

Diagnostic Accuracy of Heart-type Fatty Acid Binding Protein for the Detection of Acute Myocardial Infarction among South Indian Population: A Cross-sectional Study

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ABSTRACT

Introduction: Acute Myocardial Infarction (AMI) is a serious life threatening condition having a high mortality and morbidity rate. Hence, early detection and appropriate treatment is essential. Clinically Troponin I and Creatinine Kinase Myocardial Band (CK-MB) are currently used to detect AMI. But its rise in blood concentrations is seen only after 4-6 hours after the onset of AMI. Clinical research shows that Heart-type Fatty Acid Binding Protein (H-FABP), a novel biomarker, is beneficial in the early detection of AMI.

Aim: To determine the diagnostic accuracy of H-FABP and compare with the existing blood biochemical markers, such as Troponin I and CK-MB, in the early detection of AMI in south Indian population.

Materials and Methods: This cross-sectional study was conducted in Sree Balaji Medical College and Hospital, south Chennai, Tamil Nadu, India, from March 2017 to April 2019. A total of 50 participants, aged between 40-75 years, and diagnosed with ST elevation myocardial infarction presenting within 24 hours to the emergency room were included. Serum was collected during the time of admission (0 hour), between 4-6 hours from

the time of admission and between 12-24 hours from the time of admission for estimation of cardiac specific biomarkers such as cardiac troponin I, H-FABP, CK-MB. The sensitivity, specificity and accuracy of the cardiac-specific biomarkers were calculated using Receiving Operating Characteristics (ROC) curve analysis.

Results: There were 38 males and 12 females, with a mean age of 62.1±4.7 years. The sensitivity of H-FABP at the time of admission (0 hour) was 88%, 78% between 4-6 hours of admission, and 42% between 12-24 hours of admission. At 0 hour, the sensitivity of H-FABP (88%) was high compared to cardiac troponin I (43%) and CK-MB (40%). The accuracy of H-FABP and cTnI was equal (80% each) at the time of admission. At 4-6 hours after admission, cardiac troponin I showed higher sensitivity, specificity and accuracy compared to H-FABP. ROC analysis showed the Area Under the Curve (AUC) for H-FABP was higher (0.81) compared to cardiac troponin I and CK-MB.

Conclusion: H-FABP was found to be more sensitive compared to cardiac troponin I or CK-MB in AMI patients. Hence, early diagnosis of AMI is made possible with the H-FABP measurements.

Keywords: Cardiac biomarkers, Cardiac troponin I, Creatinine kinase myocardial band

INTRODUCTION

The AMI is a life threatening condition, leading to high mortality and morbidity rate. Annually, one million deaths are reported in the world due to AMI [1]. The World Health Organisation (WHO) estimates that 3% of rural residents and 7% of city dwellers in India have suffered a recorded AMI [2]. Data showed that almost 30% of the AMI patients die out of the hospital, 50% die during treatment, and 20% live in morbid conditions [3].

No routine diagnostic tests can rule out the manifestation of an Acute Coronary Syndrome (ACS) in the early stages in people who come with chest discomfort of suspected cardiac origin. Consequently, there are major difficulties in making an early diagnosis [4]. The management of such patients is also fraught with logistical and financial challenges. Delayed diagnosis and management has been demonstrated to increase mortality and morbidity by five fold [5].

So, a timely and accurate diagnosis is important. A simple, sensitive, specific, robust cardiac biomarker is essential for the diagnosis of AMI. Clinically, troponin I and CK-MB are the two biomarkers used for the detection of AMI. But it lacks in sensitivity because rise in the concentrations of troponin I and CK-MB in blood circulation is seen after 4-6 hours of the onset of AMI [6].

A low molecular weight protein, H-FABP, which is present in the cytoplasm of myocardial cells, is released within hours (1-2 hours) in to the blood stream after the onset of AMI [7]. Since, few studies have

reported H-FABP ability to diagnose AMI [8,9] but, previous studies measured H-FABP using Point of Care Technology (POCT) which has disadvantages like, incorrect handling and instrument calibration errors. Hence, this study was planned to determine the diagnostic efficacy of H-FABP and compare with the existing blood biochemical markers such as troponin I and CK-MB in the early detection of AMI using ELISA method in a clinical laboratory setting.

