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Serum Heart Type Fatty Acid Binding Protein (H-FABP) As an Early Marker of Myocardial Ischemia

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Abstract Original Research Article

Ischemic Heart Disease is the most common cause of cardiovascular mortality. Early detection of Acute Myocardial Infarction (AMI) at the ischemic stage is important to prevent morbidity and mortality. Heart type Fatty Acid Binding Protein (H-FABP) is a sensitive indicator of ischemia, increases earlier than other cardiac markers. With the above view, the study aimed to determine the efficacy of H-FABP in the early diagnosis of Myocardial Infarction (MI) and its correlation with Creatine Kinase –MB isoform (CK-MB) and fasting Lipid Profile. This age matched cross sectional study was conducted in a tertiary health care Centre. 90 subjects were included with age limit of 30 to 60 years. 45 cases were selected from patients admitted in ICCU within 6 hours of complaints of chest pain and 45 healthy individuals as controls. The Mean value of HFABP and CK-MB in cases were higher than the controls and the p values were 0.000 (<0.05) which are statistically significant. When compared to CK-MB, HFABP showed 76.5% detection of myocardial ischemia in the first 3 hours of symptoms, whereas CK-MB had only 58.8%. Positive correlation was also found between HFABP and duration of chest pain. Though we had significant difference in Lipid profile between cases and controls, no correlation was found with HFABP value. In this study, elevated HFABP in the early hours (0 to 3 hours) of onset of ischemic chest pain clearly shows that serum HFABP can be used as an early marker in the diagnosis of coronary artery disease.

Key words: Ischemic Heart Disease (IHD), Coronary Artery Disease (CAD), Acute Myocardial Infarction (AMI), Heart type Fatty Acid Binding Protein (H-FABP), Creatine Kinase-MB (CK-MB), Fasting lipid profile.

INTRODUCTION

Cardiovascular Disease is a major health problem across the world. By the year 2020, one in every three deaths will be due to CVD [1]. Eighty Percentages of total deaths in developing countries like India are due to cardiovascular disease [2]. Ischemic Heart Disease is the most common cause of cardiovascular morbidity and mortality. IHD occurs due to the imbalance between the oxygen supply and oxygen demand of the myocardium. The manifestations of IHD are Angina Pectoris, Unstable Angina Pectoris, Myocardial Infarction, Heart failure and sudden cardiac death [3]. Patients may have transient underlying pathology before the signs and symptoms of AMI become apparent.

Early detection of AMI at the ischemic stage is important to prevent morbidity and mortality. The diagnosis of AMI is based on history, clinical examination, and electrocardiogram and biochemical markers. ECG is not sufficient to diagnose the IHD since ST segment changes can also be observed in other conditions [4]. Cardiac markers are also important in the diagnosis of AMI. Myoglobin, CK-MB, Cardiac Troponin- T and Troponin-I am the currently used biochemical markers for diagnosing IHD.

Detection of AMI in the early hours by these markers is not satisfactory [5], since these markers tend to elevate only after 6 hours of onset of injury. Even though myoglobin level increases within 2 hours, the specificity of myoglobin towards the myocardium is low. Recent data show that H-FABP is a sensitive indicator of ischemia, increases earlier than other cardiac markers [6, 7]. HFABP is a small intracellular cytoplasmic protein consists of 132 amino acids. It weighs about 14.5 KDa and is water soluble [8].

The concentration of HFABP is 10 fold lower in skeletal muscle than cardiac muscle, and the amount in kidney, liver and small intestines are lower again [9,

10]. It appears in plasma within 2 hours of cardiac damage, peaks within 4 to 6 hours and returns to normal basal level by 20 hours [11]. Because of its low molecular weight, relative tissue specificity and high myocardial content, this marker is released earlier than other markers. HFABP is the earliest biomarker available for acute myocardial injury.

It is possible to detect the myocardial damage soon as an hour after onset of injury by H-FABP level. Its level is elevated early in the ischemic stage [12]. Diagnosing AMI at this stage helps in preventing the progression of disease. Its diagnostic accuracy may be better than other cardiac markers in the early stages. It has been proven to be an independent prognostic marker in patients with MI [13].

