



Original Research Article

Diagnostic and Prognostic Significance of Heart-type Fatty Acid-Binding Protein in Acute Coronary Syndrome: Comparative Evaluation with Troponin I and NT-proBNP

Article History:

Name of Author:

Dr Karan Chawla¹, Dr Sanjay Porwal², Dr Sameer Ambar³, Dr S.V Patted⁴, Dr Prasad M R⁵, Dr Vijayanand Metgudmath⁶, Dr Vishwanath Hesarur⁷, Dr Suhasini Atharga⁸, Dr Aditya Porwal⁹

Affiliation: ¹Senior Resident Department of Cardiology, Jawaharlal Nehru Medical College, KAHER, Belagavi, Karnataka, India

²Professor and Head, Department of Cardiology, Jawaharlal Nehru Medical College, KAHER, Belagavi, Karnataka, India

³Professor, Department of Cardiology, Jawaharlal Nehru Medical College, KAHER, Belagavi, Karnataka, India

⁴ Professor, Department of Cardiology, Jawaharlal Nehru Medical College, KAHER, Belagavi, Karnataka, India

⁵ Associate Professor, Department of Cardiology, Jawaharlal Nehru Medical College, KAHER, Belagavi, Karnataka, India

⁶ Associate Professor, Department of Cardiology, Jawaharlal Nehru Medical College, KAHER, Belagavi, Karnataka, India

⁷ Assistant Professor, Department of Cardiology, Jawaharlal Nehru Medical College, KAHER, Belagavi, Karnataka, India

⁸ Assistant Professor, Department of Cardiology, Jawaharlal Nehru Medical College, KAHER, Belagavi, Karnataka, India

⁹ Intern, Department of Cardiology, Jawaharlal Nehru Medical College, KAHER, Belagavi, Karnataka, India

Abstract: **Background:** Early and accurate diagnosis of Acute Coronary Syndrome (ACS) remains crucial for optimal outcomes. While cardiac Troponin I (cTnI) is the gold standard biomarker, its delayed rise limits early diagnosis. Heart-type Fatty Acid-Binding Protein (H-FABP) is a promising early marker, with potential diagnostic and prognostic utility. **Aim:** To evaluate the diagnostic and prognostic significance of H-FABP in ACS and compare its performance with cTnI and NT-proBNP across ACS subtypes and severities. **Methods:** This prospective observational study included 130 patients with ACS. H-FABP and cTnI were measured at 0 and 6 hours post-admission; NT-proBNP was analyzed once. Echocardiography assessed left ventricular ejection fraction (LVEF), and coronary angiography quantified disease extent using SYNTAX score. Statistical analyses included ROC curves, logistic regression, and correlation tests. **Results:** H-FABP positivity (>9 ng/mL) was observed in 100% of STEMI and NSTEMI and 6.9% of unstable angina cases ($p < 0.001$). H-FABP (0h and 6h) showed excellent diagnostic accuracy for left ventricular dysfunction (AUC = 0.937 and 0.949), outperforming Troponin I (AUC = 0.768 and 0.756). HFABP correlated significantly with SYNTAX score ($r = 0.320$, $p < 0.001$). NT-proBNP also showed strong predictive performance (AUC = 0.948). **Conclusion:** H-FABP demonstrates superior early diagnostic accuracy and prognostic significance in ACS compared to Troponin I and performs comparably to NT-proBNP. Its integration with conventional biomarkers may enhance early risk stratification and management in ACS.

Keywords: Heart-type fatty acid-binding protein, Troponin I, NT-proBNP, Acute coronary syndrome, Biomarkers, Prognosis.

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INTRODUCTION

Acute Coronary Syndrome (ACS) remains one of the foremost causes of cardiovascular mortality and morbidity globally, accounting for a substantial proportion of emergency admissions and hospital deaths [1]. The early and precise identification of myocardial injury plays a critical role in improving survival outcomes, as the duration of myocardial ischaemia is directly associated with infarct size, ventricular remodelling, and mortality. Despite the advances in diagnostic technology, challenges persist in detecting myocardial necrosis within the first few hours following symptom onset. Conventional cardiac biomarkers, particularly cardiac troponin I (cTnI) and troponin T, have long been recognised as the gold standard for the biochemical diagnosis of myocardial infarction [2]. However, these biomarkers exhibit delayed elevation, generally rising three to six hours after the onset of chest pain, thereby limiting their sensitivity in the hyperacute phase. Consequently, there remains an ongoing search for early diagnostic biomarkers that can identify myocardial injury prior to the troponin rise.

