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THE ROLE OF HEART TYPE FATTY ACID BINDING PROTEIN IN THE EARLY DIAGNOSIS OF ST SEGMENT ELEVATION MYOCARDIAL INFARCTION

Cardiology

KEYWORDS: H-FABP, Troponin T, STEMI.

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ABSTRACT

INTRODUCTION Ischemic heart disease is one of the leading causes of death all over the world and hence early diagnosis of acute coronary syndrome is crucial in prognosis. Heart type fatty acid binding protein (H-FABP) is recently studied as an early cardiac marker for the diagnosis of acute myocardial infarction. **AIM OF THE STUDY** To assess the role of heart type fatty acid binding protein in the early diagnosis of ST elevation Myocardial infarction (STEMI) and to compare its diagnostic efficacy with cardiac Troponin T. **METHODOLOGY** 75 patients who were diagnosed to have STEMI within 6 hours of onset of symptoms by WHO Definition of Myocardial infarction were included in the study and their ECG, Echocardiogram, Troponin T and H-FABP (qualitative immunological rapid test) were analysed **RESULTS** H-FABP is useful for earlier diagnosis of STEMI and it is more sensitive and specific in diagnosis of STEMI than Troponin T in patients presenting < 6 hours of onset of symptoms.

INTRODUCTION

Ischemic heart disease is one of the leading causes of death all over the world and approximately 20% of deaths due to STEMI occur before the patients reach the emergency room. Hence, early diagnosis and early treatment became the most critical and effective step in life saving. Currently used cardiac biomarkers for diagnosis of acute MI are Troponin-I, Troponin-T, Myoglobin and CK-MB, of which Troponins and CK-MB usually get elevated between 4 and 12 hours after onset of symptoms and they are not very useful for early diagnosis. Myoglobin gets elevated between 1 and 4 hours, but lacks cardiac specificity, thereby limiting its clinical utility.

Heart type fatty acid binding protein is a small cytosolic protein that is abundant in cardiac tissue. After myocardial ischemia, H-FABP can be detected in blood as early as within 1 hour after the onset of symptoms with peak value at 3-6 hours and plasma values returning to normal values within 24-30 hours. The combination of rapid initial rise after symptom onset, rapid kidney clearance from the circulation and high cardiac specificity make H-FABP an early cardiac marker for the diagnosis of acute myocardial infarction.

Gururajan et al [1] conducted a study in Chennai in 2010 in which H-FABP was compared with usual markers like Troponin and CK-MB and concluded that is an excellent tool for early detection of STEMI. McCann et al [2] it showed H-FABP is much superior to Troponin in identification of myocardial infarction with sensitivity of 71% when both FABP and Troponins were combined, the sensitivity increases to 85% for initial four hours. O Donoghue et al [3] in August 2006 published a study in Circulation showing that the high level of H-FABP in Acute coronary syndrome (in any spectrum from angina, NSTEMI to STEMI) is associated with significant increase in death and major cardiac events. Miriam Puls [4] published that H-FABP is also a predictor of perioperative mortality in patients undergoing CABG.

AIM OF THE STUDY:

To assess the role of Heart type fatty acid binding protein in the early diagnosis of ST segment elevation myocardial infarction and to compare its diagnostic efficacy with cardiac Troponin- T.

MATERIALS & METHODS

This is an Observational Cross Sectional Study conducted among 75 patients of age range 20-80 years with ST elevation Myocardial Infarction by WHO definition presenting within 6 hours of onset of symptoms in a tertiary hospital. This study was approved by the Ethical committee of the institution.

