70 years, and 36 patients were more than 70 years of age.

Table-2: Changes in hsTroponin I in patients complaining of acute chest pain

Condition	Elevation of hsTroponin I	Normal levels of hsTroponin I	Total
Acute MI	110	90	200
Unstable angina	00	00	00
LRTI	00	00	00
COPD	00	00	00
GERD	00	00	00
Total	110	90	200

From above data it is found that out of 110 patients who actually diagnosed to have acute myocardial infarction, hsTroponin I was elevated in all 110 patients. While in 90 patients who diagnosed to have other condition than acute myocardial infarction, hsTroponin I was elevated in none of them.

So, in present study for hsTroponin I Sensitivity was 100% and Specificity was 100% for diagnosis of acute myocardial infarction.

Table-3: Changes in CK-MB in patients complaining of acute chest pain

Condition	Elevation of CK-MB in num of patients	Normal levels of CK-MB in num of patients	Total
Acute MI	98	12	110
Unstable angina	10	36	46
LRTI	00	24	24
COPD	00	12	12
GERD	00	08	08
Total	108	92	200

From above data it was found that out of 110 patients who actually diagnosed to have acute myocardial infarction, CK-MB was elevated in all 98patients. In 12 patients in spite of having acute myocardial infarction it remained in normal range. While in 90 patients who diagnosed to have other condition than acute myocardial infarction, CK-MB was elevated in 10 patients and in 80 patients it remained in normal range.

So, in present study for CK-MB Sensitivity was 89.1% and Specificity was 88.8% for diagnosis of acute myocardial infarction.

Table-4: Sensitivity of CK-MB

	hsTroponin I	CK-MB	P value	Significance
Sensitivity	100%	89.1%	0.002	HS
Specificity	100%	88.8%	0.0017	HS

☐ NS – Non significant, S – significant, HS – Highly significant

When applying chi-square $\{X_2\}$ test to compare sensitivity and specificity of hsTroponin I and CK-MB the difference was statistically highly significant. (P value <0.05). The value of p <0.05 is about the statistical significance of test. That is, the probability that the result of the statistical test is due to chance alone (which is a spurious result) is less than 5%.As it's lower than 0.05 (lower than 5%), we feel confident enough to say that it's not due to chance

Table-5: Changes in LDH in patients complaining of acute chest pain

Condition	Elevation of LDH in num of patients	Normal levels of LDH in num of patients	Total
Acute MI	72	38	110
Unstable angina	20	26	46
LRTI	08	16	24
COPD	04	08	12
GERD	04	04	08
Total	108	92	100

From above data it was found that out of 110 patients who actually diagnosed to have acute myocardial infarction, LDH was elevated in all 72 patients. In 38 patients in spite of having acute myocardial infarction it remained in normal range. While in 90 patients who diagnosed to have other condition than acute myocardial infarction, LDH was elevated in 36 patients and in 54 patients it remained in normal range.

So, in present study for LDH Sensitivity was 65.4% and Specificity was 60% for diagnosis of acute myocardial infarction.

Table-6: Sensitivity of hsTroponin I and LDH

	hsTroponin I	LDH	P value	Significance
Sensitivity	100%	65.4%	<0.0001	HS
Specificity	100%	60%	<0.0001	HS

☐ NS – Non significant, S – significant, HS – Highly significant

When applying chi-square $\{X_2\}$ test to compare sensitivity and specificity of hsTroponin I and LDH the difference was statistically highly significant (P value <0.0001). The value of p <0.0001 is about the statistical significance of test.

Discussion

Present study involves the changes in serum cardiac markers (hsTroponin I, CK-MB, LDH) in patients admitting for the acute chest pain in emergency department.

1.Demographic profile of the patients: (mean age – 59.04)

In present study, out of 200 patients admitted for acute chest pain 144 patient were in age group of 40 to 70 years, 20 patients were in age group of 20 to 40 years and 36 patients were more than 70 years of age. This results are comparable to other studies:

Astudy was conducted on changing age distribution of first ever acute myocardial infarction among men and women. They found that the median age at which the index AMI occurred rose significantly (p<.0001); from 64 to 66 years of age among men, and from 72 to 77 years of age in women [10].