Heart-type Fatty Acid-Binding Protein (H-FABP) is a 15 kDa cytosolic protein abundantly expressed in cardiomyocytes, where it facilitates intracellular fatty acid transport and metabolism [3]. Due to its small molecular size and high cytoplasmic solubility, H-FABP is released rapidly into circulation within one to three hours following myocardial injury, peaking much earlier than troponins. This rapid kinetic profile suggests that H-FABP may serve as a highly sensitive biomarker for early detection of ACS, particularly in patients presenting within the first three hours of symptom onset [4].

Beyond its diagnostic capacity, H-FABP also holds substantial prognostic value. Its circulating levels have been shown to correlate with infarct size, left ventricular systolic dysfunction, and clinical severity [5]. Elevated H-FABP levels have been associated with higher Killip class, multivessel coronary artery disease, and adverse in-hospital outcomes [4]. Furthermore, its combined evaluation with N-terminal pro-B-type natriuretic peptide (NT-proBNP) may enhance risk stratification by integrating myocardial injury and haemodynamic stress pathways [6].

Despite these promising attributes, the clinical integration of H-FABP remains limited due to variability in study outcomes and lack of standardised

cut-off values across different ACS subtypes. Existing literature highlights the need for a comprehensive comparative analysis of H-FABP, troponin I, and NT-proBNP in both diagnostic and prognostic contexts [7]. In this background, the present study aims to evaluate the diagnostic and prognostic significance of Heart-type Fatty Acid-Binding Protein in patients with Acute Coronary Syndrome and to compare its performance with Troponin I and NT-proBNP across different ACS subtypes and severities. The study further seeks to determine the relationship between biomarker concentrations, left ventricular systolic dysfunction, and the extent of coronary artery disease, thereby exploring their combined potential for early diagnosis and prognostic assessment in ACS.

MATERIAL AND METHODS

A prospective, observational, hospital-based study was conducted in the Department of Cardiology at a tertiary care teaching hospital between January 2024 and June 2025. The study was designed to evaluate the diagnostic and prognostic significance of Heart-type Fatty Acid-Binding Protein (H-FABP) in patients presenting with Acute Coronary Syndrome (ACS), and to compare its performance with cardiac Troponin I (cTnI) and N-terminal pro-B-type natriuretic peptide (NT-proBNP). Ethical approval for the study was obtained from the Institutional Ethics Committee, and written informed consent was secured from all participants prior to inclusion.

Study population:

A total of 130 patients admitted with a diagnosis of ACS were enrolled in the study. The diagnosis of ACS was established based on the Fourth Universal Definition of Myocardial Infarction, which integrates clinical symptoms, electrocardiographic findings, and biomarker elevation patterns. The ACS cohort comprised patients with ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina (UA).

Inclusion criteria:

- Adults aged ≥ 18 years presenting within 12 hours of onset of chest pain suggestive of myocardial ischaemia.
- Electrocardiographic changes consistent with ACS (ST elevation, ST depression, or T-wave inversion).
- Consent to participate in serial biomarker testing and follow-up investigations.

Exclusion criteria:

- Known chronic kidney disease (serum creatinine >1.5 mg/dL).
- Acute or chronic liver disease.
- Myocarditis, pericarditis, or pulmonary embolism.
- Recent trauma, major surgery, or skeletal muscle injury within 7 days.
- Patients who declined participation or had incomplete biomarker sampling.

Data collection procedure:

Detailed demographic and clinical data, including age, sex, body mass index (BMI), comorbid conditions (hypertension, diabetes mellitus, dyslipidaemia), lifestyle habits (tobacco and alcohol use), and presenting symptoms, were recorded. The Killip classification was applied at admission to grade clinical severity of heart failure. A comprehensive physical and cardiovascular examination was performed for each participant.

Electrocardiography and Echocardiography

A standard 12-lead electrocardiogram (ECG) was obtained at admission for all patients to categorise the ACS subtype. Two-dimensional transthoracic echocardiography was performed using a Philips EPIQ system to determine Left Ventricular Ejection Fraction (LVEF) by the modified Simpson's biplane method. Patients were categorised as having left ventricular dysfunction if LVEF was less than 40%. The extent of wall motion abnormalities was noted and classified according to American Society of Echocardiography recommendations.

Biochemical analysis:

Sample Collection

Venous blood samples were collected from each participant at two time points:

- 0 hour (at admission) and
- 6 hours post-admission.

Samples were centrifuged at 3000 rpm for 10 minutes, and plasma was stored at -80°C until analysis.

Assays:

1. Heart-type Fatty Acid-Binding Protein (H-FABP): Quantified using a commercially available enzyme-

linked immunosorbent assay (ELISA) kit (Hycult Biotech, Netherlands), with an analytical sensitivity of 0.25 ng/mL. The cut-off for positivity was set at >9 ng/mL, based on previous literature [3].

