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Original Article

Diagnostic Accuracy of Heart Type Fatty Acid Binding Protein and Conventional Cardiac Troponin I in Early Diagnosis of Acute Myocardial Infarction

Hina Anwar[1]*, Muhammad Zeeshan Rana[2], Najeeb Ullah Khan[3], Mariam Saeed[1], Amal Mahmood[1], Ayesha Wahid[1]

[1]Post Graduate Resident, CMH Lahore, Pakistan.
[2]Consultant Chemical Pathologist, CMH Lahore, Pakistan.
[3]CMH Lahore, Pakistan.
Corresponding Author: Hina Anwar, Post Graduate Resident; Email: hinawahla89@gmail.com

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ABSTRACT

Background: Acute myocardial infarction (AMI) remains a leading cause of global morbidity and mortality, with early diagnosis being crucial for effective treatment and improved patient outcomes. The search for reliable early biomarkers to supplement traditional cardiac markers has been ongoing, with heart-type fatty acid-binding protein (H-FABP) emerging as a potential candidate due to its rapid post-ischemic release into the bloodstream.

Objective: This study aimed to evaluate the diagnostic accuracy of H-FABP in comparison to conventional cardiac troponin I for the early detection of AMI in patients presenting with acute chest pain.

Methods: A descriptive cross-sectional study was conducted at the Chemical Pathology Department of Combined Military Hospital Lahore from December 21, 2022, to April 21, 2023. Eighty patients presenting with symptoms suggestive of AMI were enrolled. Serum concentrations of H-FABP and cardiac troponin I were measured using the sandwich ELISA method. Diagnostic performance was assessed in terms of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and receiver operating characteristic (ROC) curves. Statistical analysis was performed using SPSS version 25.

Results: H-FABP demonstrated a sensitivity of 96.2%, specificity of 60.0%, PPV of 91.3%, and NPV of 81.8%. In contrast, cardiac troponin I had a sensitivity of 81.3% and a specificity of 60.0%, with PPV and NPV values of 91.3% and 81.8%, respectively. The area under the ROC curve (AUC) for H-FABP was 0.640 (p=0.031), slightly higher than that for cardiac troponin I, which was 0.624 (p=0.057).

Conclusion: H-FABP shows promise as a more sensitive early biomarker for AMI compared to cardiac troponin I, suggesting its potential utility in enhancing early diagnosis and improving patient care. However, its lower specificity highlights the need for its combined use with traditional markers for a more accurate diagnosis.

Keywords: Acute Myocardial Infarction, Heart-Type Fatty Acid-Binding Protein, Cardiac Troponin, Early Diagnosis, Biomarkers.

INTRODUCTION

Coronary artery disease, particularly acute myocardial infarction (AMI), continues to be the leading cause of morbidity and mortality globally, despite significant advancements in diagnostic and therapeutic modalities. In 2019, cardiovascular diseases were responsible for approximately 17.9 million deaths worldwide, with AMI and stroke accounting for 85% of these fatalities (1). AMI, characterized by irreversible damage to the cardiac muscles primarily due to oxygen supply disruption, leads to cardiac dysfunction, arrhythmias, and severe complications (2). The diagnosis of AMI traditionally relies on positive findings on electrocardiograms (ECG) and the detection of fluctuations in cardiac biomarkers, especially cardiac troponins (3,4). The significance of early reperfusion therapy in reducing AMI-related morbidity and mortality underscores the necessity for accurate and prompt diagnosis and treatment (5). Furthermore, early diagnosis has been shown to improve patient prognosis (6). Recent advancements in assay techniques have facilitated the early and rapid diagnosis of cardiac injury (7). However, about 20% of AMI cases remain undiagnosed, attributed to atypical clinical symptoms, ECG changes, or delayed elevation of cardiac biomarkers (8).

