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ORIGINAL ARTICLE

Diagnostic value of heart-type fatty acid-binding protein in the early diagnosis of acute coronary syndrome at the Emergency Medicine Department of Suez Canal University Hospital

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ABSTRACT

Background: Heart-type fatty acid-binding protein (H-FABP) is a new biochemical marker which is recently being used in the early diagnosis of acute coronary syndrome (ACS) in the early phase at 0-3 hours of chest pain onset. The aim of this study was to diagnose ACS patients early in the ER using H-FABP in the early stage during 0-3 hours of chest pain.

Methods: This is a cross-sectional descriptive study that included 41 ACS patients who presented to the emergency department of the Suez Canal University Hospital, who fulfilled the inclusion and exclusion criteria.

Results: Out of the 41 patients of ACS, 26 were male and 15 were female with a mean age of 56.8 ± 12.9 years. It was found that H-FABP was elevated in 68.3% of the patients at 0-3 hours of chest pain which increased to 80.5% at 3-6 hours of chest pain onset with 76.2% sensitivity at 0-3 hours which increased to 85.7% at 3-6 hours, while specificity was 70% at 0-3 hours but increased at 3-6 hours. The receiver operating characteristic curve was performed to find out the best cut-off value of H-FABP at 0-3 hours and at 3-6 hours' interval which was 19 ng/l for diagnosis of acute MI (ST-segment elevation myocardial infarction and non-ST-segment elevation myocardial infarction).

Conclusion: H-FABP is a promising cardiac biomarker for the early identification of myocardial ischemia and infarction. It could be a superior biomarker for earlier detection of ACS.

Keywords: Acute coronary syndrome, chest pain, heart-type fatty acid-binding protein, myocardial infarction.

Introduction

Coronary heart disease (CHD) is a major cause of death and disability in developed countries. Although CHD mortality rates worldwide have declined over the past four decades, CHD remains responsible for about one-third or more of all deaths in individuals aged over 35 years [1-3]. Acute coronary syndrome (ACS) refers to a spectrum of clinical presentations ranging from those for ST-segment elevation myocardial infarction (STEMI) to presentations found in non-ST-segment elevation myocardial infarction (NSTEMI) or in unstable angina. It is almost always associated with the rupture of an atherosclerotic plaque and partial or complete thrombosis of the infarct-related artery [4]. There are significant challenges with early accurate diagnosis of patients presenting with chest pain of possible cardiac origin because none of the standard diagnostic tests have sufficient diagnostic use to accurately rule out underlying acute coronary syndrome (ACS) in the early stages [5]. Furthermore, there are associated logistic

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and financial burdens linked to the management of these patients. Inappropriate discharge is associated with a fivefold increase in mortality and morbidity [6]. The diagnosis of ACS is presently determined by evaluating risk factors, electrocardiographic (ECG) traces, and measurement of cardiac markers. Current biochemical markers used in the diagnosis of ACS include cardiac troponins (cTn), creatinine kinase-MB, and myoglobin. They are limited by either a lack of specificity or a delay of elevation of several hours after the onset of the symptom. Therefore, their clinical use in early diagnosis of acute myocardial infarction (AMI) is limited [7].

Previous studies have established the success of heart-type fatty acid-binding protein (H-FABP) as an early biochemical marker in the detection of AMI and its use as a prognostic indicator of post-MI recovery [8].

Patients and Methods

This is a descriptive cross-sectional study that was carried out in the Emergency Medicine Department at the Suez Canal University Hospital.

The sample size was calculated from the following equation [9]:

$$n_0 = \frac{Z^2 p q}{e^2}$$

where N is the sample size of the single study group, Z is the standard normal deviate corresponding to desired confidence interval of (95%) = 1.96, e is the (margin of error) total width of the expected CI = 0.167, p is the estimated sensitivity of H-FABP alone for diagnosis of AMI (89.9%) = 0.627 [10] $q = 1 - p = 0.373$, $n_0 = 32.21$, and expected drop out of 15% will be added So, the sample should be 38 patients in the single group.

