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Original Research Article

Diagnostic utility of heart type fatty acid binding protein (H-FABP) versus cardiac troponin I in myocardial infarction

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ABSTRACT

Background: Acute myocardial infarction (AMI) management is one of the therapeutic challenges faced by the emergency physician. In the field of investigational cardiology advancements, the search of superior cardiac biomarkers has led to the discovery of sensitive biomarkers which help in the early confirmation of MI as timely intervention is the primary goal in acute coronary syndrome (ACS). Present study was aimed to evaluate the diagnostic performance of the novel biomarker H- FABP in patients with AMI especially in ST elevation MI (STEMI) and comparison of its diagnostic accuracy with the other biomarkers.
Methods: We studied 66 patients with persistent STEMI presenting within 12 hours of symptom to the department of General Medicine, Sri Manakula Vinayagar Medical College and Hospital (SMVMCH), Puducherry. Quantitative and qualitative estimation and analysis of serum biomarkers of acute myocardial infarction such as CK-MB, cardiac Troponin I (cTnI) and H-FABP were done.
Results: The sensitivity and specificity of H-FABP were 80.7 and 88.9% respectively. The positive percentage of the serum biomarkers among these patients were 64%, 65%, 86% for CK-MB, cardiac troponin I, and H-FABP respectively. The area under the curve was observed to be 0.695, with 95% confidence interval (0.514-0.876) at the optimum cut-off value of 7.0ng/ml for H-FABP.
Conclusions: H-FABP the novel biomarker, because of its early appearance in the blood stream and due to its superior sensitivity and specificity compared to Troponin I and CK-MB can be used in the early diagnosis of acute ST elevation Myocardial Infarction.

Keywords: Acute coronary syndrome, Cardiac troponin cTnI, Heart specific fatty acid binding protein, ST elevation myocardial infarction

INTRODUCTION

Acute coronary syndrome (ACS) spectrum, is one of the commonest emergencies and is most frequently catastrophic in coronary artery disease patients, and without timely intervention it has high morbidity in the affected and has a significant mortality rate especially in the first four hours of onset of the symptoms.

Early suspicion and establishment of a definitive diagnosis and stratification of acute myocardial infarction (AMI) aids in deciding the therapeutic reperfusion strategies which are essential to restore the perfusion of the ongoing ischemic necrosis of the cardiac tissue. The recent universal redefinition of myocardial infarction1 includes rise and /or fall of the serum biomarkers preferably troponin as an essential criteria for establishing the diagnosis of AMI.

For the gold standard diagnosis of myocardial infarction, cardiac markers such as CK (creatine kinase) – MB isoform, cardiac specific troponin I and T has been used as a cornerstone diagnostic biomarker over a decade according to national academy of clinical biochemistry.[2] The disadvantages in using these as biomarker are that CK – MB has gender variability and troponin is elevated in other conditions which causes myocardial necrosis apart from myocardial infarction and it starts to rise in blood stream after 6 hours after acute myocardial infarction. Hence the search for a novel biomarker for myocardial infarction which if highly specific and sensitive especially in the first few hours of myocardial infarction will decrease the diagnostic uncertainty.[3] One such biomarker is Heart Type - Fatty Acid Binding Protein (H-FABP).

The main purpose of present study is to find the diagnostic utility of Heart Type - Fatty Acid Binding Protein (H-FABP) in the diagnosis of acute MI and to compare it with cardiac troponin I and CK-MB. Present study also includes qualitative assessment of H-FABP, in comparison with cardiac troponin I (cTnI) as an early biochemical marker of myocardial infarction.

METHODS

Present study is a cross sectional study conducted in the department of General Medicine, Sri Manakula Vinayagar Medical College and Hospital (SMVMCH), Puducherry, from September 2014 to December 2015. The study got approval from the institutional ethical committee. Around 66 consecutive acute coronary syndrome patients above 18 years with persistent ST elevation myocardial infarction based on the American College of Cardiology/ American Heart Association STEMI diagnosis guideline and Sgarbossa criteria for myocardial infarction in LBBB, presenting within 12 hours of symptom onset were included in present study.[4,5]

Those patients whopresentedlate or with evidence of liverdisease, chronic kidney disease, and those suspected to have pulmonary thromboembolism were excluded from present study.[6]

The recruited patients after signing the informed consent underwent a series of investigations such as Electrocardiography, Random blood sugar, Urea, Creatinine, liver function test estimation of cardiac biomarkers such as CK-MB, cardiac Troponin I (cTnI) using electro chemiluminescence immunoassay-2 antibodies sandwich principleand H-FABP by Enzyme Linked Immune Sorbent Assay (ELISA), based on biotin double antibody sandwich technology.