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Cardiac troponins, including types I and T, are highly sensitive biomarkers for AMI but often do not elevate until at least two hours after the onset of acute myocardial ischemia, complicating the early diagnosis (10). Moreover, studies have indicated a lack of specificity of these biomarkers, further challenging their diagnostic utility (11,12). This has led to the exploration of early diagnostic biomarkers for AMI, among which heart-type fatty acid-binding protein (H-FABP) has emerged as a promising candidate. H-FABP, a small cytoplasmic protein comprising 132 amino acids, plays a crucial role in the metabolism of fatty acids in cardiomyocytes (13). It is released into the bloodstream shortly after myocardial ischemia, typically within one hour, offering a potential for earlier diagnosis of AMI (14). Unlike troponins, which are released following the necrosis of cardiomyocytes, H-FABP is released from both ischemic and necrotic cardiac muscle cells. However, its adoption in clinical laboratories remains limited (15).

Several studies have suggested that H-FABP may either surpass or add diagnostic value to other biomarkers in the rapid identification of AMI (11,15,16). Conversely, other research has found traditional biomarkers to be superior in diagnosing AMI (12,17,18). Pyati et al. highlighted that the sensitivity, specificity, positive, and negative predictive values of H-FABP were lower than those of troponin I, with receiver operating characteristic (ROC) curves indicating a marginally lesser diagnostic capability for H-FABP (AUC = 0.906, $p < 0.001$) compared to Troponin I (AUC = 0.99, $p < 0.001$) (12). Another study reported a sensitivity of 60% for H-FABP, against 18.8% for cardiac troponin I (19). The rationale behind this study was to evaluate the role of H-FABP as an early biomarker for the swift detection of AMI and to compare its efficacy with other biomarkers, which take a longer time to appear in circulation and confirm the diagnosis. This research aims to aid clinicians in the early diagnosis and prompt management of AMI, potentially reducing morbidity and mortality rates and improving patient outcomes.

MATERIAL AND METHODS

A descriptive cross-sectional study was conducted at the Chemical Pathology Department of Combined Military Hospital Lahore from December 21, 2022, to April 21, 2023. The study's sample size was determined to be 80, calculated to achieve a 95% confidence interval and a 10% margin of error, assuming the expected sensitivity of heart-type fatty acid-binding protein (H-FABP) to be 100%, its expected specificity 75%, and the expected prevalence of acute myocardial infarction (AMI) 7.6% (12). Data collection was performed using a convenient sampling method after obtaining approval from the ethical committee and informed consent from the participants. The study included patients admitted to the Cardiac Unit of Combined Military Hospital, Lahore, presenting with acute crushing chest pain of less than 2 hours in duration, radiating to the arms, neck, and/or stomach, and diagnosed with AMI, categorized into either ST-elevation myocardial infarction (STEMI) or Non-ST elevation myocardial infarction (NSTEMI). Exclusion criteria comprised patients with cardiac arrhythmias, spasm, chronic renal failure, acute left bundle branch block, or non-ischemic myocardial injury due to myocarditis, septicemia, and chemotherapy. Demographic data were collected for each participant.

Blood samples were drawn under aseptic conditions and immediately transported to the laboratory, where sera were separated using centrifugation at 3000 revolutions per minute for 5 minutes and subsequently stored at -70°C until analysis. The ELISA for cardiac troponin I and H-FABP was performed using the sandwich ELISA method. The assay for cardiac troponin I involved four unique monoclonal antibodies directed against different antigenic determinants on the troponin I molecule. Three of these antibodies were used for solid-phase immobilization on the microtiter wells, while the fourth was conjugated with an enzyme in the solution. The process facilitated the formation of a "sandwich" of troponin I molecules between the solid-phase and enzyme-linked antibodies. Following a 90-minute incubation at room temperature and subsequent thorough washing, tetramethylbenzidine (TMB) reagent was added, resulting in a blue color formation. The reaction was stopped by adding hydrochloric acid, changing the color to yellow, with absorbance measured spectrophotometrically at 450 nm within 15 minutes. The concentration of cardiac troponin I was directly proportional to the test sample's color intensity and was determined by comparing the sample's absorbance with a standard curve. Similarly, the ELISA for H-FABP was conducted using a sandwich ELISA method, with micro ELISA plate wells coated with antibodies specific to human H-FABP. After adding samples and specific antibodies to the wells, biotinylated detection antibodies specific for human H-FABP and Avidin-Horseradish Peroxidase conjugate were sequentially added and incubated. Following incubation, unbound components were washed away, and TMB was added to develop a blue color, which turned yellow upon the addition of hydrochloric acid. The optical density (OD) was measured at 450nm, with the color intensity directly related to the H-FABP concentration in the samples, quantified by comparing the OD with the standard curve.