Inclusion criteria

All patients presented with chest pain for less than 3 hours to the emergency room, which fulfills our inclusion criteria.

All patients ≥18 years presented to the emergency room with chest pain for no more than 3 hours suggesting ACS like the following:

1. Substernal chest discomfort, pressure, or tightness located centrally in the chest and radiated mainly to arms, jaw, or upper back more than 30 minutes.
2. Pain evoked by exertion or emotional stress or may be with minimal exertion or even at rest.
3. Pain not relieved by rest and/or nitroglycerine.
4. Pain with or without ECG changes (STEMI or NSTEMI).

Exclusion criteria

1. Patients presenting with traumatic chest pain.
2. Patients referred from other hospitals and treated with appropriate management but passed the 3- Hours window.

Data were collected in pre-organized data sheet by a researcher and the following variables and procedures were taken:

A. Demographic data regarding age, gender, smoking status, and residence.

B. Clinical data past history of any chronic illness (e.g., diabetes, hypertension, renal disease, chronic heart disease, and previous history of CCU admission).

C. Clinical examination with regard to vital signs general examination for heart failure and immediate ECG at time of presentation.

D. Laboratory tests are the blood samples drawn on arrival to the ER for all patients focusing on cardiac markers (CPK), creatine kinase myocardial band (CKMB), and lactate dehydrogenase (LDH), and risk factors assessment (RBS, sr. creatinine).

E. H-FABP was performed from serum samples at 0-3 hours of chest pain onset and 3-6 hours of chest pain onset.

Heart-type fatty acid-binding protein was performed in serum using a solid phase ELISA. Venous blood samples were collected using a serum separator tube and the samples were allowed to clot for 30 minutes before centrifugation for 15 minutes at approximately 1,000 × g. The serum was removed and the samples were stored at −20°C or −80°C.

Data were collected throughout the history and clinical examination, and laboratory investigations were coded, entered, and analyzed using Microsoft Excel software. Data were imported to Statistical Package for the Social Sciences (SPSS) software program. According to the type of data, the chi-square test was used to test for significant differences and the one-way analysis of variance was used to test for least significance differences. Chi-square test and non-parametric tests were used to compare categorical variables. p-value set at <0.05 was considered to be statistically significant.

Results

Overall, 41 patients met the inclusion criteria; 26 (63.4%) of them were male and 15 (36.6%) were female (M:F = 1.7:1), as shown in Figure 1. Mean age of the study population was calculated to be 56.8 ±12.9 years, as shown in Figure 2. Evaluation of coronary artery disease risk factors revealed that 34.1% were diabetics, 61% were hypertensive, 51.2% of the patients had a history of ischemic heart disease, and 65.9% of patients were active smokers, as shown in Figure 3.

Regarding that final diagnosis of studied populations, it was found that 21 (51.2%) was STEMI, 12 (29.3%) was NSTEMI, while 8 (19.5%) was UA (Figure 4).

It was found that H-FABP elevated in 68.3% at 0-3 hours which increased to 80.5% at 3-6 hours of chest pain, as shown in Figures 5 and 6, with sensitivity of 76.2% at 0-3 hours which increased to 85.7% at 3-6 hours, while specificity was 70% at 0-3 hours but that increased at 3-6 hours. The receiver operating characteristic (ROC) curve was performed to find out the best cut-off value of H-FABP at 0-3 hours and at 3-6 hours intervals which