EXCLUSION CRITERIA:

- Known case of heart diseases like heart failure, cardiomyopathy, rheumatic heart disease, myocarditis.
- Aortic Dissection
- Pulmonary Embolism
- Known case of Chronic Kidney disease, skeletal muscle disorders like myositis and myopathy
- Critically ill patients

METHODOLOGY:

After obtaining consent and checking for exclusion criteria, the detailed history, clinical examination findings were noted. Relevant investigations such as blood glucose, blood urea, serum creatinine, routine urine analysis, hemogram, ESR, C reactive Protein, CK-MB, serum lipid profile, Chest X-ray, electrocardiography and echocardiogram were done for all patients. Troponin T and H-FABP were checked simultaneously in all patients using Cardio-detect qualitative immunological rapid test combi kit. The test field for both troponin I and H-FABP was filled with 3 to 4 drops of whole blood, serum or plasma. The result is read after 15 minutes. If both the test (T) and control (C) lines were seen then it was taken as positive result. If only control (C) was seen then it was taken as negative result. If no line was seen then it was taken as invalid result.

STATISTICAL ANALYSIS:

Data was entered in Microsoft excel spread sheet and analysed statistically using SPSS software version 23. Results were considered significant if the p-value was below or equal to 0.05. Chi – square test and Pearson's correlation test were done for statistical analysis. ROC curve was drawn to find the sensitivity and specificity of H FABP in comparison with Troponin T.

RESULTS

40%of the patients in the study belong to the age group between 41 and 50 years (30 out of 75). Males were more commonly affected when compared to females (62.66% versus 37.33%) as shown in table 1 and Figure 1. Out of 75 patients in the study, 52% had diabetes, 45% had hypertension and 39% had both diabetes and hypertension. 25.3 % of patients presented within 2.5 hours, 18.6% of patients presented from 2.5 to 4 hours and 56.1% of the patients in the study group presented between 4-6 hours of onset of symptoms.

Table 1: Age & Sex distribution of study group

Age in years	Male	Female	Total	Percentage
21-30 years	2	1	3	4%
31-40 years	5	8	13	17.33%
41-50 years	20	10	30	40%
51-60 years	11	5	16	21.33%
61-70 years	6	3	9	12%
71-80 years	3	1	4	5.3%
Total	47	28	75	100%

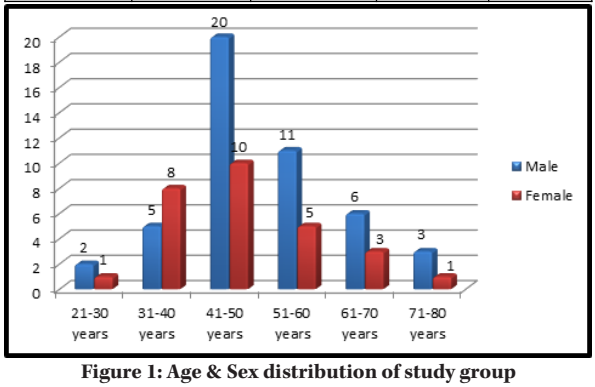


Figure 1: Age & Sex distribution of study group

Among 75 patients who presented in the study group, 90.6% (n=68) showed H-FABP positivity when compared to 34.6% (n=26) who showed Trop T positivity (p value<0.001) and 9.3% patients (n=7) were negative for both as shown in table 2 and Figure 2.

Table 2: Frequency of H-FABP and Troponin T test results

TIME OF PRESENTATION	ONLY H-FABP POSITIVE	BOTH H-FABP & TROPONIN T POSITIVE	BOTH NEGATIVE	P value
0-2.5 hours	12	6	7	<0.001
2.5-4 hours	14	5	0	
4-6 hours	42	15	0	
TOTAL	68	26	7	