Data analysis was performed using SPSS version 25. Quantitative variables, such as age, were presented as mean and standard deviation, while qualitative variables, including gender, smoking status, alcohol consumption, hypertension, diabetes mellitus, history of myocardial infarction, and ECG changes, were presented as frequencies and percentages. A p-value of ≤ 0.05 was considered statistically significant. The comparison between cardiac troponin I and H-FABP focused on their sensitivity, specificity, positive predictive value, and negative predictive value. Receiver operating characteristic (ROC) curve analysis was employed to assess the diagnostic validity of each biomarker.

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RESULTS

In the conducted study, which involved a sample size of 80 participants, the baseline characteristics of the patients revealed a mean age of 52.78 years with a standard deviation of 7.44. The gender distribution was fairly balanced, with 41 males (51.2%) and 39 females (48.8%), illustrating a diverse demographic profile (Table 1). Smoking habits were observed in half of the participants (50%), whereas alcohol consumption was notably low, with only one participant (1.3%) reporting consumption. A significant majority of the patients had hypertension (93.8%) and diabetes mellitus (82.5%), indicating a prevalent comorbidity among the study population. Regarding the ECG findings, there was a near even split between those diagnosed with STEMI (46.2%) and NSTEMI (53.8%), highlighting the variety of acute myocardial infarction presentations within the sample.

Table 1 Baseline Characteristics of Patients (n=80)

Characteristic	Detail
Age of patients* (years)	52.78 ± 7.44
Gender of patients	
- Male	41 (51.2%)
- Female	39 (48.8%)
Smoking	40 (50%)
Alcohol consumption	1 (1.3%)
Hypertension	75 (93.8%)
Diabetes mellitus	66 (82.5%)
ECG Findings	
- STEMI	37 (46.2%)
- NSTEMI	43 (53.8%)
*Continuous data are presented as mean ± standard deviation; discrete data are presented as number (percentage).	

The descriptive statistics for cardiac biomarkers in the study participants showed that the mean concentration of cardiac troponin I was 1.88 ng/ml with a standard deviation of 0.61, where 65 participants (81.3%) tested positive based on the cutoff value of 1.5 ng/ml. In contrast, 15 participants (18.7%) were found to be negative for cardiac troponin I (Table 2). For H-FABP, the mean concentration was significantly higher at 12.20 ng/ml with a standard deviation of 4.32, with 69 participants (86.3%) testing positive using a cutoff value of 6.4 ng/ml, and 11 participants (13.7%) testing negative. This indicates a higher detection rate of AMI through H-FABP compared to cardiac troponin I among the participants.

Table 2 Descriptive Statistics of Cardiac Troponin I and H-FABP in Study Participants (n=80)

Biomarker	Status	Mean ± S.D.	Number (%)
Cardiac troponin I (ng/ml)	Positive	1.88 ± 0.61	65 (81.3%)
	Negative		15 (18.7%)
H-FABP (ng/ml)	Positive	12.20 ± 4.32	69 (86.3%)
	Negative		11 (13.7%)
N = Number of study participants; S.D. = Standard deviation; % = percentage; cutoff value for troponin I = 1.5 ng/ml; cutoff value for H-FABP = 6.4 ng/ml.			