Statistical analysis

The diagnostic accuracy of H-FABP was assessed by estimating the sensitivity, specificity, positive predictive value and negative predictive value and compared with that of cardiac troponin I.

The results were statistically analyzed and compared using chi-square test. ROC (Receiver operating characteristic) curve was plotted with sensitivity and specificity for H-FABP.

RESULTS

In the study of 66 STEMI patients, majority of patients belonged to the age group 61-70 years (28.8%) and the mean age of presentation was 55 years as from various studies we know that increasing age is a risk factor for atherosclerosis, the main bulk of the study population between 40 to 70 years of age as shown in Table 1.

Table 1: Age wise distribution of patients.

Age in years	Upto 30	31-40	41-50	51-60	61-71	71-80
Patients	3	7	14	17	19	6

The sex distribution of patients was 77% males, and 23% females, majority of the study population were male (77%) as shown in the Figure 1.

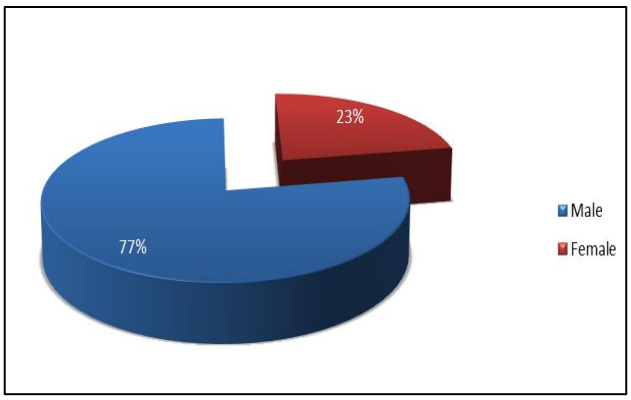

Figure 1: Gender wise distribution of patients.

The cutoff for the normal value of H-FABP from our study was 7.0 ng/ml.

The range of H-FABP value in our study subjects ranged from 0.6ng/ml -11.2ng/ml, and the average value of H-FABP in our study was 8.19ng/ml. The main objective of the study was comparison of H-FABP with the routinely used cardiac biomarkers (CKMB and Troponin I).

The sensitivity and specificity of H-FABP were found to be 80.7 and 88.9% respectively which was found to be better compared to troponin I with sensitivity and specificity of 66.7% and 77.8%.

It was found to be statistically significant with p value <0.001 as shown in Table 2.

Table 2: Sensitivity, specificity, positive predictive value and negative predictive value, of H-FABP and cardiac troponin I.

Parameters	H-FABP	P value	cTnI	P value
Sensitivity	80.7%	<0.001	66.7%	0.011
Specificity	88.9%		77.8%	
Positive predictive value	97.9%		95.0%	
Negative predictive value	42.1%		26.9%	

Receiver operating characteristic (ROC) curve was created to identify the value above which H-FABP is considered positive in patients with STEMI. Area under the ROC curve was observed to be 0.695, with 95% confidence interval (0.514-0.876) as shown in Figure 2 at the optimum cut-off value of 7.0ng/ml for H-FABP.

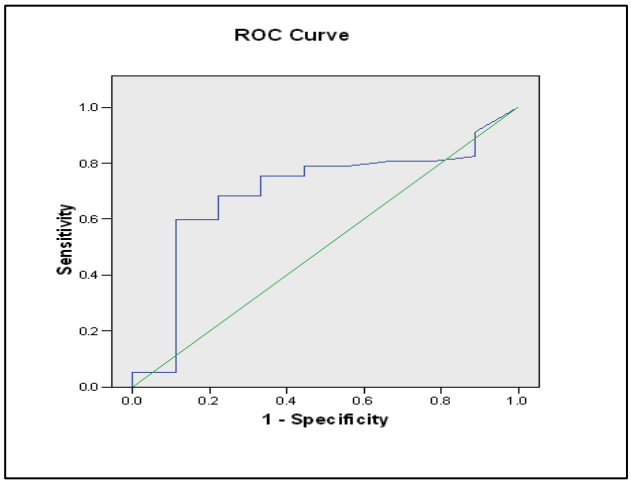

Figure 2: Receiver operating characteristic curve for H-FABP.

Based on the ROC curve the positive percentage of H-FABP was 86%, superior compared to troponin I with a percentage of 66 and CKMB 64Percentage of STEMI patients who had negative results for these biomarkers were 36%, 35%, 14% for CK-MB, cardiac troponin I, and H-FABP respectively. The positive predictive value and negative predicitive value of H-FABP was statistically significant with a p value of <0.001. From the results of this study H-FABP was found to be a better indicator of acute coronary syndrome compared to troponin and CKMB and Troponin I and in future may be used in clinical practice as a marker of ACS.