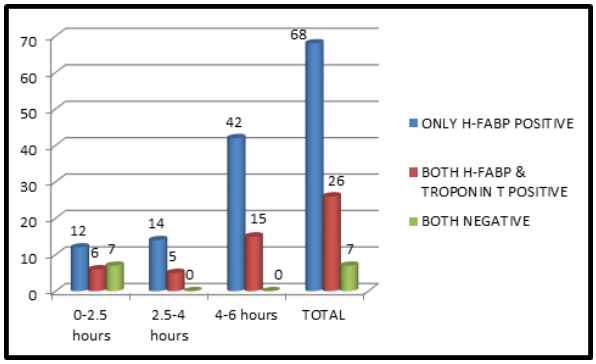


Figure 2: Frequency of H-FABP and Troponin T test results

The sensitivity and specificity of H-FABP in diagnosing STEMI within 6 hours are 82.4% and 100% while the sensitivity and specificity of Troponin T in diagnosing STEMI within 6 hours are 57.7% and 45% respectively. Thus H-FABP is a better marker for earlier diagnosis of STEMI. Among 19 patients presenting within 2.5 hours of onset of symptoms, 12 patients (63%) showed H-FABP positivity and 7 patients (37%) showed H-FABP negativity. The ROC curve derived for H-FABP is shown in figure 3.

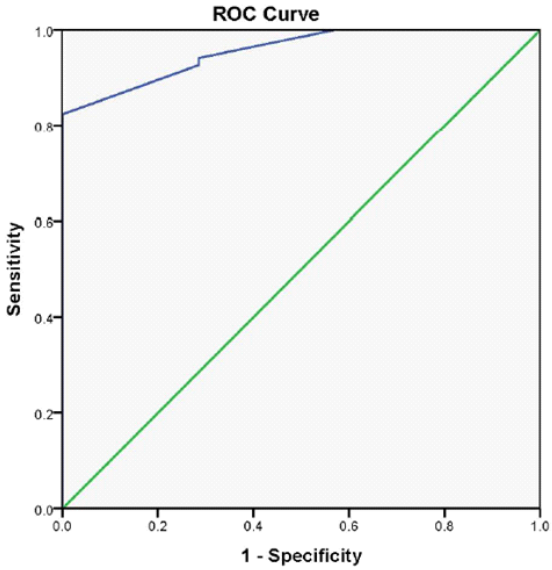


Figure 3: ROC curve of H-FABP in diagnosis of STEMI

In our study, 69% patients showed wall motion abnormality and all were troponin positive and 38% were H-FABP positive. The mean ejection fraction of Troponin positive patients was much lower than FABP positive patients. This showed that H-FABP is helpful earlier diagnosis of STEMI compared to troponin T.

DISCUSSION

Cardiovascular disease accounts for approximately 12 million deaths annually. Early treatment of myocardial ischemia have improved outcome [5]. The diagnosis of acute myocardial infarction (AMI) [6] is usually with the two well-known biomarkers namely Creatine Kinase-MB isoform and Cardiac Troponin. In 2000, Cardiac Troponin replaced CK-MB as the biomarker of choice for diagnosing a myocardial infarction [7].

Cardiac Troponins are detectable only after a latency period of 4-6 hours following the onset of injury, and recommendations call for serial measurements. Troponin may be raised in coronary, non-coronary cardiac as well as non-cardiac conditions such as sepsis. Hence the search for an ideal biomarker of MI is still going on.

H-FABP is a small low molecular weight (i.e., 15 kDa), 132 amino acid, soluble protein, with general characteristics resembling myoglobin. H-FABP is a cytosolic protein involved in fatty acid transport and metabolism which displays a very early raise after an AMI (i.e., increased concentrations can be detected as soon as 30 min after the onset of an ischemic episode), peaks in blood after ~6–8 hours, and returns to baseline values after nearly 24–30 hours. It is unsuitable as a test for patients presenting >6 hours from onset of symptoms due to rapid renal clearance [8], [9], [10]. H-FABP has also been shown to independently predict mortality in patients with ACS [11]. Although the kinetics of H-FABP after an AMI thus mirrors that of other early AMI biomarkers such as myoglobin, soluble CD40 ligand, ischemia modified albumin, pregnancy-associated plasma protein A (PAPP-A) and myeloperoxidase, this protein is reported to be more myocardium-specific [12], thus making it a promising biomarker to be used in combination with conventional troponin tests. Another advantage is represented by the availability of rapid bedside chromatographic as well as fully automated turbidimetric immunoassays, which allow rapid measurement and short turn around time.

