ORIGINAL RESEARCH

Quantitative Estimation of Cardiac Markers in Acute Myocardial Iinfarction: A Study in A Tertiary Care Hospital

N. Jaya[1], Nasika Chowdeswari[1]

ABSTRACT

Introduction: Myocardial Infarction is one of the leading cause of death in the world. CK-MB, Myoglobin and Troponin T are the main cardiac markers, whose levels rise durine an MI. we have tried to compare the sensitivity, specificity, Positive predictive value and Negative Predictive Value of Myoglobin, CK-Mb mass, CK-MB act and Troponin T.

Materials and Methods: 167 patients who presented with angina or similar symptoms of MI in <48 hours duration and had an elevated ST segment of >1mm in at least 2 consecutive leads were included in the study. First blood sample was collected at 0 hours and then at 1, 2, 3, 6, hours and once between 12-24 hours of onset of symptoms. Then they were collected once every day. All the blood samples were tested for myoglobin, CK-MB_{mass}, and Troponin T and CK-$MB_{activity}$.

Results: We had observed 61 patients out of a total of 167 patients (37%) to have MI. 63% (106) patients did not have AMI. The ages of 167 patients ranged between 37-74 years in our study with the mean age being 62.5 years ± 3.4. majority of the patients were males compared to females, although this had no relevance in our study. Among the patietns with AMI, based on the CK-MB levels, the size of the infarcts were divided into small, medium and large (Fig: 2) More than half of the infarcts were of the small size. Many of the large size infarcts had a history of previous AMI. The Negative Predictive value rose to the peak within 6 hours in myoglobin while it did not reach 90% mark with Troponin T. Sensitivity with myoglobulin was above 90% within 6 hours but the levels decreased soon after. But the other cardiac markers retained high level of sensitivity even after 24 hours.

Conclusion: We conclude that Troponin T, though a highly efficient marker in the diagnosis of MI is not as good marker in ruling out AMI as Myoglobin or CK-MB_{mass} or CK-MB_{act}. Of these also, myoglobin is a better marker as it rises to the peak very early compared to the others.

Keywords: Myocardial Infarction, Cardiac markers, Myoglobin, Troponon T, CK-MB_{mass}, CK-$MB_{act.}$

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INTRODUCTION

Myocardial infarction (MI) or acute myocardial infarction (AMI), commonly known as a heart attack, occurs when blood flowstops to a part of the heart causing myocardial cell death. Coronary heart disease (CHD) is the number one cause of death in the Western world and as such constitutes an immense public health problem.[1] In 2006, an estimated 935,000 people experienced an acute MI, of which more than 150,000 resulted in death in the United States.[2] In the past four decades, the life expectancy has seen a marked increase, but it is obscured by the fact that the decline largely represents the postponement of CHD deaths until older age. Thus the burden of coronary heart disease is increasing along with the life expectancy. Since myocardial infarction is life threatening, and events may be sudden and unpredictable, early detection and diagnosis is important to limit myocardial damage and preserve cardiac function.[2]

The World Health Organization (WHO) defines the diagnosis of Acute Myocardial Infarction to be two out of the three: characteristic chest pain, diagnostic electrocardiogram changes and elevation of the biochemical markers in the blood samples.[3]

In the early stages of MI, the electrocardiogram (ECG) may not always show the classical features of ST elevation and new Q waves hampering in the clear diagnosis.[4] Among the biochemical markers, the most sensitive and specific markers are elevated levels of creatinine kinase (CK-MB), Troponin T, and myoglobin which are useful in early diagnosis of acute coronary syndrome. These can be rapidly and easily measured in the serum.[5,6]

ST- segment elevation occurs shortly after coronary artery occlusion and is highly diagnostic for MI.[7,8] Other than the elevated ST segment, measurement by newer and highly specific markers of the myocardial damage is done by cardiac structural proteins like Troponin T (TnT) and Creatinine kinase. TnT isnot detectable in the normal population and is released into the circulation during MI earlier than

CK-MB.[9-11] In the acute coronary syndrome of unstable angina pectoris, the presence of this marker in the plasma is diagnostically superior, because it identifies minor myocardial damage missed by other biochemical markers. It is also known to have prognostic significance, because if present, it identifies a subgroup of patients who are at high risk for early cardiac events.[12-14]

The purpose of this study was to estimate the elevation of the Cardiac Markers with reference to time of onset of symptoms, the sensitivity and specificity of these markers along with their Positive and Negative Predictive Values.