DISCUSSION

India is at the verge of facing an epidemic of cardiovascular diseases (CVD). Recent epidemiological data shows a rise in the proportion of coronary artery disease in younger age groups, affecting the productive population which in turn may have an impact on the country's development and economy.[7]

Table 3: Comparison of H-FABP with troponin I, CK-MB.

Parameters	H-FABP	Troponin I	CK-Mb
Positive percentage	86	65	64
Negative percentage	14	35	36

Table 4: Comparison of H-FABP with troponin I.

Troponin I		H-FABP	
		Positive (>7.0)	Negative (<7.0)
Positive	Count	46	1
	% within Troponin I	97.9	2.1
	% within H-FABP	80.7	11.1
Negative	Count	11	8
	% within troponin I	57.9	42.1
	% within H-FABP	19.3	88.9
Total	Count	57	66
	% within troponin I	86.4	100.0
	% within H-FABP	100.0	100.0

The total years of life lost due to cardiovascular deaths are predicted to rise among Indians when compared to other nations.[8] Asians in particularly Indians have a low median age of first presentation of AMI which in a study was found to be 53 years.[9] According to the country wide statistics by WHO, non-communicable deaths (NCD) accounts to about 53% of deaths, of which 24% are due to cardiovascular deaths.[9] Non communicable disease (NCD) is fast replacing the proportion of deaths due to infections and malnutrition due to the epidemiological transitions. These could be attributed to the westernisation of dietary habits, lack of awareness about the risk factors for coronary artery disease among the lower socioeconomic strata, and the need to intervene at the earliest.

STEMI may be the initial presentation of chronic coronary artery disease and is due to acute transmural ischemia typically occurs after abrupt disruption of a cholesterol-laden plaque, resulting in thrombus formation, causing interruption of blood flow resulting inmyocardial cell necrosis. Clinical diagnosis of acute myocardial infarction comprises of clinical symptoms, electrocardiographic findings, rise in cardiac specific biomarkers consistent with ischemic necrosis of cardiac tissue. Though 12-lead electrocardiogram (ECG) plays a pivotal role in the diagnosis of AMI, cardiac biomarkers are needed to distinguish unstable angina (UA) from non-ST segment MI (NSTEMI) and to assess the magnitude of ST-segment elevation MI (STEMI). This stresses the need for serial blood sampling, as the gold standard biomarkers appear late after the onset of myocardial infarction. So, the search for an ideal biomarker which can aid in establishing the diagnosis of AMI at the earliest still continues. Availability of highly sensitive serum cardiac markers enables the clinicians to diagnose MI in an additional one third of patients who would not

have fulfilled the criteria for MI in the past. An ideal biomarker for diagnosing myocardial infarction should be highly concentrated in the myocardium and hence it should get released in blood soon after the myocardial injury due to ischemia. It should remain elevated in blood for hours to days, so that patients who present late to the hospital can also be diagnosed. One such cardiac specific biomarker is Heart type fatty acid binding protein (H-FABP).

Heart type fatty acid binding protein (H-FABP), discovered by Ockner in 1972, is a low molecular weight cytoplasmic protein with a molecular weight of 15 kDa, is present abundantly in the cardiac myocytes (0.5 mg/g). It is involved in the long chain fatty acid homeostasis in cardiac tissue.[10] In case of myocardial necrosis due to acute myocardial infarction, H-FABP gets released into the blood stream as early as 30 minutes of myocardial injury. It is highly specific, as it is predominantly expressed in cardiac muscle than the skeletal muscle, liver, kidney. Hence it is a potential marker for early diagnosis of myocardial infarction, and it also has the potential for usage as a prognostic indicator.[11] Further, repeated blood samples are not needed as in cardiac troponin, as H-FABP is detectable early in the blood stream and it lasts for 12-24 hours. Various studies across the world were done to evaluate the performance of H-FABP in myocardial infarction. But very few studies are available to know the diagnostic utility of H-FABP in STEMI. Hence this study was conducted to evaluate the diagnostic utility of H-FABP in acute myocardial infarction-STEMI. Demographic profile of present study population showed an increased prevalence of myocardial infarction among males and higher age groups, which is similar to the observation noted in National Health and Nutritional Survey 2009-2012.[12]