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This is an observational cross sectional study conducted among patients presenting with STEMI within 6 hours of onset of symptoms in a tertiary hospital to assess and compare diagnostic efficacy of H-FABP with cardiac Troponin T. Majority of study population belonged to age group between 41 and 50 years (30 out of 75). Males were more commonly affected when compared to females (62.66% versus 37.33%).Similar observation was made by Canto J.G. et al [13] in a study conducted between 1994 to 2006 in 11,43,513 patients. He concluded that significant interaction between sex and myocardial infarction (more prevalent in male) especially in younger age group which attenuated as age increases. Shah [14] observed that Male : Female ratio is 3.5: 1. Out of 75 patients in the study, 52% had diabetes, 45% had hypertension and 39% had both diabetes and hypertension. 25.3 % of patients presented within 2.5 hours, 18.6% of patients presented from 2.5 to 4 hours and 56.1% of the patients in the study group presented between 4-6 hours of onset of symptoms.

Among 75 patients who presented in the study group 90.6% (n=68) showed H-FABP positivity when compared to 34.6% (n=26) who showed Trop T positivity (p value<0.001) and 9.3% patients (n=7) were negative for both. The sensitivity and specificity of H-FABP in diagnosing STEMI are 82.4% and 100% while the sensitivity and specificity of Troponin T in diagnosing STEMI within 6 hours are 57.7% and 45% respectively. Thus H-FABP is a better marker for earlier diagnosis of STEMI. Similar observation was made by McCann et al [2] in 2008 in a study conducted in 664 patients showed H-FABP were more sensitive than Troponin in patients presenting within 4 hours of symptoms (85% vs. 73%). Valle HA et al [15] observed that chest pain of duration less than 3 hour, the sensitivity of H-FABP is 60% and that of Troponin is 19%. Among 19 patients presenting within 2.5 hours of onset of symptoms, 12 patients (63%) showed H-FABP positivity and 7 patients (37%) showed H-FABP negativity.

According to a study by Okamoto et al [16] the overall sensitivity within 12 hours of symptom onset was 92.9% for H-FABP, 88.6% for myoglobin and 18.6% for CK-MB. The overall specificity was 67.3% for H-FABP, 57.1% for myoglobin and 98.0% for CK-MB. Gururajan et al showed H-FABP to be a good discriminator between patients with and without IHD [1]. It also showed that troponin levels rise more than six hours after symptom onset, H-FABP is usually positive within first four hours. At the optimum cut-off value (17.7 ng/ml), the sensitivity and specificity were found to be 87% and 93% respectively.

A study by Ruzgar et al showed sensitivity of 38% with troponin, 76% with CK-MB and 95% with H-FABP in patients admitted within 6 hours of chest pain onset [10]. In another study conducted by Mad P et al., in 280 patients presenting to the hospital with a median time of three hours of symptom onset, H-FABP had a sensitivity of 69% and specificity of 74% and AMI was diagnosed significantly earlier than by troponin [9].

This study also showed that RWMA and low ejection fraction were found to be more prevalent in those with troponin t positivity compared to H-FABP positivity. This implied that the latter in useful in earlier diagnosis. FABP was also shown to be a potential prognostic marker of STEMI in few studies [17], [18].

CONCLUSION

H-FABP is elevated very early (< 2hours) after onset of symptoms when compared to Troponin T which takes an average of 4-6 hours to be elevated(p value < 0.001). H - FABP is more sensitive and specific in diagnosis of STEMI than Trop T in patients presenting < 6 hours of onset of symptoms.

LIMITATIONS

The main limitation of the study was the small sample size because of resource constraints. Serial evaluation of the biomarkers were not done. Quantitative measurement of biomarkers could not be done which could have helped to assess the prognosis.

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