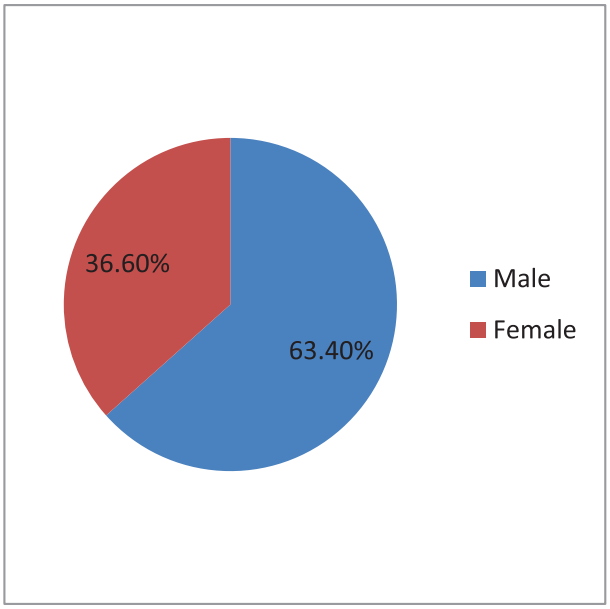

Figure 1. *Gender distribution between studied patients (n = 41).*

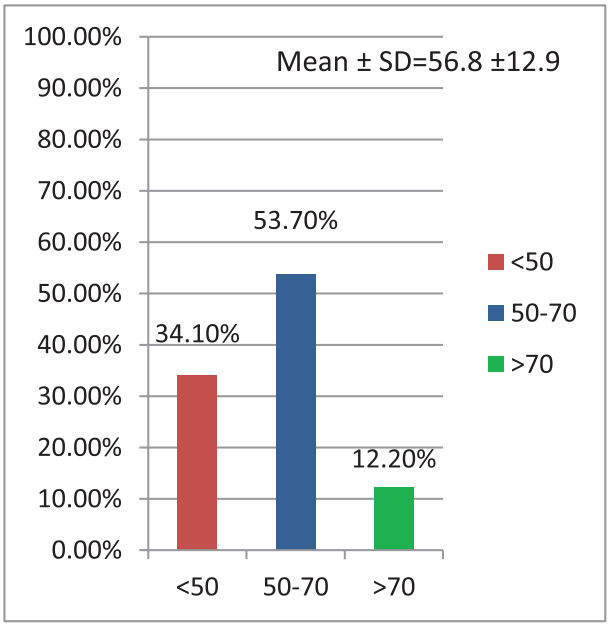

Figure 2. *Age distribution between studied patients.*

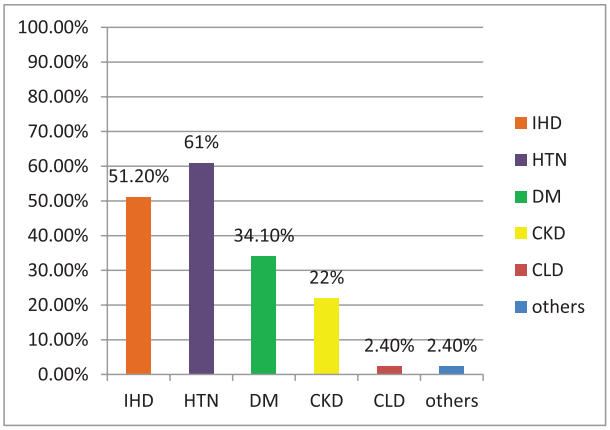

Figure 3. *Frequency of chronic diseases among studied patients (n = 41).*

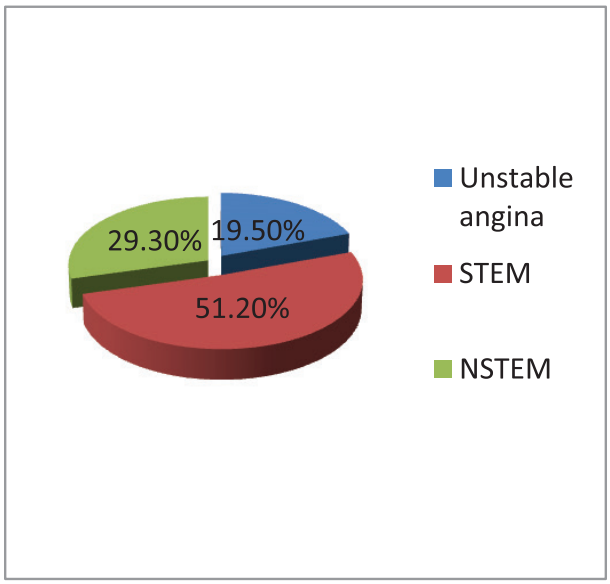

Figure 4. *Final diagnosis among studied population (n = 41).*

was 19 ng/l for the diagnosis of acute MI (STEMI and NSTEMI) (Figure 7).