AIMS & OBJECTIVES

Aims

To estimate the serum concentration of Heart type Fatty Acid Binding Protein (H-FABP) in Patients within 6 hours of onset of chest pain.

Objectives

- To correlate H-FABP Level with CK-MB
- Correlation of H-FABP with Lipid Profile which includes
  - Total cholesterol
  - High density Lipoprotein(HDL)
  - Low density Lipoprotein (LDL)
  - Very Low density Lipoprotein (VLDL)
  - Triacylglycerol (TAG)

MATERIALS & METHODS

This age matched cross sectional study was conducted in a tertiary health care hospital for a period of 9 months and included 90 subjects with age limit of 30 to 60 years. Out of 90, 45 cases were selected from patients admitted within 6 hours of onset of chest pain in ICCU and diagnosed to have coronary artery disease and 45 healthy individuals as controls. Informed and written consent were obtained from both cases and control group.

Inclusion Criteria

- Chest pain of duration less than 6 hours
- ECG showing abnormal ST-T Segment changes- ST elevation or depression, T wave inversion

Exclusion Criteria

- Hepatic disease
- Renal disorders
- Heart failure
- Pulmonary edema
- Cardiomyopathy
- Stroke
- Patient underwent CABG, Coronary Angioplasty within 30 days.

Under aseptic precautions, blood samples were collected from cases and controls by venipuncture. Fasting blood sample was collected from patients and controls for the estimation of Total Cholesterol, Triglycerides and HDL. HFABP was measured by Quantitative Sandwich Elisa Method and CK-MB by Immuno inhibition method. Total cholesterol, HDL and TGL were estimated by cholesterol oxidase peroxidase (CHOD-PAP) method, Selective Inhibition Method (Direct Method) and enzymatic method respectively. FRIEDEWALDS formula was used to calculate LDL = TC – (HDL + TGL / 5). The normal reference range of HFABP is 0 to 6 ng/ml. Cut-off value for AMI is >19 ng/ml.

RESULTS

Statistical analysis was done using SPSS-16. Student t test was employed for statistical analysis of data. Mann Whitney U test was also performed because of wide standard deviation. Correlation between the measured parameters was done by Pearson's correlation. The data are expressed in terms of mean and standard deviation. P value <0.05 is taken as significant.

Table-1: Statistical Analysis of HFABP and other parameters in cases and Controls

VARIANCE	CASES (n=45)	CONTROLS (n=45)	p-value
	Mean ± SD	Mean ± SD	
HFABP	35.81 ± 19.28	2.78 ±1.45	0.000*
CK- MB	53.71 ±42.93	13.51 ±3.94	0.000*
CHOLESTEROL	211.4 ±41.91	170.15 ±20.51	0.000*
TGL	150.51 ±33.82	117.13 ±25.38	0.000*
HDL	38.44 ±7.66	42.02 ±7.15	0.025*
LDL	142.9 ±41.48	104.70 ±20.45	0.000*
VLDL	30.10 ±6.76	23.42 ±5.07	0.000*

*significance at 0.05 level

Table- 2: Mann Whitney U Test for Comparison of HFABP & CK-MB in cases and controls

Variance	CASES (n=45)		CONTROLS (n=45)		Z score	p-value
	Mean Rank	Sum of Ranks	Mean Rank	Sum of Ranks		
HFABP	23.02	1036.00	67.98	3059.00	-8.163	0.000*
CK MB	62.97	2833.50	28.03	1261.50	-6.348	0.000*

*significance at 0.05 level

Mean value of HFABP in cases was higher than control group and the p value was 0.000 (<0.05) which is statistically significant. In Mann-Whitney U test, Mean rank of HFABP in case and control group were 23.02 and 67.98. p value was 0.000(<0.05). Mean value of CK-MB and lipid parameters were higher in cases when compared to controls and the differences were statistically significant.