MATERIALS AND METHODS

This study was conducted in the Department of Biochemistry at ACSR GovernmentMedical College between May 2013 to July 2015.167 patients who came to our hospital with angina or similar symptoms of MI in <48 hours duration and had an elevated ST segment of >1mm in at least 2 consecutive leads were included in the study. Informed consent was taken from all the patients. Patients with severe skeletal damage, who underwent cardiac resuscitation and those who refused to give informed consent were excluded from the study.

Patients who had abnormal ECG readings, suggestive of Acute Myocardial Infarction were given thrombolysis on the attending physician's advice and appropriate therapy was given. Similar was the case with patients with symptoms of unstable angina who were treated accordingly. Detailed history, physical examination and ECG was taken for all the patients and the probability of Myocardial Infarction was noted based on the ST-segment elevation.

First blood sample was collected at 0 hours and then at 1, 2, 3, 6, hours and once between 12-24 hours of onset of symptoms. Then they were collected once every day. All the blood samples were tested for myoglobin, CK-MB_{mass}, and Troponin T. CK-$MB_{activity}$ was evaluated till the elevated levels came back to the base line.

CK-MB_{act} was measured by column chromatograohy method. The upper limit for this test was 8 U/L. CK-Mb_{mass} was measured by immunochemical method, with the upper reference limit being 8.0 ng/mL; linearity was from 0 to 500 ng/mL. Myoglobin was measured by immunoturbidimetry method. The measuring range was 50-650ng/ml, with the upper reference level being 9 ng/ml. Troponin T was measured by ELISA. The upper reference limit was 0.1 ng/mL, and the linearity range was 0 to 15 ng/mL.

RESULTS

The diagnosis of Acute myocardial infaction was based on the WHO criteria which includes a typical history and chest pain, with elevated levels of CK-MBact above the diagnostic threshold concentration with or without the development of changes in the Q waves on ECG.[15]

We had observed 61 patients out of a total of 167 patients (37%) to have MI. 63% (106) patients did not have AMI (fig: 1)

The ages of 167 patients ranged between 37-74 years in our study with the mean age being 62.5 years ± 3.4. majority of the patients were males compared to females, although this had no relevance in our study. Other general details of the patients is shown the table: 1

Among the patietns with AMI, based on the CK-MB levels, the size of the infarcts were divided into small, medium and large (Fig: 2) More than half of the infarcts were of the small size. Many of the large size infarcts had a history of previous AMI.

The blood samples were tested for the markers of MI and the sensitivity, specificity, Positive Predictive value and Negative Predictive value were calculated. After 6 hour, CK-MB-mass showed a sensitivity of 87.3% and rose to 93.5% only around 24 hours, while sensitivity of myoglobin crossed the 90% mark in 6 hours itself, but the levels decreased within 12 hours (Fig:3).

High levels of specificity was seen in all the cardia markers with most of them being above 90% within 2 hours while myoglobin was over 90% sprcific only after 3 hours (Fig:4). The Negative Predictive value rose to the peak within 6 hours in myoglobin while it did not reach 90% mark with

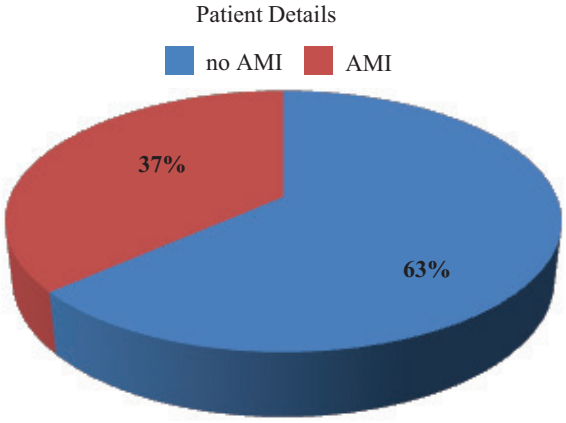

Figure-1: No. of patients with or without Acute myocardial infarction

Mean Age (in years)	**62.5 ± 3.4**
Males	108 (64.7%)
Hypertension	23%
Diabetes	28%
Smoker	42%
Previous MI	34%
Accelerated angina	35
Previous bypass / graft	15%
Admission rest pain	64
Mean time to hospital from worst pain	5.2
Medication with Beta blockers	25%
With nitrates	34%
With Ca antagonists	21%
Impaired renal function (creatinine >120mmol/L	0.5%