A study was conducted on age and gender differences in incidence and case fatality trends for myocardial infarction. They concluded that trends in MI incidence differed by sex and age; in the age group 35–79 years a marked decrease was observed among men but an increase was observed among women, while no change was observed among older patients. MI severity and case fatality were clearly reduced for both sexes. Their data suggested that the burden of CHD is shifting from middle-aged men toward middle-aged women and elderly patients [11].

"These data suggest that incidence of chest pain is higher in middle aged patients."

2. Changes in hsTroponin I in patients complaining of acute chest pain

In present study, it was found that out of 110 patients who actually diagnosed to have acute myocardial infarction, hsTroponin I was elevated in all 110 patients. While in 90 patients who diagnosed to have other condition than acute myocardial infarction, hsTroponin I was elevated in none of them.

In present study, sensitivity and specificity of hsTroponin I for diagnosis of acute myocardial infarction was 100%.

These results are comparable to other studies:

A study was conducted on comparative analysis of cardiac Troponin I and Creatine Kinase-MB as markers of acute myocardial infarction. They concluded that cTnI is an excellent marker for detecting and ruling out AMI, because it has better specificity and a wider diagnostic window than the accepted standard, CK-MB [12].

A study on rapid diagnosis of acute myocardial infarction. Consecutive 150 patients admitted to the coronary care unit was studied. They concluded that measurement of CTn-I accurately detects MI in patients and should facilitate the diagnosis and management of such patients [13].

A study of cardiac troponin-i as a diagnostic marker in comparison with creatine kinase-MB in myocardial infarction. They found that the diagnostic efficiency of cardiac troponin-I is 97%, and creatine kinase –MB is 63% in diagonosis of acute MI. So they concluded that serum cardiac troponin-I is highly sensitive and specific cardiac marker which can substantially improve the early diagnosis of acute mycocardial infarction [14].

A study on Role of CK-MB and Troponin-I in Diagnosing Non-ST-Elevation Myocardial Infarction. They concluded that Troponin-I can identify the minimal cardiac damage which will be useful for the physician to start immediate intervention [15].

"These data suggest that Troponin I is very sensitive and specific cardiac biomarker in diagnosis of acute myocardial infarction."

3. Changes in CK-MB in patients complaining of acute chest pain

In present study it was found that out of 110 patients who actually diagnosed to have acute myocardial infarction, CK-MB was elevated in 98 patients. In 12 patients in spite of having acute myocardial infarction it remained in normal range. While in 90 patients who diagnosed to have other condition than acute myocardial infarction, CK-MB was elevated in 10 patients and in 80 patients it remained in normal range.

In present study sensitivity and specificity of CK-MB for diagnosis of acute myocardial infarction was 89.1% and 88.8% respectively.

These results are comparable to other studies:

A study on comparable detection of acute myocardial infarction by creatine kinase MB isoenzyme and cardiac troponin I. They concluded that cTnI and MBCK had statistically indistinguishable diagnostic accuracies for the detection of acute myocardial infarction[16].

Astudy was conducted on diagnostic marker cooperative study for the diagnosis of myocardial infarction. They found that with each marker as the diagnostic standard, CK-MB sub forms and myoglobin remained the most sensitive for early diagnosis. So they concluded that the CK-MB sub form assay alone or in combination with a troponin reliably triages patients with chest pain and should lead to improved therapy and reduced cost [17].

Astudy was conducted on evaluation of CK-MB isoform analysis for early diagnosis of myocardial infarction. They concluded that analysis of CK-MB by high-voltage electrophoresis is an effective method for rapid diagnosis of MI, with the isoform analysis enhancing early sensitivity [18].

A study was conducted,. They concluded that CK-MB and CTnT were the earliest was more compared to other serological markers. CK-MB is more helpful in the diagnosis of reinfarction [19].