Sensitivity and specificity of H-FABP was significantly high in present study which is consistent with various other studies such as Tanaka et al, Glatz et al, Okamoto et al, Seino et al which also have shown that H-FABP as a sensitive marker for the diagnosis of acute myocardial infarction (AMI).[13,14] In a study done by Gururajan et al, the sensitivity and specificity was found to be 82% and 91% respectively.[15] Mad et al has evaluated H-FABP in 280 patients presenting with 24 hours of onset of chest pain, in which sensitivity of H-FABP was 69% and specificity of 74% which are less when compared to present study, which is attributed to inclusion of patients within 24 hours of symptom onset, as compared to 12 hours in present study.[15] H-FABP not only confirms the diagnosis but also can be used to rule out acute myocardial infarction because of its high specificity. There ceiver operator characteristic curve (ROC) analysis showed H-FABP as a good discriminator between patients with ischemic and non ischemic heart disease. In Gururajan et al study the area under the ROC curve (AUC) was found to be 0.965 at 95% CI (0.945-0.979). This is in similarity with present study which also showed that H-FABP immuno test accurately discriminates the presence of AMI -STEMI from its absence.

Quantitative assessment of the serum biomarkers such as CK-MB, Troponin I in our STEMI patients showed that the even the gold standard diagnostic biomarkers such as CK-MB and Troponin were negative in 36% and 35% of the study population respectively. A study conducted by Conor J et al, stated, only 55% of sensitivity for Troponin I during the first four hours of acute myocardial infarction. This is due to the release kinetics of CK-MB and Troponin I.[17] A study by de Lemos JA et al states, troponin begins to appear in the blood after 6 to 8 hours of onset of acute myocardial infarction, this is because of the relative larger size of the location bound within the contractile apparatus of the cardiomyocyte, makes its release typically delayed for several hours after the onset of ischemic injury.[18] In a study by Klenie AH et al H-FABP was detected as early as one hour in the blood stream.

In present study, sensitivity of Troponin I (66.7%) was less when compared to other markers and is similar to study done by Kim et al which also had the sensitivity of cTnT as 60.5%, which was low when compared with previous reports in which sensitivities ranged from 74.2% to 100%.[19] This difference might be due to differences not only in URL level, but also in the characteristics of study subjects. Their study also revealed that cTnT and CK-MB showed low sensitivity in patients admitted within 6 hours after onset of chest pain and high sensitivity in patients admitted 6 to 8 hours after onset of symptoms, and there was a significant difference in sensitivity between the 2 patient groups. Thus, blood for cardiac troponin I must be sampled at least 6 h after the onset of ischemic discomfort in order to achieve adequate sensitivity. As such, for a large number of patients without classic symptomatology or electrocardiographic changes, significant irreversible myocardial injury might occur before a definitive therapeutic plan is implemented. In addition, troponin levels remain elevated for 7-14 days after the initial ischemic insult, thereby limiting sensitivity for detecting recurrent myocardial injury. A study by, Figiel et al compared the sensitivity of H-FABP, Cardiac Troponin I and Glycogen Phosporylase isoenzyme BB. They documented 84% sensitivity for H-FABP and 64% sensitivity for GP-BP and Cardiac Troponin I. A Study done on 2005 by, Ruzgar et al has compared 40 patients admitted with chest pain and compared H-FABP with CK-MB and Troponin I and claims the sensitivity of H-FABP as 90% and CK-MB was 76% and Troponin the least of 38.1%.[20] But the drawback is his sample size was smaller than present study. A Study done by McCann et al. has compared novel biomarkers such as, H-FABP, GP-BB, Cardiac troponin I, NT-pro BNP, D-dimer, hsCRP, MPO, MMP9, PAPP-A in about 400 patients admitted as ACS. Of all the markers compared, cardiac Troponin I was the most sensitive marker followed by H-FABP. Conor also mentioned in the study that the sensitivity and the

positive predictive value is very high, when H-FABP and Troponin I were both used together, compared with all the list of above new and novel markers available till date.

CONCLUSION

Despite the growing amount of information and public awareness on the prevention of certain risk factors for coronary heart disease, it remains the leading cause of death in developed countries. Present study was done to confirm the theoretical report that H-FABP is a better marker compared to Troponin I in patients presenting early with ST elevation myocardial infarction. As per the third Universal Definition of Myocardial Infarction, ECG along with a positive biomarker becomes necessary for documenting the diagnosis of myocardial infarction. H-FABP can be detected as early as 30 minutes in the circulation in patients with STEMI. Because of its early appearance in the blood stream and its high sensitivity and specificity compared to Troponin I, H-FABP can be used in the early diagnosis of acute ST elevation Myocardial Infarction. Also, combining with the available markers like CK-MB and Troponin I, H-FABP can provide a very high diagnostic utility and can benefit the patients from an aggressive therapeutic strategy.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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