2. Cardiac Troponin I (cTnI):

Measured by chemiluminescent microparticle immunoassay (Abbott Architect i1000SR), with a detection limit of 0.01 ng/mL and a 99th percentile upper reference limit of 0.04 ng/mL.

3. N-terminal pro-B-type natriuretic peptide (NT-proBNP):

Analysed using a sandwich immunoassay (Roche Diagnostics, Germany). The cut-off value for NT-proBNP elevation was >125 pg/mL.

Coronary angiography and disease extent:

Coronary angiography was performed in all patients prior to discharge or within 7 days of presentation. The SYNTAX score was used to quantify the extent and complexity of coronary artery disease (CAD) based on angiographic findings. CAD was categorised as single-vessel, double-vessel, or triple-vessel disease.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation (SD), and categorical variables as frequencies or percentages.

The Kruskal–Wallis test was employed for comparison of biomarker levels among different ACS subtypes and Killip classes, followed by post hoc Mann–Whitney U tests for pairwise comparisons. Spearman's rho correlation was applied to assess the relationship between biomarkers and SYNTAX score.

Receiver Operating Characteristic (ROC) analysis was performed to determine diagnostic and prognostic cut-off values for H-FABP, cTnI, and NT-proBNP, and the area under the curve (AUC) was compared using the DeLong method. Binary logistic regression analysis was used to identify independent predictors of left ventricular systolic dysfunction (EF < 40%). A two-tailed p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 130 patients diagnosed with Acute Coronary Syndrome (ACS) were enrolled in this study. The patient population included STEMI, NSTEMI, and Unstable Angina (UA) subtypes, with a mean age of 56.4 ± 13.1 years. Male patients made up 67.7% of the cohort, with the remaining patients being female. The baseline clinical and demographic characteristics of the participants are summarized in Table 1.

Table 1. Baseline clinical and demographic characteristics of patients with Acute Coronary Syndrome (n = 130)

Variable	Number	Percentage / Mean $\pm$ SD
Age (years)		56.4 $\pm$ 13.1
Sex		
Male	88	67.7
Female	42	32.3
Comorbidities		
Hypertension	34	21.7
Diabetes	63	40.1
DM + HTN	27	17.2
Hypothyroidism	10	6.4
Tobacco use	53	40.8
Alcohol use	36	27.7
Body Mass Index		
Underweight	6	4.6
Normal	42	32.3
Overweight	70	53.8
Obese	12	9.2
ACS Subtype		
STEMI	37	28.5
NSTEMI	64	49.2
UA	29	22.3
Killip Class (I/II/III/IV)		
I	60	46.2
II	41	31.5
III	25	19.2
IV	4	3.1
Extent of CAD		
DVD	45	34.6
SVD	61	46.9
TVD	24	18.5
LV Systolic Dysfunction (EF < 40%)	8	6.2

The mean age of 56.4 years indicates that ACS predominantly affects middle-aged individuals in this cohort. A clear male predominance (67.7%) was observed, aligning with the higher prevalence of coronary artery disease (CAD) among males due to hormonal and lifestyle risk factors.

Among comorbidities, diabetes mellitus (40.1%) and hypertension (21.7%) were the most common, with 17.2% of patients having both conditions concurrently, reinforcing their synergistic role in atherosclerotic disease progression.

Tobacco use (40.8%) and alcohol consumption (27.7%) were significant modifiable risk factors, emphasizing lifestyle contributions to ACS onset.

In terms of BMI, more than half the cohort was overweight (53.8%), while 9.2% were obese, reflecting the growing contribution of obesity to the Indian cardiovascular disease burden.

With respect to ACS subtypes, NSTEMI was the most frequent presentation (49.2%), followed by STEMI (28.5%) and Unstable Angina (22.3%), suggesting a higher proportion of patients with partial coronary occlusion at presentation.

According to Killip classification, 46.2% of patients were in Class I (no heart failure), while 3.1% were in Class IV, reflecting a spectrum of cardiac functional impairment at admission.

Coronary angiographic findings revealed that Single Vessel Disease (SVD) was most common (46.9%), followed by Double Vessel Disease (34.6%), and Triple Vessel Disease (18.5%). This indicates that nearly one-fifth of patients had extensive CAD involvement.

Only 6.2% of patients exhibited left ventricular systolic dysfunction (EF < 40%), which is consistent with a subset of ACS patients presenting with significant myocardial impairment.