Table-1: General details of the patients

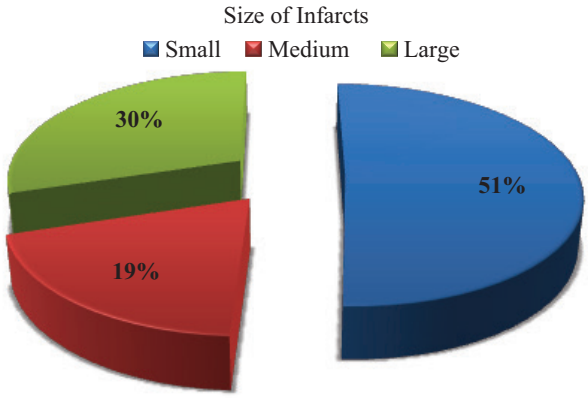

Figure-2: Size of Infarcts

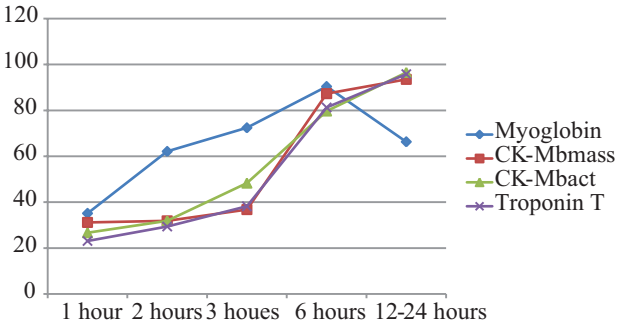

Figure-3: Sensitivity of CK-MBmass, CK-MBact, Myoglobin and Troponin T

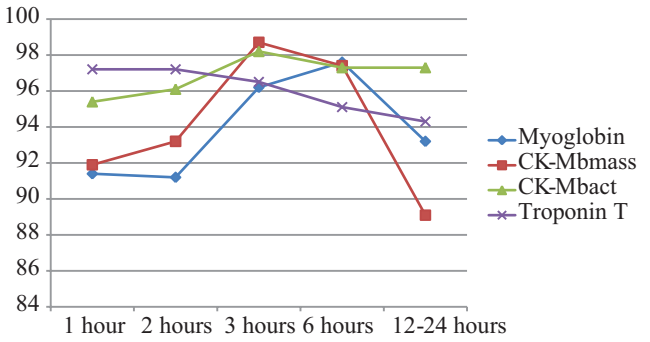

Figure-4: Specificity of CK-MBmass, CK-MBact, Myoglobin and Troponin T

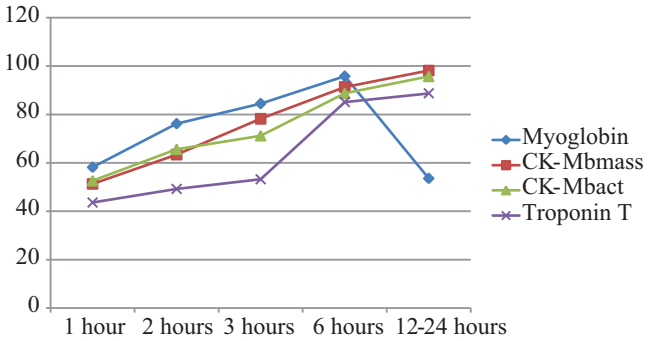

Figure-5: NPV of CK-MBmass, CK-MBact, Myoglobin and Troponin T

Marker	Test positive in (hours)	Peak levels (in hours)	After 1 hour	After 2 hours	After 3 hours	After 6 hours	Between 12-24 hours
$CK\text{-}MB_{mass}$	3-8	12-24					
Sensitivity			31.2	31.9	36.8	87.3	93.5
Specificity			91.9	93.2	98.7	97.4	89.1
PPV			95.4	94.3	91.7	90.3	90.6
NPV			51.3	63.4	78.2	91.3	98.1
$CK\text{-}MB_{act}$	4-6	12-24					
Sensitivity			26.7	31.9	48.3`	79.7	96.5
Specificity			95.4	96.1	98.2	97.3	97.3
PPV			93.8	98.1	92.6	93.2	93.1
NPV			52.6	65.6	71.2	88.7	95.7
Myoglobin	2	6 -8					
Sensitivity			35.1	62.1	72.4	90.4	66.3
Specificity			91.4	91.2	96.2	97.6	93.2
PPV			84.3	93.2	97.8	96.3	94.2
NPV			58.2	76.2	84.5	95.8	53.6
Troponin T	4-10	8-28					
Sensitivity			23.1	29.4	38.2	81.3	95.8
Specificity			97.2	97.2	96.5	95.1	94.3
PPV			78.5	80.9	83.3	97.1	88.4
NPV			43.6	49.2	53.2	85.1	88.7

Table-2: Characteristics of $CK\text{-}MB_{mass}$, $CK\text{-}MB_{act}$, Myoglobin and Troponin T Assays

Troponin T (Fig:5).

The characteristics of all the assays in given in the table 2.

DISCUSSION

Of late the protocols being used to exclude Acute Myocarial Infarction involve the measurement of the cardiac markers over 6 to 12 hours of onset of symptoms.It is estimated that about 1/3rd of the patients are not diagnosed with AMI because the chest pain is atypical or absent.[16,17] ECG may be misleading in 8% of the cases and indeterminate in about 12% of them.[18] About 50% of the patients with AMI may

have nondiagnostic ECGs initially.[19] To rule out an AMI in these cases depends chiefly on the cardiac markers like CK-MB, myoglobin and Troponin T.[20]

Taking into account the importance of the quickest diagnosis possible of myocardial infarction, our study mainly attempt to assess the diagnostic value of the various markers for AMI.