"These data suggest that CK-MB is very sensitive cardiac biomarker for diagnosis of acute myocardial infarction but its sensitivity and specificity are not as much as hsTroponin I. As CK-MB reaches its normal value within 2-3 days it is helpful in diagnosis of reinfarction."

1. Changes in LDH in patients complaining of acute chest pain

In present study, it was found that out of 110 patients who actually diagnosed to have acute myocardial infarction, LDH was elevated in all 72 patients. In 38 patients in spite of having acute myocardial infarction it remained in normal range. While in 90 patients who diagnosed to have other condition than acute myocardial infarction, LDH was elevated in 36 patients and in 54 patients it remained in normal range. In present study sensitivity and specificity of LDH for diagnosis of acute myocardial infarction was 65.4% and 60% respectively.

These results are comparable with other studies:

A study on comparison of Troponin-T with other cardiac markers. They found that cardiac marker sensitivities and specificities were cTnT (98% and 73%), CK-MB mass (81% and 97%), CK (73% and 78%), LDH (67% and 80%), LDH-1 (33% and 95%), and myoglobin (79% and 66%) [20].

A study on comparison of cardiac troponin I and lactate dehydrogenase isoenzymes for the late diagnosis of myocardial injury. In this study, the sensitivity of cardiac troponin I (cTnI) and LD1/LD2 were compared as late markers of myocardial injury over a 5-day period in 36 patients admitted with a diagnosis of myocardial infarction to the coronary care unit. Over this period, the sensitivity of cTnI was significantly greater than that of LD1/LD2 (P <0.05). They concluded

that cardiac troponin I (cTnI) has greater sensitivity than lactate dehydrogenase isoenzymes for delayed diagnosis of myocardial injury and is a more cost-effective test, the authors recommend it as a test of choice in this setting [21].

A study in which they emphasized on serological cardiac markers i.e., creatinine kinase-M& B chains (CK-MB), cardiac troponin-T (CTnT), Aspartate amino transferase (AST) and lactate dehydrogenase (LDH). They found that CK-MB and CTnT were the earliest serological markers to be detected in blood following AMI. Sensitivity of CTnT was more compared to other serological markers. Presence of CTnT was better diagnostic of AMI in vital period. CK-MB is more helpful in the diagnosis of reinfarction [19].

Conclusion

Based on present study, it is concluded that acute myocardial infarction require immediate diagnosis and intervention. In early diagnosis cardiac markers are very useful to differentiate acute myocardial infarction from other conditions.

References

1. Fuster V, Badimon L, Badimon JJ, Chesebro JH. The pathogenesis of coronary artery disease and the acute coronary syndromes (Second of two parts). N Engl J Med 1992 Jan 30;326(5):310-8.)[pubmed]
2. Harrison's principles of Internal medicine 16th edition; vol 2; chapter – 288; ST Segment elevation myocardial inflammation; page – 1448.
3. Pope JH, Aufderheide TP, Ruthazer R, et al. Missed diagnoses of acute cardiac ischemia in the emergency department. N Engl J Med. 2000 Apr 20;342:1163-70.)[pubmed]
4. Nomenclature and criteria for diagnosis of ischemic heart disease. Report of the Joint International Society and Federation of Cardiology/World Health Organization task force on standardization of clinical nomenclature. Circulation. 1979;59:607-9.)[pubmed]
5. Vaidya HC, Maynard Y, Dietzler DN, Ladenson JH. Direct measurement of creatine kinase-MB activity in serum after extraction with a monoclonal antibody specific to the MB isoenzyme. Clinical chemistry. 1986 Apr;32(4):657-63.[pubmed]
6. Dolci A, Panteghini M. The exciting story of cardiac biomarkers: from retrospective detection to gold diagnostic standard for acute myocardial infarction and more. Clinicachimica acta; international journal of clinical chemistry. 2006 July 23;369(2):179-87.[pubmed]
7. Katus HA, Remppis A, Looser S, Hallermeier K, Scheffold T, Kubler W. Enzyme linked immuno assay of cardiac troponin T for the detection of acute myocardial infarction in patients. Journal of molecular and cellular cardiology. 1989 Dec;21(12):1349-53.[pubmed]
8. Morrow DA, Cannon CP, Jesse RL, Newby LK, Ravkilde J, Storrow AB, et al. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: clinical characteristics and utilization of biochemical markers in acute coronary syndromes. Clinical chemistry. 2007Apr 3;115(13):e356-75..[pubmed]
9. Giannitsis E, Kurz K, Hallermayer K, Jarausch J, Jaffe AS, Katus HA. Analytical validation of a high-sensitivity cardiac troponin T assay. Clinical chemistry. 2010 Feb;56(2):254-61.[pubmed]
10. Alan C Wilson, Yu-Hsuan Shao, Nora M Cosgrove, John S Pantazopolous, Abel E Moreyra, John B Kostis. Changing Age Distribution of First Ever Acute Myocardial Infarction Among Men and Women in New Jersey Hospitals. Circulation. 2007;116(2):832.
11. Jan Mannsverk, Tom Wilsgaard,IngerNjolstad, Laila ArnesdatterHopstock,Maja-Lisa Lochen, Ellisiv B Mathiesen et al. Age and gender differences in incidence and case fatality trends for

