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CORRELATION OF URINARY HUMAN HEART FATTY ACID BINDING PROTEIN WITH THE CONVENTIONAL CARDIAC MARKER OF STEMI

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Abstract:

Aim: To analyze the blood levels of cardiac enzymes and urinary and serum levels of human heart-type fatty acid-binding protein (HH-FABP) in patients with ST-elevation myocardial infarction (STEMI); to analyze and assess the correlation of urinary protein HH-FABP with the blood levels of troponin I and creatine kinase (CK-MB) in patients with STEMI and to assess the correlation between serum and urine levels of HH-FABP in patients with STEMI

Background: STEMI is one of several medical challenges. There is still lack of highly sensitive and specific cardiac markers for early detection of AMI and scope to develop. In this study the diagnostic yield of Human Heart type fatty acid binding protein (HH-FABP), an emerging biomarker was assessed in patients with STEMI in both serum and urine and correlated its diagnostic efficacy was correlated with other conventional markers (Troponin I and CKMB)

Methods: Cross-sectional observational study**.** 41 patients with STEMI were studied. Serum and urine samples were collected within seven hours of onset of symptoms. HH-FABP was quantified using Enzyme Linked Immunosorbent Assay (ELISA) reader of Bio-Rad and the test result was correlated with data of Troponin I and CKMB collected from Laboratory information system (LIS).

Results: Our investigation highlighted the link between plasma Troponin I and serum CKMB. However, there was no statistically significant correlation between serum and urine HH-FABP and with other markers.

Conclusion: Plasma troponin I and CKMB were found to be consistently elevated in patient with STEMI. A significant correlation between serum and urine HH-FABP and other identified cardiac biomarkers was not found.

INTRODUCTION

Acute myocardial infarction (AMI) is the most common cause of death in the world. Comprehensive risk assessment of patients presenting with chest pain and eliminating undesirable results should decrease morbidity and mortality rates, increase the quality of life of patients, and decrease health expenditure. HH-FABP is a cytosolic protein which carry fatty acids in the cytosol and is, are found in all cells utilizing fatty acids. It is abundantly found in heart tissue. It is expected to be rapidly released from cardiac myocytes into the circulation shortly after the onset of cell damage and has the potential to be used as marker for myocardial damage in blood and urine.[1]It is thought to be involved in the fatty acid metabolism in the cardiomyocytes. When the cell is injured, the protein leaks from the cell and appear in the blood and urine.[2]The levels start to appear in 90 minutes of symptomatic presentation of infarction, peaking at around 6 hours and return to baseline in 24 hours. Prognostic utility of HH- FABP in acute coronary syndromes assessed in a large cohort showed increased association with death and adverse cardiovascular events.[3]

Plasma levels of fatty acid binding protein 3 (pFABP3) are elevated in patients with peripheral artery disease (PAD). Since the kidney filters FABP3 from circulation, urinary levels of it were investigated and found to have a stronger association between urinary fatty acid binding protein 3 with PAD, as a potential diagnosticbiomarker.[4]

Human urine is an ideal candidate for use in clinical diagnostics. The collection is non-invasive and does not require personnel, and it is suitable for repeated collection. There is a paucity of studies on urinary HH-FABP in acute coronary syndrome and their correlation with conventional cardiac markers of blood.

Since then, several biomarkers, including lactate dehydrogenase (LDH), myoglobin, creatine-kinase (CK), its cardiac-specific iso-enzyme CK-MB were used, but they have been superseded by cardiac troponins (cTn).[5]

MATERIAL AND METHODS

This cross-sectional observational study on 41 patients of acute ST elevation Myocardial infarction cases (STEMI), was carried out in the Department of Biochemistry and cardiology, at Father Muller Medical college Hospital. Patients were aged between 30 to 60 years. It was a purposive sampling of STEMI. History of malignancy, infectious diseases, sepsis and kidney injury, urinary tract infection, stroke, and history of MI was excluded. The total duration of the study was of two years, after obtaining clearance from institutional ethics committee (FMIEC/CCM/714/2020).Voluntary, informed consent was obtained from the study subjects. Taking aseptic precautions urine samples were collected. The left-over serum after analysis of CK-MB activity was used for serum HH-FABP evaluation. Separated serum was stored at −20∘ C until analysis and the samples were thawed only once. The samples were analyzed for HH-FABP in the serum and urine samples, using enzyme linked immunosorbent assay (ELISA) reader of Biorad. The procedure was followed as per the manufacturer’s instruction. For each batch of sample analysis, the standards and controls were run. The data of whole blood

Troponin I estimated by fluorescent Immunoassay and serum CK-MB by enzymatic spectrophotometric method were collected from the laboratory information database.

