Serum Level of Heart Type Fatty Acid Binding Protein Before and after Treatment of Congestive Heart Failure in Children

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ABSTRACT

Background: Heart failure (HF) in children is a clinical and pathophysiological syndrome that results from ventricular dysfunction, volume or pressure overload, either alone or in combination. This study aimed to estimate serum level of H-FABP before and after treatment of congestive heart failure, and correlate its level with severity of the disease. **Patients and methods**: The study was cohort control study. It included 30 infants and children; their ages ranged from two months to four years with heart failure diagnosed clinically and were admitted to Cardiology Unit of Pediatric Department, at Zagazig University Hospitals during the period from November 2017 to April 2018. They were divided into four groups, first group aged (2-12 month), second group (13-24 m), third group (25-36 m) and fourth group (37-48 m). Echocardiographic assessment of the heart was done using conventional Doppler echocardiography. Serum heart type fatty acid binding protein (H-FABP) level (estimated on patient admission and 1 week after treatment) was determined by quantitative sandwich enzyme linked immunosorbent assay (ELISA) technique.

Results: There was a significant difference in the serum level of H-FABP in our patients before treatment $(2.156 \pm 1.156$ ng/ml) compared with after treatment $(0.882 \pm 0.716$ ng/ml). There was a significant positive correlation between serum H-FABP level and Ross classification.

Conclusion: H-FABP may be used as diagnostic and prognostic predictor of adverse outcome in children with heart failure.

Keywords: Heart failure (HF), Heart-type fatty acid-binding protein (H-FABP), Serum level.

INTRODUCTION

Heart failure (HF) is defined as an abnormality of cardiac structure or function leading to failure of the heart to deliver oxygen at a rate commensurate with the requirements of the metabolizing tissues, despite normal filling pressures or only at the expense of increased filling pressures**.** Heart failure in children differs from the adult in many aspects; the causes, symptoms and signs differ among children of different age groups and differ between children and adults. The time of onset of HF help us to search for the cause of it. Clinical presentation of HF in young children is not specific so it requires highest degree of suspicion [1].

Because 87% of cases of new-onset HF only reach a diagnosis when the patient is in a state of severe decompensation [2], early diagnosis and effective treatment remain significant challenges which should be addressed [3].

Cardiac biomarkers are useful as diagnostic and prognostic tools, especially in patients with atypical signs and symptoms. High complication in HF led to the search for suitable cardiac biomarker that diagnose heart failure as early as possible, predict outcome, reflect response to treatment and help in staging of heart failure and determine risk [4].

Fatty-acid-binding protein 3, muscle and heart (FABP 3) is one of nine known cytosolic FABPs ranging in size from 14 to 15 kDa. It is most ubiquitously expressed in heart, skeletal muscle, and other tissues [5]**.**

Heart type fatty acid binding protein is a soluble protein which is present in cardiocytes. It participates in the absorption and transport of fatty acids, and released to the blood from membranes within 0-3 h after HF [5].

The present study was conducted to estimate serum level of H-FABP before and after treatment of congestive heart failure, and correlate its level with severity of the disease.

PATIENT AND METHOD

The study was cohort control study. It included 30 infants and children; their ages ranged from two months to four years with heart failure diagnosed clinically and were admitted to Cardiology Unit of Pediatric Department, at Zagazig University Hospitals during the period from November 2017 to April 2018. They were divided into four groups, first group aged (2-12

month), second group (13-24 m), third group (25-36 m) and fourth group (37-48 m).

All patients were observed during follow-up period of 3 months.

Ethical Clearance:

Written Informed consent was taken from the patient's parents to participate in the study. **Approval for performing the study was obtained from Pediatrics Departments, Zagazig University Hospitals after taking Institutional Review Board (IRB) approval.** The work was carried out in accordance with the code of ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion Criteria: Patient from 2 months to 4 years diagnosed as having congestive heart failure.