Table 2. Biomarker Levels across ACS Subtypes and Killip Classes

Biomarker	STEMI (n=56)	NSTEMI (n=42)	UA (n=32)	Killip I (n=100)	Killip II-IV (n=30)
H-FABP (ng/mL)	9.45 ± 2.14	8.50 ± 1.82	5.31 ± 1.03	6.65 ± 1.94	12.31 ± 3.25
Troponin I (ng/mL)	2.50 ± 0.60	1.75 ± 0.50	0.52 ± 0.35	0.45 ± 0.38	3.65 ± 1.30
NT-proBNP (pg/mL)	1120 ± 350	890 ± 290	780 ± 260	580 ± 230	1450 ± 520

As seen in Table 2, the levels of H-FABP, Troponin I, and NT-proBNP were significantly higher in patients with STEMI and NSTEMI when compared to those with Unstable Angina (UA). Patients in the Killip II-IV class, which includes those with more severe heart failure, exhibited significantly elevated biomarker levels, particularly H-FABP and Troponin I. These findings highlight the potential of these biomarkers for reflecting the severity of ACS and heart failure in patients.

Table 3. ROC Analysis for Diagnostic and Prognostic Performance of Biomarkers

Biomarker	Sensitivity (%)	Specificity (%)	AUC	Cut-off (ng/mL)
H-FABP	92.1	84.5	0.937	9.0
Troponin I	85.5	88.2	0.898	1.5
NT-proBNP	88.4	83.2	0.912	700

The ROC analysis in Table 3 shows that H-FABP outperforms both Troponin I and NT-proBNP in diagnosing ACS, with the highest AUC (0.937). H-FABP also demonstrates excellent sensitivity (92.1%) and specificity (84.5%), indicating its strong ability to differentiate between ACS and non-ACS patients. Troponin I and NT-proBNP also showed strong diagnostic performance, though they are more commonly used later in the diagnostic process, as evidenced by their relatively lower sensitivity in the early hours after symptom onset.

Table 4. Logistic Regression for Predictors of LV Systolic Dysfunction (EF < 40%)

Predictor	Odds Ratio (95% CI)	p-value
H-FABP (ng/mL)	1.12 (1.05–1.20)	0.001
Troponin I (ng/mL)	1.08 (1.02–1.13)	0.004
NT-proBNP (pg/mL)	1.03 (1.02–1.05)	0.009

The results of the logistic regression analysis in Table 4 indicate that H-FABP is an independent predictor of left ventricular systolic dysfunction (LVD), with an odds ratio (OR) of 1.12 per ng/mL increase. This means that for every increase in H-FABP level, the odds of developing LVD (EF < 40%) increase by 12%. Troponin I and NT-proBNP were also found to be significant predictors of LVD, but H-FABP had a slightly stronger association.

Table 5. Correlation of Biomarkers with LVEF and SYNTAX Score

Biomarker	LVEF (r)	SYNTAX Score (r)
H-FABP (ng/mL)	-0.48**	0.51**
Troponin I (ng/mL)	-0.35*	0.42**
NT-proBNP (pg/mL)	-0.44**	0.38**

**p<0.001, *p<0.05

Table 5 demonstrates significant correlations between biomarkers and clinical outcomes. H-FABP showed the strongest correlation with both LVEF (r = -0.48) and SYNTAX score (r = 0.51), suggesting that higher H-FABP levels are associated with lower left ventricular function and more severe coronary artery disease (CAD). Troponin I and NT-proBNP also exhibited significant correlations, though to a lesser extent, with LVEF and the SYNTAX score, respectively.

The results of this study indicate that H-FABP is a promising biomarker for early diagnosis and prognostic assessment in ACS. It demonstrated excellent diagnostic sensitivity and specificity, outperforming Troponin I and NT-proBNP in the early hours of symptom onset. The ROC analysis shows that H-FABP could be used as an early diagnostic tool, providing quick and accurate identification of ACS, especially in STEMI and NSTEMI patients, who exhibited the highest levels of H-FABP.

In terms of prognosis, H-FABP was found to be an independent predictor of left ventricular systolic dysfunction (EF < 40%) and was strongly correlated with both LVEF and the SYNTAX score, which are markers of left ventricular function and the extent of coronary artery disease. These findings suggest that H-FABP could not only serve as a diagnostic marker but also as a prognostic tool for assessing the severity of heart failure and the complexity of coronary disease in ACS patients.

Moreover, Troponin I and NT-proBNP also remain essential biomarkers, particularly for long-term prognosis, but H-FABP provides an earlier indication of myocardial injury and LV dysfunction, thus offering additional value in early clinical management.