All patients admitted to ICCU with diagnosis of ST-elevation acute coronary syndrome based on clinical symptoms and 12 lead ECG were selected. Time of collection of samples was on an average of 7 hours from the onset of symptoms.

Ethical approval:

All procedures performed in studies involving human participants were as per the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by Father Muller Institutional ethics committee. (FMIEC/CCM/714/2020)

Statistical Analysis:

Statistical analysis was done using SPSS version 23.0 software. The descriptive statistics median and IQR, nonparametric bivariate correlations were tested by Spearman's coefficient (rho). P<.05 was considered statistically significant.

Study protocol:

Information regarding patient demographics and relevant clinical data, such as that concerning the patient's cardiac history and contact address, was recorded on a data collection sheet. Blood samples were taken upon arrival to the casualty.

RESULTS

Forty one patients were evaluated in the casualty and H-FABP was estimated.

Table 1 - IQR of Serum CK-MB, Plasma Troponin I, serum HFABP and Urine HFABP.

VARIABLES	MEDIAN	INTERQUARTILE RANGE
Serum CK-MB (IU/mL)	50	63
Plasma Troponin I (ng/mL)	0.97	4.51
Serum HFBP (ng/mL)	0.4	0.2
Urine HFBP (ng/mL)	1.16	0.9

Table 2: Correlation between Serum HFBP vs. Time (min) of sample collection after the appearance of acute MI symptoms.

variables	Median	Q1, Q3	r	p
Serum HFBP (ng/mL)	0.38	0.32,0.49	0.242	0.255
Time in min	426.5	242.0,511.5		

Table 3: Correlation between Urine HFBP vs. Time (min) of sample collection after the appearance of acute MI symptoms.

Variables	Median	Q1, Q3	r	p
Urine HFBP (ng/mL)	1.16	0.60,1.50	0.371	0.082
Time in min	420	225.0,570		

Table 4: Correlation between various biomarkers in Acute STEMI by Non-parametric Spearman's rho test.

N=41	Spearman's rho	Serum CKMB	Plasma Troponin I	Serum HH-FABP	Urine HH-FABP
Serum CKMB	Correlation coefficient	1.000	.661**	.207	.172
	Significance	.	.000	.193	.282
Plasma Troponin I	Correlation coefficient	.661**.	1.000	.001	.198
	Significance	.000	.	.996	.254
Serum HH-FABP	Correlation coefficient	.207	.001	1.000	.237
	Significance	.193	.996	.	.136
Urine HH-FABP	Correlation coefficient	.172	.198	.237	1.000
	Significance	.282	.254	.136	.