Table 3 Diagnostic Accuracy of H-FABP in Comparison with Cardiac Troponin

Measure	H-FABP Positive	H-FABP Negative	Total	Cardiac Troponin I	p-value*	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic Accuracy (%)
Positive (+)	63	2	65		<0.0001	96.2	60.0	91.3	81.8	90.0
Negative (-)	6	9	15							
Total	69	11	80							
+ = positive;- = negative; PPV = Positive predictive value; NPV = Negative predictive value; % = percentage; *Chi-square test was used to determine the p-value, and a p-value less than 0.05 is considered significant.										

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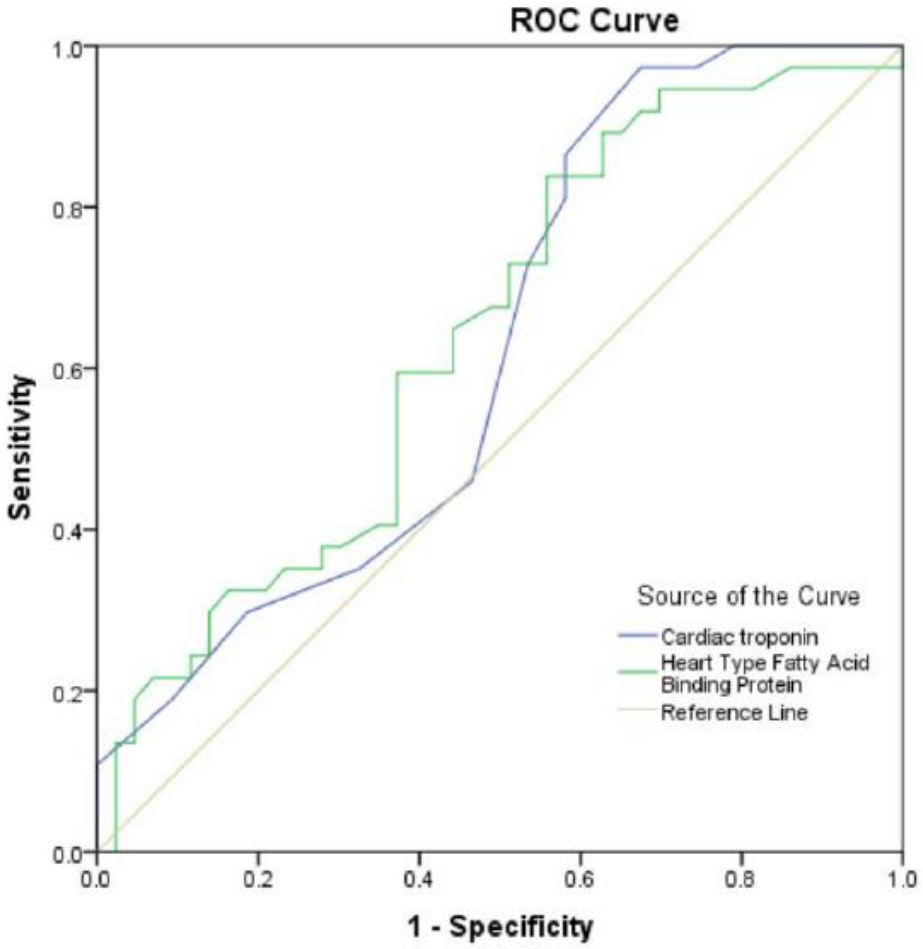

Figure 1 ROC Curve of H-FABP and cardiac Troponin I in AMI

The diagnostic accuracy of H-FABP in comparison to cardiac troponin I was assessed (Table 3), revealing that H-FABP had a sensitivity of 96.2% and a specificity of 60.0%, with a positive predictive value (PPV) of 91.3% and a negative predictive value (NPV) of 81.8%. The overall diagnostic accuracy was determined to be 90.0%. A statistically significant difference was observed, as evidenced by a p-value of less than 0.0001, suggesting that H-FABP could be a more sensitive marker for the early detection of AMI compared to cardiac troponin I. These findings underscore the potential of H-FABP as a crucial biomarker in the rapid identification and management of acute myocardial infarction, offering implications for clinical practices and patient outcomes.