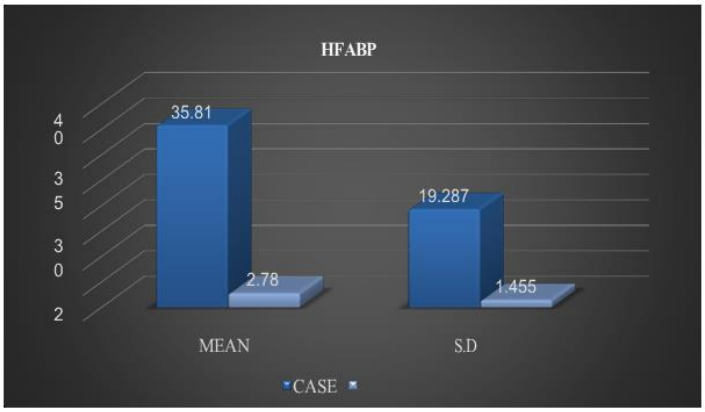

Fig-1: Mean and S.D of HFABP in cases and Controls

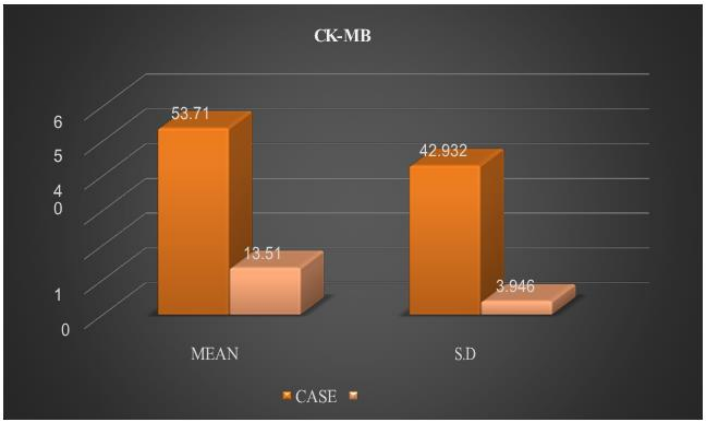

Fig: 2 Mean and S.D of CK-MB in cases and Controls

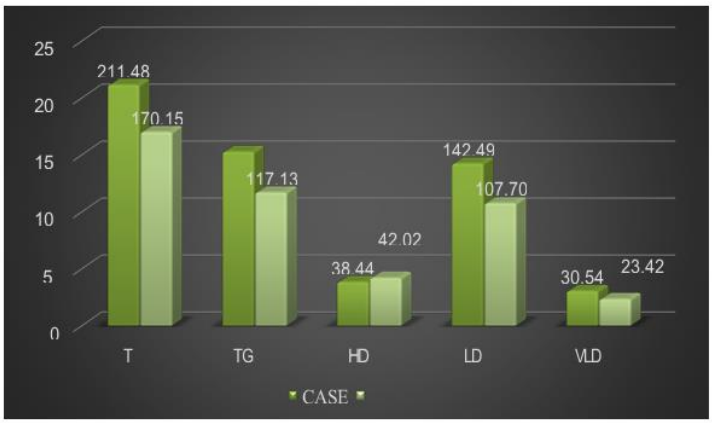

Fig-3-Mean Value of Lipid Profile in cases and Controls

Table- 3: Frequency table for Serum Levels of HFABP, CK- MB and Duration of Chest Pain in cases

Variables		Hours				Total	
		< 3 hours		3 to 6 hours			
		count	%	count	%	count	%
HFABP (ng/mL)	Below 19 ng/mL	4	23.5%	3	10.7%	7	15.6%
	Above 19 ng/mL	13	76.5%	25	89.3%	38	84.4%
CK-MB (U/L)	Below 24 U/L	7	41.2%	4	14.3%	11	24.4%
	Above 24 U/L	10	58.8%	24	85.7%	34	75.6%

HFABP showed 76.5% detection in first 3 hours whereas CK-MB had only 58.8%. There was no significant difference between HFABP and CK-MB in the 3 to 6 hours of duration.

Table -4: Pearson Correlation between HFABP with other Parameters in Study group

	Variables	Correlation value	p value	Statistical Inference
HFABP	Duration	**0.365**	**0.014**	**S**
	CK-MB	**0.318**	**0.033**	**S**
	Total Cholesterol	-0.056	0.714	NS
	TGL	-0.030	0.845	NS
	HDL	-0.217	0.152	NS
	LDL	-0.012	0.939	NS
	VLDL	0.020	0.896	NS

Table 4 shows significant positive correlation between HFABP with duration and CK-MB.

