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Role of Serum Fatty Acid Binding Protein and High Sensitive Cardiac Troponin in Diagnosis and Differentiation of Acute Coronary Syndrome

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ABSTRACT

Background Acute coronary syndrome (ACS) refers to any group of clinical symptoms compatible with acute myocardial ischemia including unstable angina, Non-ST-segment elevation myocardial infarction & ST-segment elevation myocardial infarction. Heart - type fatty acid binding protein (H-FABP) also known as mammary-derived growth inhibitor is a protein that in humans is encoded by the FABP3 gene, The diagnostic potential of the biomarker H-FABP for heart injury. The aim was to To evaluate serum levels of FABP in patients with Acute Coronary Syndrome subgroups and investigate its role in differentiation among them.

Patients & Methods: The present study was conducted at the Department of Biochemistry, College of Medicine/ University of Baghdad during the period from December 2017 until August 2018. Thirty three patients with ACS were included as 11 with unstable angina (UA), 11 with non ST elevation myocardial infarction (NSTEMI), & 11 ST elevation myocardial infarction (STEMI) patients. Also this study included 18 non-ischemic chest pain subjects who served as pathological control. Blood samples were obtained for measurements of FABP and hs-cTn by ELISA method.

The Results: The mean (±SD) value of FABP was significantly increased in NSTEMI (3.80 ± 1.45ng/ml, p< 0.001) and UA (3.62 ± 0.42 ng/ml, p < 0.001) compared to that of STEMI (1.88 ± 1.60 ng/ml). Also, the mean value of serum H-FABP levels of pathological controls (3.17 ± 0.73 ng/ml) was significantly higher than that of STEMI group (p < 0.001). Regarding hs-cTn, it did not differ significantly among the groups of UA (2.82 ± 0.69), NSTMI (4.08 ± 2.35), and STMI (4.53 ± 2.06)

Conclusion:

FABP showed significant elevation in UA and NSTMI and may be used as a biochemical marker in assessment of these two conditions and to differentiate them from STEMI. It used in ACS differentiation is superior of that of Tn.

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Introduction

Acute coronary syndrome (ACS) is defined as sudden coronary obstructions resulting in UA, myocardial infarctions (MI), or ischemic deaths. Most of the time, ischemia develops as a result of endothelial damage and subsequent obstructions of coronary arteries with thrombus formed in atherosclerotic plaque ruptures (1).

ACS usually occurs as a result of one of three problems: ST elevation myocardial infarction (STEMI), non ST elevation myocardial infarction (NSTEMI), or unstable angina (UA) (2). These types are named according to the appearance of the electrocardiogram (ECG) as Non-ST segment elevation myocardial infarction and ST segment elevation myocardial infarction (1).

The transition from stable coronary artery disease to the ACS of STEMI and NSTEMI infarction and unstable angina is characterized by coronary plaque disruption and subsequent thrombosis, which constitute the major pathogenetic components of unstable or vulnerable plaques (3).

In addition to clinical and ECG findings, several Biochemical markers are assessed in patients with chest pain to diagnose myocardial ischemia; such as cardiac enzymes (CK-MB) and cardiac troponins; others are still under research (4). Heart-type fatty acid binding protein (H-FABP) also known as mammary-derived growth inhibitor is a protein that in humans is encoded by the FABP3 gene, The diagnostic potential of the biomarker H-FABP for heart injury was discovered in 1988 by Prof. Jan Glatz (5). It is found at ten-fold lower levels in skeletal muscle than heart muscle and the amounts in the kidney, small intestine, liver, brain, lactating mammary glands and the placenta are even lower again (6). H-FABP is recommended to be measured with troponin to identify MI and acute coronary syndrome in patients with chest pain. H-FABP measured with troponin shows increased sensitivity of 20.6% over troponin at 3-6 hr. Following chest pain onset (7).

Patients & Methods:

The present study was conducted at the Department of Biochemistry, College of Medicine/ University of Baghdad, Baghdad Teaching Hospital, period from December 2017 until August 2018. This study was done on 51 subjects (33 acute coronary syndrome patients and 18 pathological controls).Thirty three patients with ACS were included and divided into three groups:

Group (1): included 11 UA patients.

Group (2): included 11 STEMI patients.

Group (3): included 11 NSTEMI patients.

The diagnosis of ACS in every patient was done by Cardiologist based on clinical presentation and history of ischemic heart disease, which was confirmed by ECG and cardiac troponin. Also the study included (18) non-ischemic chest pain persons served as control. Blood samples were obtained for measurements of serum FABP by ELISA method for all participants (8).