DISCUSSION

Coronary artery disease remains the preeminent cause of global mortality, accounting for around 7 million deaths annually (20). Acute myocardial infarction (AMI), a primary consequence of coronary artery disease, significantly contributes to global morbidity and mortality, displaying a prevalence of 3.8% in individuals under 60 years and 9.5% in those older than 60 years (21). The imperative for early diagnosis and management to preserve cardiac function and mitigate ischemic damage has been well-documented (19), despite the challenges posed by the delayed elevation of gold-standard cardiac markers post-myocardial injury (22) and the limited diagnostic utility of ECGs in approximately half of the patients presenting to emergency departments with AMI (19).

Heart-type fatty acid-binding protein (H-FABP) has emerged as a focal point of interest due to its potential for early AMI detection in various studies (7,15,22,23). Initially highlighted by Sohmiya et al., H-FABP's detectability within an hour of symptom onset, peak levels at 2-4 hours, and rapid clearance within 16-24 hours underscore its utility as an early biomarker (24). Despite this, debates regarding its reliability persist, with some studies questioning its diagnostic efficacy both independently and in conjunction with cardiac troponins (28).

This study's evaluation of serum concentrations of H-FABP and cardiac troponin I in 80 patients for early AMI diagnosis revealed H-FABP's superior sensitivity, positive predictive value (PPV), and negative predictive value (NPV), albeit with lower specificity (60.0%). The area under the curve (AUC) for H-FABP was slightly higher (0.640, p=0.031) compared to cardiac troponin I (0.624, p=0.057), suggesting a marginally better diagnostic capability for H-FABP.

Consistent with previous findings, Kabekkodu et al. and Vupputuri et al. reported higher sensitivity for H-FABP compared to cardiac troponin I, particularly in patients presenting within the first few hours of symptom onset (19,29). Moreover, a combined measurement of cardiac troponin I and H-FABP increased sensitivity significantly, with the highest diagnostic capability for H-FABP

indicated by AUCs at various post-symptom onset intervals (22). Agnello et al.'s findings of higher H-FABP sensitivity yet lower specificity and PPV compared to cardiac troponin I further corroborate the potential of H-FABP as an adjunctive biomarker (30).

However, the study faced limitations, including prolonged patient presentation times to the emergency department, which potentially compromised H-FABP's efficacy as an early biomarker. Additionally, the lack of automation in H-FABP measurement resulted in increased turnaround times and possibly suboptimal results.

Despite these challenges, the findings advocate for the inclusion of H-FABP alongside cardiac troponin I in the AMI diagnostic process, which could significantly expedite diagnosis and thereby reduce morbidity and mortality associated with delayed treatment. Implementing H-FABP measurement could enhance the early diagnostic capability for AMI, emphasizing the need for broader accessibility to and automation of H-FABP assays. Future research should focus on overcoming the identified limitations and exploring the integration of H-FABP into standard diagnostic protocols to improve patient outcomes in acute coronary syndromes.

CONCLUSION

The study underscores the potential of heart-type fatty acid-binding protein (H-FABP) as a valuable early biomarker for acute myocardial infarction (AMI), demonstrating superior sensitivity and diagnostic accuracy compared to traditional cardiac troponin I, despite its lower specificity. The incorporation of H-FABP into the AMI diagnostic protocol could significantly expedite the identification and management of AMI, offering a promising avenue to reduce the associated morbidity and mortality. This finding has profound implications for clinical practice, suggesting that augmenting current diagnostic approaches with H-FABP measurement can enhance early detection and treatment outcomes for patients presenting with AMI symptoms.

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