Discussion

Acute coronary syndrome remains a dominant cause of high morbidity and mortality, despite advancements in treatment and poses a high economic burden [11]. Both NSTEMI and STEMI share similar long-term prognosis, whereas STEMI is associated with worst short-term prognosis [12]. Numerous biomarkers have been studied in the past to assist in the earlier diagnosis of STEMI in addition to troponins, especially in the window period of the initial 4 hours since the onset of symptoms. Heart-type fatty acid-binding protein (H-FABP), involved in the intracellular transport of free fatty acids in the myocardium, has also been studied for this purpose [13]. Owing to the smaller size of H-FABP (15 kDa) and higher concentration in the cardiac myocytes (2-10 times) than skeletal muscle, it appears early in the circulation than cTnI in response to myocardial injury [12]. This was a descriptive cross-sectional study which had been carried out in the Emergency Medicine Department at the Suez Canal University Hospital to evaluate the diagnostic value of heart-type fatty acid-binding protein (H-FABP) for early diagnosis of ACS. A total of 41 patients matching the inclusion criteria were enrolled in this study.

Our study showed that the mean age of the studied patients was 56.8 ± 12.9 years and (53.7%) of them were between 50 and 70 years old; 63.4% of them were male, with male to female ratio of 1.7:1; 65.9% of them were smokers. Similar to our study, Muhammad Saleem et al. [14] conducted a study which revealed that the mean age