MATERIALS AND METHODS

The cross-sectional study was conducted in Sree Balaji Medical College and Hospital located in south Chennai, Tamil Nadu, India, from March 2017 to April 2019. This study was approved by Institutional Ethical Committee (IEC) board (SBMCH/IEC/2017/933). Written informed consent was obtained from all the study participants.

Inclusion criteria: A total of 50 participants aged between 40-75 years, diagnosed with ST elevation MI, presenting within 24 hours to the emergency room were included in the study.

Exclusion criteria: Subjects with pulmonary thromboembolism, respiratory diseases, kidney diseases, liver diseases, musculoskeletal diseases, gastrointestinal diseases or any other acute systemic illnesses were excluded from the study.

Sample size: Sample size was calculated using the formula:

$$N = Z^2 pq / d^2$$

Z=Confidence level

$P = \text{Expected prevalence} [10]$

$q = 100 - P$

$d = \text{precision}$

$Z = 1.96, P = 3, q = 100 - 3 = 97, d = 5.$

Substituting the above values in the formula gives N of 45. Hence, a sample size of 50 was taken in present study.

Data collection: Demographic details (age, gender) and clinical details (chest pain, dyspnoea, dyslipidaemia, smoking, alcohol, hypertension, diabetes, aspirin use) were recorded from all the study participants.

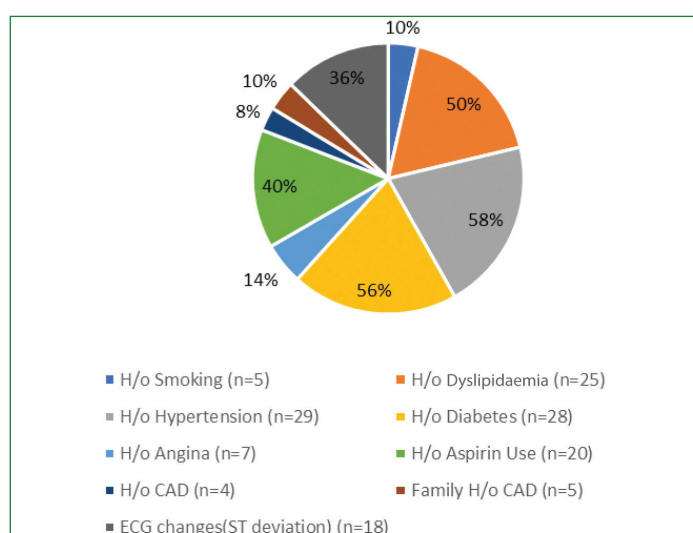
A 5 mL of blood (serum) was collected during the time of admission (0 hour), between 4-6 hours from the time of admission, and between 12-24 hours from the time of admission for estimation of cardiac specific biomarkers such as cardiac troponin I, H-FABP, CK-MB. Sensitivity, specificity and accuracy of these biomarkers were assessed according to the time of admission and duration of chest pain. Troponin I and CK-MB was estimated using Siemens ADVIA CENTURA immunoassay analyser based on sandwich electrochemiluminescence immunoassay principle [11,12]. H-FABP was measured using sandwich double body ELISA principle [13]. The cut-off values for H-FABP was ≥ 1.6 ng/mL, Troponin I was ≥ 0.3 ng/mL, CK-MB was ≥ 25 U/L [11-13].

STATISTICAL ANALYSIS

The sensitivity, specificity, and accuracy of H-FABP, troponin I, CK-MB were calculated using Statistical Package for the Social Sciences (SPSS) software version 28.0. Study data were presented as percentage, mean and standard deviation. Data were statistically analysed using Analysis of Variance (ANOVA), Student's t-test, Chi-square test. The diagnostic accuracy of H-FABP, Troponin I, CK-MB was assessed using ROC analysis. The p-value < 0.05 was considered significant.