Results:

The mean (±SD) value of age of pathological control group (49.4 ± 14.1 years) was significantly lower than that of NSTEMI group (65.7 ± 9.8 years, p<0.002) and UA group (65.4 ± 7.1 years, p<0.003). However, there was no significant difference between pathological controls and STEMI group (60.6 ± 10.4 years) as well as among ACS subgroups in age mean value. Twenty six subject of study were males while 25 subject were females. Table (1)

The of mean (±SD) value of serum FABP levels was significantly increased in NSTEMI (3.80 ± 1.45 ng/ml, p< 0.001) and UA (3.62 ± 0.42 ng/ml, p < 0.001) compared to that of STEMI (1.88 ± 1.60 ng/ml). Also, the mean value of serum H-FABP levels of pathological controls (3.17 ± 0.73 ng/ml) was significantly higher than that of STEMI group (p < 0.001). The mean values of serum hs-cTn concentrations did not differ significantly among the groups of ACS (Table 2), (figure 1,2).

Table (3), show the ROC analysis of the validity of serum FABP predictor of NSTEMI and UA from pathological control: H-FABP (ROC: 0.717 and 0.712, respectively) had fair ability to diagnose and differentiate NSTEMI and UA from control with optimal cut points >3.5 ng / ml (SN=73%, SP=78%) for NSTEMI, and >3.5 ng / ml (SN=73%, SP=78%) for UA, respectively.

Table1: Mean (±SD) Values of Demographic Data of Non-Ischemic Chest pain Group, ACS Chest Pain Subgroups (STEMI, NSTEMI, UA)

Parameter	Pathological Control (n=18)	STEMI GIII (n=11)	NSTEMI GIII (n=11)	UA GIII (n=11)
Age	49.4 ± 14.1 *, NS	60.6 ± 10.4 NS	65.7 ± 9.8 *	65.4 ± 7.1 *
BMI NS	28.4 ± 4.8	29.5 ± 2.6	29.7 ± 3.0	28.3 ± 2.1
Gender				
Female NS	8 (44.4%)	6 (54.5%)	3 (27.3%)	8 (72.7%)
Male NS	10 (55.6%)	5 (45.5%)	8 (72.7%)	3 (27.3%)

STEMI: ST elevation myocardial infarction, NSTEMI : non ST elevation myocardial infarction, UA : unstable angina

*ANOVA & t-test revealed significant decrease in age in control group compared with GIII NSTEMI and UA, NS: non - significant differences in (BMI, Gender) between groups and controls and non-significant differences in age between GIII (STEMI) subgroup compared to controls.

Table 2: Mean (±SD) Values of Biochemical Marker of ACS Chest Pain Subgroups (STEMI, NSTEMI, UA) and Pathological Control

Parameter	Pathological Control (n=18)	STEMI (n=11)	NSTEMI (n=11)	UA (n=11)
H-FABP (ng/ml)	3.17 ± 0.73	1.88 ± 1.60 *	3.80 ± 1.45	3.62 ± 0.42
Hs-cTn (ng/ml) NS	3.98 ± 1.08	4.53 ± 2.06	4.08 ± 2.35	2.82 ± 0.69

All data presented as mean ± SD. ANOVA and t test reveled *significant increase in H-FABP level in each of NSTEMI (p value<0.001), UA (p value=0.001) , and pathological control (p value=0.004), compared to STEMI. NS: non significant difference in Hs-cTn

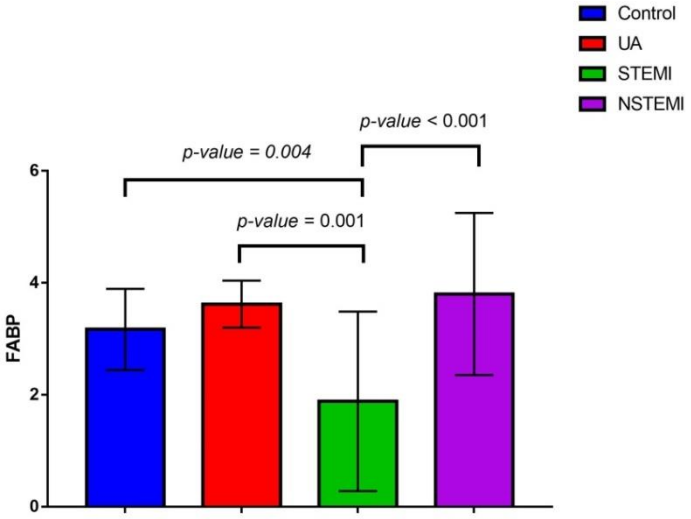

Figure 1: Differences in serum H-FABP level among the subgroups of ACS (UA, STEMI, and NSTEMI) and pathological controls