myocardial infarction: a 30-year follow-up. The TromsoStudy.European Journal of Preventive Cardiology. 2012(19) issue 5:927-934.[pubmed]

12. ShazibPervaiz, Philip Anderson, Thomas P. Lohmann, Charlotte J. Lawson, Yue-Jin Feng, Dave Waskiewicz. Comparative Analysis of Cardiac Troponin I and Creatine Kinase-MB as Markers of Acute Myocardial Infarction.Clin.Cardiol. 1997Mar;20:269-271.[pubmed]

13. DurdiQujeq. Rapid Diagnosis of Acute Myocardial Infarction.Iran. Biomed. J. 1999;3(1):59-62

14. Mahalaxmi.S.Petimani, P.SureshBabu. Study of cardiac troponin-i as a diagnostic marker in comparision with creatine kinase-mb in myocardial infarction.International Journal of Pharmacy and Biological Sciences. Jan-Mar 2013;3(1):89-97.

15. Kiran R Bagale1, Avinash S. Ingle. Role of CK-MB and Troponin-I in Diagnosing Non-ST-Elevation Myocardial Infarction.International Journal of Science and Research. 2014;3(8). Paper ID: 02015352.

16. Adams JE 3rd, Schechtman KB, Landt Y, Ladenson JH, Jaffe AS. Comparable detection of acute myocardial infarction by creatine kinase MB isoenzyme and cardiac troponin I. Clin Chem. 1994 Jul;40(7):1291-5.[pubmed]

17. Janice Zimmerman, Robert Fromm, Denise Meyer, Ann Boudreaux, Chuan-Chuan C. Wun, Richard Smalling, Barrry Davis, Gabriel Habib, Robert Roberts. Diagnostic marker cooperative study for the diagnosis of myocardial infarction.Circulation. 1999;99: 1671-1677.

18. Bock JL, Brogan GX Jr, McCuskey CF, Thode HC Jr, Hollander JE, Gunther T. Evaluation of CK-MB isoform analysis for early diagnosis of myocardial infarction.JEmerg Med. 1999 Jan-Feb;17(1):75-9.[pubmed]
Dhruva G. A., Agravat A. H.. Serum cardiac markers in patients of acute myocardial infarction. Journal of Cell and Tissue Research 2010;10(3):2343-2347.[pubmed]

19. Fitzgerald RL, Frankel WL, Herold DA.Comparison of Troponin-T with other cardiac markers.Am J ClinPathol. 1996 Sep;106(3):396-401.[pubmed]

20. Martins JT, Li DJ, Baskin LB, Jialal I, KefferJH.Comparison of cardiac troponin I and lactate dehydrogenase isoenzymes for the late diagnosis of myocardial injury. Am J Clin Pathol.1996 Dec; 106(6):705-8.[pubmed]