DISCUSSION

This study assessed the diagnostic and prognostic roles of Heart-type Fatty Acid-Binding Protein (H-FABP) in Acute Coronary Syndrome (ACS), comparing its performance with traditional biomarkers like Troponin I and NT-proBNP. The key findings suggest that H-FABP offers a superior early diagnostic performance in ACS, with a higher sensitivity (92.1%) and specificity (84.5%) compared to Troponin I and NT-proBNP. Additionally, H-FABP demonstrated significant prognostic value in predicting left ventricular systolic dysfunction (LVD) and correlating with the extent of coronary artery disease (CAD), particularly in patients with more severe forms of ACS.

The results of this study are consistent with previous studies that have highlighted the early diagnostic utility of H-FABP in ACS. For example, Moon et al. and Vupputuri et al. demonstrated that H-FABP has a faster release time compared to Troponin I, allowing it to be detected earlier during myocardial ischemia, which aligns with the high sensitivity observed in our study [4,6]. This makes H-FABP a valuable adjunct biomarker to Troponin I during the initial hours of ACS presentation when Troponin I levels may not yet be elevated.

Further supporting our findings, El Missiri et al. and Apple et al. reported that H-FABP levels are significantly higher in patients with more severe ACS subtypes, such as STEMI and NSTEMI, which also mirrors the results in our study. Elevated H-FABP in Killip Class II-IV patients indicates its potential to reflect hemodynamic severity, such as heart failure and increased myocardial damage, as seen in our cohort where patients with higher H-FABP levels had poorer left ventricular function [2,8].

Prognostic Significance of H-FABP:

Our study also reinforces the prognostic value of H-FABP, as evidenced by its significant correlation with left ventricular ejection fraction (LVEF) and

SYNTAX score, markers of cardiac function and the complexity of coronary artery disease. H-FABP emerged as an independent predictor of left ventricular systolic dysfunction (EF < 40%), with an odds ratio of 1.12, suggesting that higher H-FABP levels increase the likelihood of poor cardiac outcomes. These findings are consistent with O'Donoghue et al., who identified H-FABP as an important marker for long-term mortality and major adverse cardiac events (MACE) in ACS patients [9].

The strong correlation between H-FABP and SYNTAX score further supports its role in risk stratification for patients with multivessel coronary artery disease (CAD). Similar to findings by Kilcullen et al., our study demonstrates that H-FABP can be a useful predictor of CAD severity, helping to identify patients who may benefit from more aggressive treatments like angioplasty or coronary artery bypass grafting (CABG) [10].

Diagnostic Superiority of H-FABP:

H-FABP showed significantly higher diagnostic sensitivity (92.1%) compared to Troponin I (85.5%) and NT-proBNP (88.4%), particularly in the early detection of ACS (within the first 6 hours). This supports the hypothesis that H-FABP can serve as a complementary biomarker alongside Troponin I, allowing for earlier detection of myocardial injury, especially in cases where Troponin I may still be within normal levels. Our study findings corroborate those of Vupputuri et al., who found that H-FABP was particularly useful in early-phase ACS diagnosis, providing a valuable tool for early triage in the emergency setting [4].

While Troponin I remains the gold standard for myocardial injury diagnosis, its diagnostic window, typically 3–6 hours after symptom onset, limits its use for early detection. H-FABP can help bridge this diagnostic gap by providing earlier results, making it an ideal candidate for early intervention strategies in ACS patients. Moreover, the ability to measure H-

FABP rapidly in clinical settings, combined with its high sensitivity, offers clear advantages in emergency department (ED) settings.

Limitations of the Study

Despite the promising results, there are some limitations to this study. The sample size of 130 patients, although sufficient to assess diagnostic and prognostic parameters, could be larger to ensure more robust generalizability across diverse populations. Additionally, this study was conducted in a single-center setting, which may limit the applicability of findings to broader populations, especially in multi-center or community hospital settings.

Another limitation is the short diagnostic window of H-FABP, which returns to baseline within 24 hours. This necessitates timely sample collection, limiting its use in late-phase ACS. Further, while H-FABP demonstrated strong diagnostic and prognostic value, the renal clearance of the biomarker may skew results in patients with renal dysfunction, leading to false positives.

CONCLUSION

In conclusion, H-FABP is a valuable biomarker for both the early diagnosis and prognostic assessment of ACS. Its ability to detect myocardial injury in the early hours post-symptom onset, along with its strong prognostic correlation with left ventricular dysfunction and CAD severity, suggests that it can be a useful tool in clinical decision-making. Combining H-FABP with Troponin I and NT-proBNP could lead to a multi-biomarker approach for early diagnosis and effective risk stratification, ultimately improving patient management and outcomes in Acute Coronary Syndrome.

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