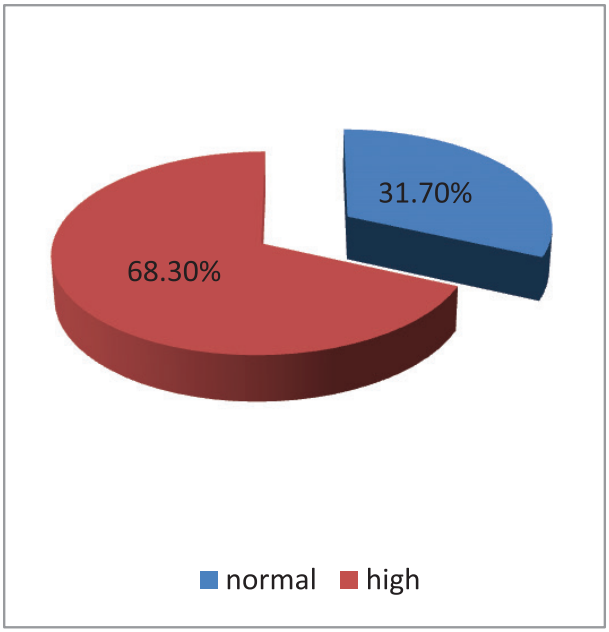

Figure 5. *H-FABP level at 0-3 hours among studied patients.*

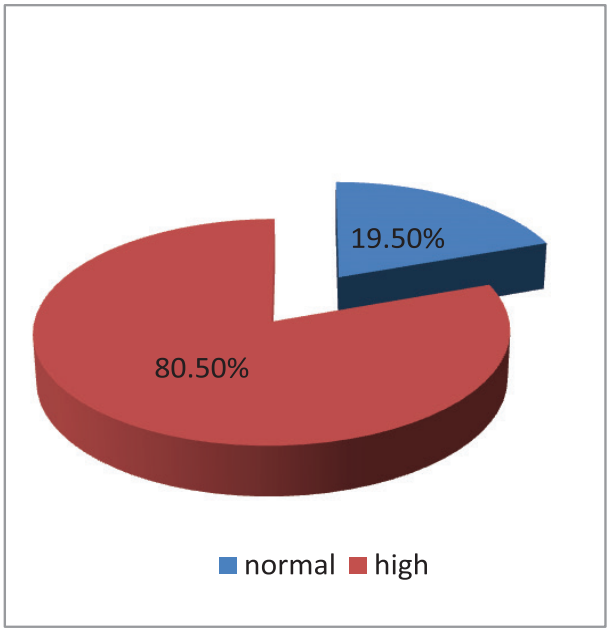

Figure 6. *H-FABP level at 3-6 hours among studied patients.*

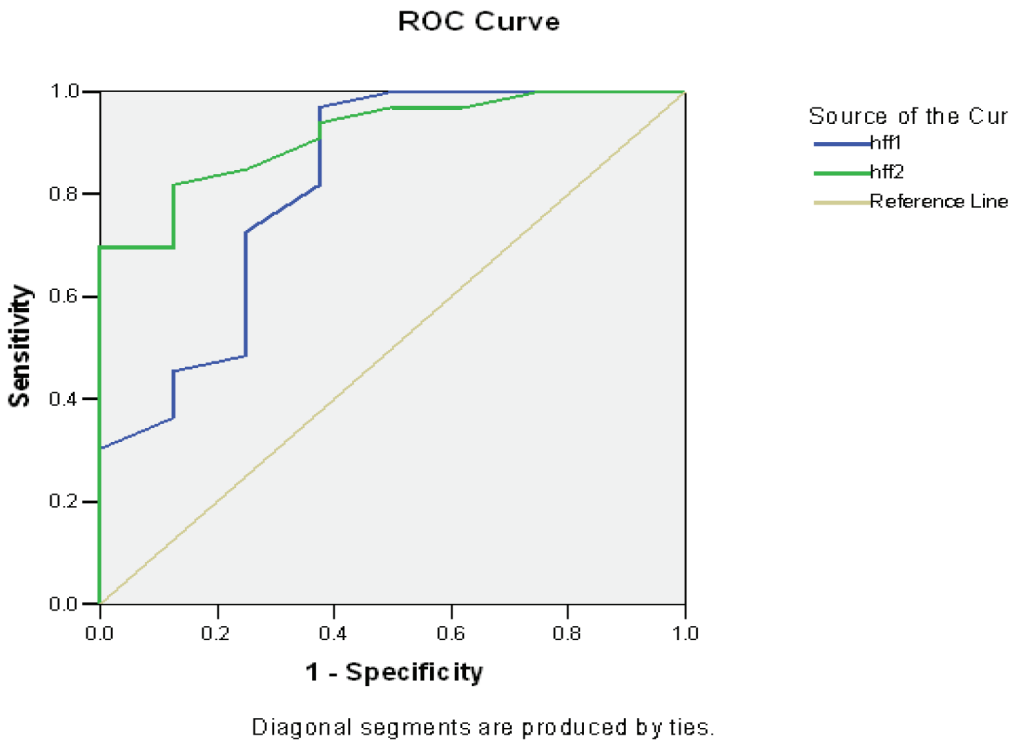

Figure 7. *ROC for cut-off values of H-FABP at first and second assessments in the diagnosis of acute MI.*

of the studied patients was 54.26 ± 9.53 years and 89.6% of them were males and 67.2% of them were smokers. These results were similar to our study and this is due to increasing age and smoking being the risk factors for atherosclerosis and CAD, while in contrast to our present study 89.6% of their studied patients were male, and this may be due to increased sample size (125 patients) in comparison to the present study (41 patients) [14].