We have observed in our study that by consequent and serial samples for the markers shows that the negative predictive value in myoglobin after 6 hours is above 89%, showing that AMI can be ruled out in so many cases. Myoglobin as a useful marker in diagnosis of AMI has been reported in several other studies.[21-23] However the levels of myoglobins disappear much faster that the other cardiac marker, making it not so efficient after some time Our study showed a decline of myoglobin NPV to less than 53% with 12 – 24 hours. We have observed that Ck-MB_{mass} NPV rises much earlier than $CK\text{-}MB_{act}$ and rises to over 96% within 6 hours while the same value if obtained by $CK\text{-}MB_{act}$ only after 12 hours duration.

Tropinin T rose late but did not attain 90% NPV even after 24 hours duration. We found troponin T not a very reliable marker as compared to CK-MB during AMI. But it is said to be elevated in unstable angina where other markers are not very useful. Although our study did not concentrate on the Troponin NPV in unstable angina, there have been many reports which have favoured Troponin to be a better marker in such cases.[24-26] It has been observed that even low levels of troponin that are below typical cutoff values to define myocardial necrosis appear to have prognostic significance for future cardiac events

The sensitivity of the markers showed that $CK\text{-}MB_{mass}$, $CK\text{-}MB_{act}$ and Troponin T showed a marked increase in the sensitivity >90% at the peak concentrations as compared to myoglobin, which though rises early, did not reach a peak of 90%. This was observed by Apple et al in a similar study.

The specificity for most of the markets were complarable but that in Troponi T, unstable angina also should be traken into account that probably gave high specificity as Troponin was highly elevated in these cases

CONCLUSION

We conclude that Troponin T, though a highly efficient marker in the diagnosis of MI is not as good marker in ruling out AMI as Myoglobin or $CK\text{-}MB_{mass}$ or $CK\text{-}MB_{act}$. Of these also, myoglobin is a better marker as it rises to the peak very early compared to the others.

As there have been many reports on the efficacy of Troponin T in the diagnosis of unstable angina, we recommend further study to corroborate this.

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