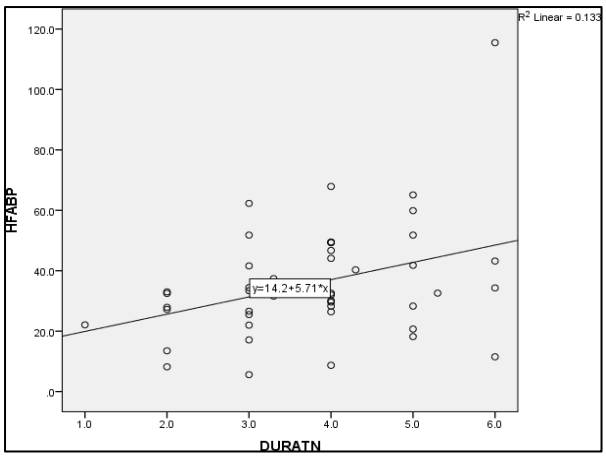

Fig-4: Correlation between HFABP and Duration

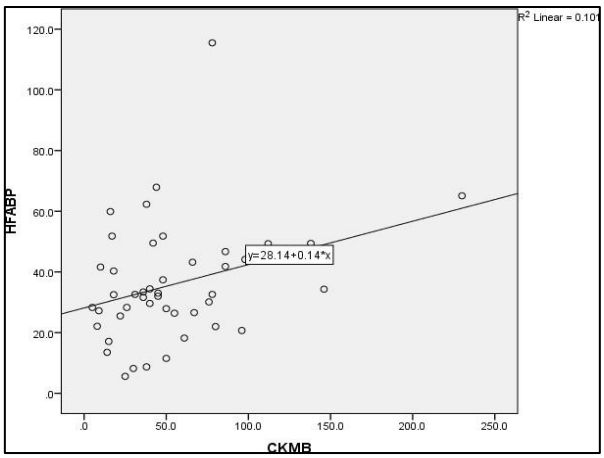

Fig-5: Correlation between HFABP and CK-MB

DISCUSSION

The present study establishes the characterization of HFABP, its association with the early diagnosis of myocardial ischemia in patients and its comparison with CK-MB, the commonly used early biochemical marker of coronary artery disease.

In our study serum concentration of HFABP is found to be increased in patients with coronary heart disease when compared to control group and it is statistically significant (p value <0.01).The mean value of cases and controls are 35.811 ± 19.2871 and 2.787 ± 1.4556. These findings are in accordance with the study of Bhakti .N. Gami *et al*. who reported an increased level of HFABP in CAD than normal healthy individuals [14].

Mean value of CK-MB is higher in cases than controls. When compared to CK-MB, HFABP showed 76.5% increase in the first 3 hours, whereas CK-MB had 58.8%. At 3 to 6 hours, HFABP showed 89.3% and CK- MB had 85.7%. Elevated HFABP values in the early hours than CK-MB correlates with the findings of HaticePasaoglu *et al*. [15] our findings also correlate with study by McMahon *et al*. who showed that

HFABP had the sensitivity of 64.3% at 0 to 3 hours and 85.3% at 3 to 6 hours [16].

Positive correlation of HFABP and CK-MB levels with duration is also found in this present study. This correlates with the study done by P. Mad *et al*.[17]. Traditional risk factors used in the prediction of atherosclerosis are Total Cholesterol, Triglycerides, LDL, VLDL and HDL. The value of lipid parameters shows significant increase in cases than controls. We have no significant correlation between HFABP and lipid profile.

CONCLUSION

The ability to detect ischemia before myocyte destruction is necessary for earlier and more accurate management decisions in patients suspected to have CAD. Myoglobin rises within 2 hours but it is a less specific marker. CK-MB, a commonly used early marker, lacks early sensitivity because their blood concentration does not increase until 4 to 8 hours after onset of AMI. HFABP, a small molecular size protein which has absolute specificity towards myocardium, is released in to the circulation at the early stage of injury and presence of trace amount of HFABP in circulation under physiological conditions implies detection of the marker in serum is possible even with minimal increase. Estimation of Serum HFABP would be an important diagnostic as well as a prognostic marker for CAD.

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