Our study showed that 51.2% of the studied patients had IHD, 61% of them were hypertensive, and 34.1% of them were diabetic. Similar to our study, Vupputuri et al. [15] found that CAD, hypertension, and type 2 diabetes account for 46.3%, 63%, and 63%, respectively. On the other hand, McMahon et al. [16] found that (34.5%) of the studied patients were hypertensive, 26.4% of them had IHD, and 7.7% of them were diabetic. This difference may be due to sample size in McMahon et al.'s [16] study, which was 1128 patients, while the present study's sample size was 41 patients.

Our study showed that 51.2% of the studied patients had STEMI, 29.3% of them had NSTEMI, and 19.5% of them had UA. In disagreement with our study, McMahon et al.

[16] revealed that 5.1% of the patients had STEMI, 5.2% of them had NSTEMI, and 14.9% of them had UA. This difference may be due to the sample size in McMahon et al.'s [16] study, which was 1128 patients, while the present study's sample size had only 41 patients. Also, it included patients with chest pain other than ACS (e.g., stable angina, arrhythmia, heart failure, and non-cardiac origin chest pain) [16]. The present study showed that H-FABP had high sensitivity at the early time of 0-3 hours (76.2%) which increased to 85.7%. In accordance with our study, McMahon et al. [16] found that H-FABP had the greatest sensitivity at 0-3 hours (64.3%) and within 3-6 hours of chest pain, the sensitivity of H-FABP was 85.3%. The present study showed that H-FABP had 70% specificity at the early time of presentation at 0-3 hours which increased to 75% at 3-6 hours of chest pain. In accordance with our study, Ibrahim Elmadbouh et al [17] revealed that the specificity of H-FABP was 88.2% and it became 88.9% at 3-6 hours.

Recommendation

All patients presenting with chest pain should be assessed carefully and full history, physical examination, and ECG should be done at a probable time in order to determine patients with chest pain of cardiac origin to avoid losing time and for rapid withdrawal of blood samples for laboratory investigations. H-FABP can be used to ensure earlier ACS diagnosis and earlier discharge of inappropriate patients. Using the absolute cut-off value (19 ng/l) of H-FABP assay will provide an excellent rule out capacity for AMI at 0-3 hours since symptoms onset. Adding H-FABP to routine use of troponin I for early diagnosis of acute coronary syndrome patients at early presentation to ED during 0-3 hours of chest pain is recommended. Application of training programs and workshops about updated and approved guidelines of management ACS patients to improve outcome of these patients is recommended. Finally, we suggest further multicenter studies with a larger sample size or duration to have more accurate estimation of diagnostic value of H-FABP for early diagnosis of ACS patients and for improvement in their outcome.

Conclusion

It was found that H-FABP had a high sensitivity (76.2%) at the early stage during 0-3 hours of chest pain while during 3-6 hours of chest pain the sensitivity of H-FABP was 85.7%.

It was also found that H-FABP specificity was 70% during 0-3 hours of chest pain, while during 3-6 hours it became 75%.

Use absolute cut-off value (19 ng/L) of H-FABP assay will provide an excellent rule out capacity for AMI at 0-3 hours since symptoms onset.

Conflict of interests

The authors declare that there is no conflict of interest regarding the publication of this article.

Funding

None.

Consent to participate

Written consent was obtained from all the subjects.

Ethical approval

Approval of local ethical committee of Faculty of Medicine, Suez Canal University) was taken. Ethics approval was sought from the Institutional Review Board at its meeting on (21/10/2015) and the ethical clearance was given.