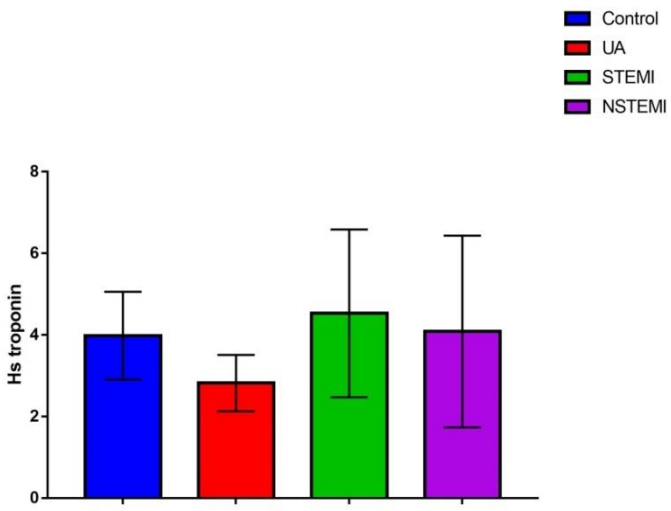

Figure 2: Differences in serum h-scTn level among the subgroups of ACS (UA, STEMI, and NSTEMI) and pathological controls

Table (2), show the ROC analysis of the validity of serum FABP predictor of NSTEMI and UA from pathological control: H-FABP (ROC: 0.717 and 0.712, respectively) had fair ability to diagnose and differentiate NSTEMI and UA from control with optimal cut points >3.5 ng / ml (SN=73%, SP=78%) for NSTEMI, and >3.5 ng / ml (SN=73%, SP=78%) for UA, respectively.

Table 3: ROC analysis of the validity of the H-FABP marker as predictor of STEMI, NSTEMI and UA from control

Parameter	ROC	p-value	Cut point	SN	SP	AC	PPV	NPV
H-FABP (ng/ml) with NSTEMI	0.717	0.069	>3.5	73%	78%	76%	67%	82%
H-FABP (ng/ml) with UA	0.712	0.038	>3.5	73%	78%	76%	67%	82%

ROC: receiver operator characteristics, SN: sensitivity, SP: specificity, AC: accuracy, PPV: positive predictive value, NPV: negative predictive value

Discussion

The present study found significant increased of FABP with fair discriminator utility power in patients with UA and NSTEMI compared with hs-cTn. The PPV and NPV of FABP was found to be 67% and 82%.

The study conducted by Missiri et al (9) has demonstrated that a significantly larger number of patients with NSEMI were detected by point-of-care H-FABP test available in the ER compared to cTnT for patients and accordingly it can be used to rapidly rule out acute myocardial infarction especially in those presenting early after the onset of chest pain.

Kilcullen et al (10) showed increased levels of HFABP in high risk patients with a negative value of troponin levels. In another study of unstable angina patients with H-FABP levels <5.8□g/l are at risk of death at 1 year was 2.1% first, much smaller than in patients with high levels of H-FABP> 5.8□g/l at 22.9%. Increase in H-FABP in UA patients showed recurrent infarction incidence and risk of repeatable ischemic events. The increased levels of H-FABP in UA ischemia caused by expansion of an ongoing process and myocyte injury with the risk of death and cardiovascular events in the future (11).

Rrobert et al (12) study investigated the optimal cut-off point of FABP and assessed the possible diagnostic potency of plasma H-FABP in patients presenting with chest pain to the GP. The cut-off value for ACS of H-FABP, where sensitivity and specificity reached optimal values, is 4.0 ng/ml. Using this cut-off value for H-FABP, sensitivity for AMI of the H-FABP (hs-cTn) tests was 77.5% (73.0%) for all patients at presentation and the sensitivity for ACS was 73.9% (70.6%). Based on the results of this study, H-FABP with a cut-off value of 4.0 ng/ml could reach an overall NPV for AMI of 93.9% and for ACS of 90.8% in an unselected primary care population (estimation based on a prevalence of ACS of 22%).

Several studies have shown that sensitivity and specificity of H-FABP ranged from 39 to 78.5% and 78.2 – 94%, respectively in early diagnosis of ACS (13). Orak et al (14) was found 98% specificity and 71% sensitivity different from those study. The most important cause of the different results in these studies which used qual¬itative techniques is thought to be the low cut-off levels. 100% sensitivity and 27-38% specificity were found in two studies which used quantitative H-FABP measurement (15).

Furthermore, elevated H-FABP levels were associated with increased risk of MI or recurrent ischemia within 30 days, especially in unstable angina patients, when they were determined the +negative troponin I (16). H-FABP for confirming AMI has a higher significance and sensitivity, compared with myoglobin, troponin, CK-MB elevation, and at the same time H-FABP has a high specificity (17). Moreover, the elevated H-FABP level within 30 days also was associated with the risk of recurrent ischemia (18). Normal levels of troponin and H-FABP were associated with very low risk of death (10).

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