**. Correlation is significant at the 0.01 level (2-tailed).

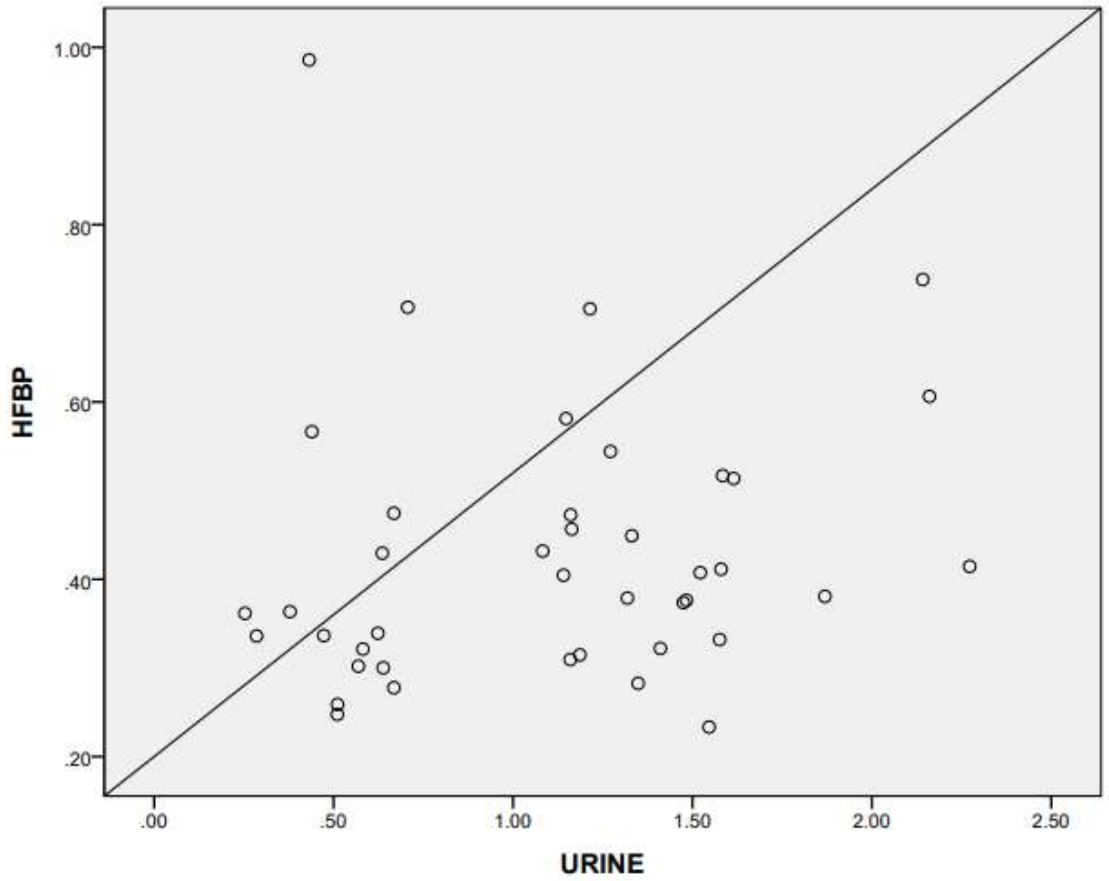

Figure 1: Scatter plot graph between the serum H- FABP and urine H-FABP values.

DISCUSSION

Our study showed a significant correlation between serum CKMB and plasma Troponin I. However, the correlation between serum and Urine HH-FABP and with other conventional markers was not statistically significant.

Study done by Takao Tanaka et al.,[1]a competitive enzyme immunoassay was developed, and they measured timely serum and urine levels of HH-FABP to study the time course changes in acute myocardial infarction cases. The results showed that values increased between 5-10 hours after the development of the symptoms and then declined afterwards. In our study the samples were collected after 6-7 hours of onset of symptoms. The values did not show high results as there was a difference in the time of admission of the patient to the hospital and thus sample collection.

Case control study done by Chandran PA et al.[6]Onevaluation of serum human fatty acid binding protein on diagnosing of non-ST elevation of acute coronary syndrome. ROC curve of HH-FABP was more when compared to Cardiac troponin I and T. The HFABP level above 6.5 ng/mL showed 56.7% sensitivity, 0.5 negative likelihood ratio 100% specificity, and 100% positive predictive value, 62.9%negative predictive value (NPV). However, in our study the

serum values did not correlate with urine values and with other conventional cardiac markers, serum CK-MB and plasma troponin I. This may be attributed to various factors like infarct size and glomerular filtration rate.[7]

Zamzam, A et al. examined the possibility of using urine fatty acid binding protein 3 (uFABP3) as a diagnostic biomarker for peripheral artery disease (PAD). Patients with PAD had 1.7-fold higher levels of uFABP3 normalised for urine creatinine (uFABP3/uCr) [median (IQR) 4.41 (2.79–8.08)] than non-PAD controls and by regression analysis uFABP3/Cr levels were independently associated with PAD for prior history of coronary arterial disease and other risk factors.[4]

Hayashida N et al., evaluated the levels of plasma and urinary levels of HH-FABP in patients undergoing cardiac surgery. And the study showed that levels increased after reperfusion. The levels reached earlier than other cardiac biomarkers. Urine also showed peak levels. It correlated with cardiac function.[2]On the contrary, in our study serum HH-FABP did not show any significant increase in levels.

CONCLUSION

Among the biomarkers evaluated, plasma troponin I and CKMB showed consistently high levels. Serum and Urinary HH-FABP did not show any significant correlation with each other and with other established cardiac biomarkers.

The specificity of HH-FABP alone for diagnosis of acute MI is poor. The elevation was also found in patients with chest pain and significant stenosis on CAG without myocardial infarction. This sensitive detection of myocardial ischemia by HH-FABP may also be applied in patients with unstable angina though further studies are required.

Limitation of study-In this study only assessed the potential benefit from a single measurement of HH-FABP at the time of admission. Sequential measurements were not investigated. Myoglobin was not measured for comparison purposes. Unlike myoglobin, the concentration of HH-FABP in cardiac muscle is higher than in skeletal muscle. This may mean that HH-FABP is potentially more suitable than myoglobin as an early marker of myocyte injury. This study was designed taking cTnI done after 12 h of admission as a gold standard for diagnosis of AMI though it is not 100% specific. Finally the small sample size. Future studies are required with large sample size and the serial measurement of the concentration to evaluate its diagnostic utility

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CONFLICT OF INTEREST

Authors declare that there is no conflict of interest.

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