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References

1. Rosamond W, Flegal K, Furie K, Go A, Greenlund K, Haase N, et al. Heart disease and stroke statistics--2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2008;117(4):e25–146. https://doi.org/10.1161/CIRCULATIONAHA.107.187998
2. Lloyd-Jones D, Adams RJ, Brown TM et al. Executive summary: heart disease and stroke statistics--2010 update: a report from the American Heart Association. Circulation. 2010;121:948. https://doi.org/10.1161/CIRCULATIONAHA.109.192666
3. Nichols M, Townsend N, Scarborough P, Rayner M. Cardiovascular disease in Europe 2014: epidemiological update. Eur Heart J. 2014;35:2950. https://doi.org/10.1093/eurheartj/ehu299
4. Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2011;32:2999–3054. https://doi.org/10.1093/eurheartj/ehr236
5. Goldmann L, Kirtane A. Triage of patients with acute chest pain and possible cardiac ischemia: the elusive search for diagnostic perfection. Ann Intern Med 2003;139:987–95. https://doi.org/10.7326/0003-4819-139-12-200312160-00008
6. Collinson PO, Premachandram S, Hasehmi K. Prospective audit of incidence of prognostically important myocardial damage in patients discharged from emergency department. BMJ. 2000;320:1702–5. https://doi.org/10.1136/bmj.320.7251.1702
7. McCord J, Nowak RM, McCullough PA, Foreback C, Borzak S, Tokarski G, et al. Ninety-minute exclusion of acute myocardial infarction by use of quantitative point-of-care testing of myoglobin and troponin I. Circulation. 2001;104(13):1483–8. https://doi.org/10.1161/hc3801.096336

8. Viswanathan K, Kilcullen N, Morrell C, Thistlethwaite SJ, Sivananthan MU, Hassan TB, et al. Hearty-type fatty-acid binding-protein (H-FABP) predicts long-term mortality and reinfarction in consecutive patients with suspected acute coronary syndrome who are troponin negative. J Am Coll Cardiol. 2010;55(23):2590–8. https://doi.org/10.1016/j.jacc.2009.12.062
9. Armitage P, Berry G, Matthews JNS. Statistical methods in medical research, 4th ed. Oxford, UK: Blackwell; 2002. https://doi.org/10.1002/9780470773666
10. McMahon CG, Lamont JV, Curtin E, McConnell RI, Crockard M, Kurth MJ, et al. Diagnostic accuracy of heart-type fatty acid- binding protein for the early diagnosis of acute myocardial infarction. Am J Emerg Med. 2012;30:267–74. https://doi.org/10.1016/j.ajem.2010.11.022
11. Kolansky DM. Acute coronary syndromes: morbidity, mortality, and pharmacoeconomic burden. Am J Manag Care. 2009;15(2):36–41.
12. Marceau A, Samson JM, Laflamme N, et al. Short and long-term mortality after STEMI versus NON-STEMI: a systematic review and meta-analysis. J Am Coll Cardiol. 2013;61(10):E96. https://doi.org/10.1016/S0735-1097(13)60097-2
13. Banu S, Tanveer S, Manjunath CN. Comparative study of high sensitivity troponin T and heart-type fatty acid-binding protein in STEMI patients. Saudi J Biol Sci. 2015;22(1):56–61. https://doi.org/10.1016/j.sjbs.2014.05.011
14. Abbasi WA, Saleem M, Rasheed S, Kiyani AM. Utility of heart type fatty acid binding protein (H-FABP) point of care test in the early hours of STEMI compared with troponin-I in Pakistani population. J Ayub Med Coll Abbottabad. 2017;29(1):107–11.
15. Vupputuri A, Sekhar S, Krishnan S, Venugopal K, Natarajan KU. Heart-type fatty acid-binding protein (H-FABP) as an early diagnostic biomarker in patients with acute chest pain. Indian Heart J. 2015;67:538–42 https://doi.org/10.1016/j.ihj.2015.06.035
16. McMahon CG, Lamont JV, Curtin E, McConnell RI, Crockard M, Kurth MJ, et al. Diagnostic accuracy of heart-type fatty acid-binding protein for the early diagnosis of acute myocardial infarction. Am J Emerg Med. 2012;30:267–74. https://doi.org/10.1016/j.ajem.2010.11.022
17. Elmadbouh I, Mahfouz R, Bayomy N, Faried W, Ghanayem N. The value of human heart-type fatty acid binding protein in diagnosis of patients with acute chest pain. Egypt Heart J. 2012;64:179–84. https://doi.org/10.1016/j.ehj.2012.06.004