RESULTS

In present study, out of total 50 study participants, 38 were male and 12 were female, with a mean age of 62.1 ± 4.7 years. There were about 29 participants (58%) with hypertension, 25 participants (50%) with dyslipidaemia, 28 participants (56%) with history of diabetes [Table/Fig-1].



[Table/Fig-1]: Distribution of risk factors among the study participants (N=50).
H/o: History of; CAD: Coronary artery disease

Variable	Mean \pm SD		p-value	Sensitivity			Specificity			Accuracy		
	<6 hrs	>6 hrs		<6 hrs N=23	>6 hrs N=27	Total N=50	<6 hrs N=23	>6 hrs N=27	Total N=50	<6 hrs N=23	>6 hrs N=27	Total N=50
H-FABP (ng/mL)	3.1 \pm 1.2	1.8 \pm 1.6	<0.0001	100%	70%	89%	85%	46%	65%	93%	70%	80%
cTnI (ng/mL)	1.82 \pm 0.7	2.1 \pm 1.9	0.33	45%	68%	72%	100%	100%	100%	70%	88%	80%
CK-MB (U/L)	21.3 \pm 1.4	29.7 \pm 0.6	<0.0001	30%	56%	45%	90%	89%	90%	62%	70%	67%

[Table/Fig-2]: Association of cardiac markers in relation to duration of chest pain (N=50).
Student t-test; chi-square test

Twenty three patients presented to the department within six hours of chest pain and 27 presented after six hours of experiencing chest pain. The overall sensitivity of H-FABP (89%) was high when compared with cardiac troponin I (72%) and CK-MB (45%) in relation to the duration of chest pain. Overall, the accuracy of H-FABP and cardiac troponin I was equal (80% each), but H-FABP (93%) showed a high accuracy in less than six hours of duration of chest pain compared to Cardiac Troponin I (70%) and CK-MB (62%). The specificity of H-FABP (65%) was low compared to cardiac troponin I (100%) and CK-MB (90%) [Table/Fig-2].

At 0 hour, the sensitivity of H-FABP (88%) was high compared to cTnI (43%) and CK-MB (40%). The accuracy of H-FABP and cTnI was equal (80% each) at the time of admission. At 4-6 hours after admission, cardiac troponin I showed higher sensitivity, specificity and accuracy compared to H-FABP. Overall, H-FABP showed a low specificity, sensitivity and accuracy as compared to cardiac troponin I and CK-MB after 4-6 hours, 12-24 hours of admission [Table/Fig-3].

The diagnostic accuracy of H-FABP, cardiac troponin I, CK-MB was assessed using the ROC curve analysis. It shows that the AUC for H-FABP was higher (0.81) compared to cardiac Troponin I (0.75) and CK-MB (0.67) [Table/Fig-4].

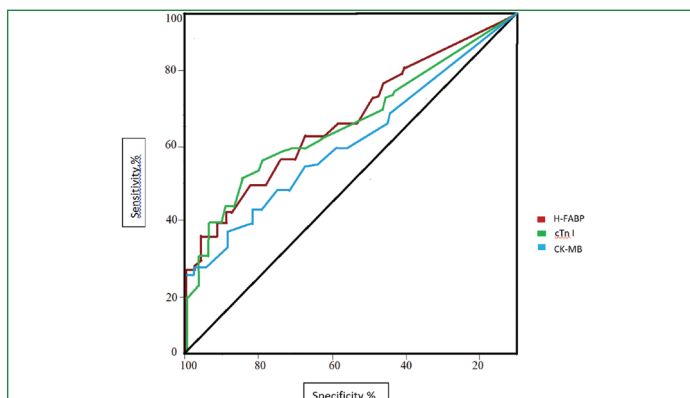
DISCUSSION

The study demonstrated that H-FABP showed higher sensitivity than troponin I and CK-MB in the patients admitted within 4 hours of onset of AMI. This study results were consistent with a few previous studies [14,15]. McCann CJ et al., did a prospective study with 664 patients over the period of three years in the United Kingdom. They found that measurement of H-FABP within four hours of symptoms was 86% sensitivity (95% CI 72-94) superior to measurement of cardiac troponins {65% sensitivity (95% CI 50-78)} for the diagnosis of AMI [16]. The present study also found that H-FABP had higher (88%) sensitivity than Troponin I (43%), when measured within 4 hours of admission. H-FABP, due to its low molecular weight, is immediately released within 20-30 minutes in to the circulation after the myocardial injury in the diagnosis of AMI is high. H-FABP is present predominantly in the myocytes, and its cardiac specificity is high. But the lack of specificity of H-FABP in the current experiment could be attributed to a multitude of different factors. Starting with all of the patients, regardless of how long they had been feeling chest discomfort, H-FABP was assessed. The reason for low specificity, both ischaemia and infarcted myocardium can cause the release of H-FABP. Another reason for low specificity may be that H-FABP is detected in skeletal muscle, though in lower concentrations than in other tissues. There was no information gathered regarding recent physical activity, injuries, or intramuscular injections within the purview of this investigation.

H-FABP was used as an early marker of AMI in various studies before cardiac troponins became widely used in clinical practice [17,18]. A study done by Ruzgar O et al., found that troponin sensitivity was 38%, CK-MB sensitivity was 76% of the AMI cases and H-FABP sensitivity was 95% of the AMI cases. Over 6-24 hours, the sensitivity to troponin and CK-MB increased to 100% and 90%, respectively, but after the same time period the sensitivity of H-FABP increased to 91% [19]. In the present study, the AUC for H-FABP was 0.81. A study by Suresh K et al., analysed 66 AMI patients and reported an AUC of 0.69 [20]. Similar findings were also in line with a research conducted by Inoue K et al., in Japan on roughly 400 patients [21].

Variable	Mean±SD			p-value	Sensitivity			Specificity			Accuracy		
	0 hrs	4-6 hrs	12-24 hrs		0 hrs	4-6 hrs	12-24 hrs	0 hrs	4-6 hrs	12-24 hrs	0 hrs	4-6 hrs	12-24 hrs
H-FABP (ng/mL)	1.96±0.7	3.42±1.1	0.12±1.6	0.01	88%	78%	42%	85%	75%	63%	80%	71%	60%
cTnI (ng/mL)	0.12±1.2	1.91±0.6	2.49±1.4	0.04	43%	90%	95%	100%	95%	100%	80%	85%	100%
CK-MB (U/L)	18.3±2.1	22.12±1.5	30.2±1.9	0.02	40%	75%	91%	90%	95%	92%	65%	85%	87%

[Table/Fig-3]: Comparing the cardiac markers in relation to the time of admission (N=50). ANOVA, chi-square test



Cardiac biomarkers	Area Under the Curve (AUC)
H-FABP	0.81
Cardiac Troponin I (cTnI)	0.75
CK-MB	0.67

[Table/Fig-4]: Receiving Operating Characteristics Curve (ROC) representing the diagnostic accuracy of Heart type fatty acid binding protein (H-FABP), Cardiac Troponin I (cTnI), Creatine kinase-Myocardial Band (CK-MB) in Acute Myocardial infarction (AMI).

According to Inoue K et al., despite the high sensitive troponin T (hsTnT) assay having superior diagnostic performance in the absence of ACS, it is more likely to produce false-positive results than H-FABP, which has comparable overall diagnostic performance [21].

Limitation(s)

The limitations of this include the fact that it was only carried out in a single centre.

CONCLUSION(S)

H-FABP can be considered as the most promising marker for the early detection of AMI. Also, the data showed that sensitivity and accuracy of H-FABP was high compared to cardiac troponins and CK-MB. Early rise (less than 6 hours) of serum H-FABP after myocardial injury would definitely assist the clinician in a right way to early diagnose AMI and to prevent the patients from mortality.

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