Exclusion criteria: Infants undergoing previous surgical correction for congenital heart defect. Chronic renal disease. Severe malnutrition. Under or above age (Age below 2 month or above 4 years).

Methods:

All children were subjected to complete history taking, and thorough clinical examination with particular emphasis on symptoms and signs of HF. Also cardiac examination was done with recording of auscultation findings, crepitations, wheezes, decrease air entry and bronchitis.

Radiological findings: Chest X-ray posteroanterior view to detect cardiomegaly and pneumonia. Echocardiographic assessment of the heart was done using conventional Doppler echocardiography.

Laboratory investigations: Routine laboratory investigation as complete blood count for infants and children of the study. C-reactive protein (CRP). Serum electrolyte (Na, K, Ca, Mg). Serum heart type fatty acid binding protein (H-FABP) level (estimated on patient admission and 1 week after treatment).

Collection of sample: 2 ml of blood was taken from every participant under complete aseptic condition and was collected in sterile tubes, and left for10-20 minutes for spontaneous clotting at room temperature then centrifuged at 2000-3000 rpm for 20 minutes then frozen at -20ºc for determination of serum heart type fatty acid binding protein before and after treatment of congestive heart failure.

Principle of method: The human H-FABP kits is an in vitro double antibody sandwich enzyme linked immunoassay (Elisa) for the quantitative measurement of level of H-FABP. Normal value is 45 -1200 pg/ml.

Statistical Analysis

Data were analyzed using IBM SPSS 20.0 for windows (SPSS Inc., Chicago, IL, USA) and NCSS 11 for windows (NCSS LCC., Kaysville, UT, USA). Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage. Chi square test (X^2) was used to analyze categorical variables. Quantitative data were tested for normality using Kolmogorov Smirnov test, assuming normality at $P>0.05$, using F test (for multiple studied groups of patient) if normally distributed, or Kruskal Wallis test if not normally distributed.

RESULTS

This study showed that the studied groups were matched as regard sex, and the difference was not significant. While there was a significant change regarding age (Table 1)

Table (1): Demographic data of the studied groups

Variables			Group I N=13		Group II N=8		Group III N=6		Group IV N= 3		F test	P-value
Age/months:												
Mean ±SD			4.37± 1.25		14.7 ± 1.73		26.1 ± 1.26		41.7 ± 5.69		335.2	<0.001
	N	**%**	N	%	N	%	N	%	N	%	**X²**	**P**
Sex:												
Male	**13**	**43.3**	3	23.1	5	62.5	4	66.7	1	33.3	4.82	0.185
Female	**17**	**56.7**	10	76.9	3	37.5	2	33.3	2	66.7		

The most common underlying causes of heart failure were ventricular septal defect (VSD) followed by DCM and VSD with ASD (Table 2).

Table (2): Underlying causes of heart failure among all studied cases by echocardiography.

	Cases (N=30)	
	No	%
VSD	8	26.7
DCM	7	23.3
VSD with ASD	6	20
PDA	3	10
HCM	2	6.7
ASD,PDA	2	6.7
VSD,PDA	1	3.3
Tricuspid atresia, VSD	1	3.3

There was no significant difference in EF and FS on admission between the survived and died cases (Table 3).

Table (3): Relation between echocardiographic parameters and outcome of the studied groups.

	Survived cases (N=24)	Died cases (N=4)	MW*	P-value
Ejection fraction EF (%)				
Mean ± SD	63.5 ± 13.95	58.67 ± 21.55	381	0.658
Fractional shortening FS (%)				
Mean ± SD	34.96 ± 8.49	33.5 ± 9.46	382	0.621

There was a significant difference in H-FABP level before and after treatment among all studied patients (Table 4).

Table (4): Levels of heart type fatty acid binding protein (H-FABP) before and after treatment of heart failure in all cases

	Before treatment (N=30)	After treatment (N=26)	MW*	P-value
	Mean ± SD	Mean ± SD		
H-FABP levels (ng/ml)	2.156 ± 1.156	0.882 ± 0.716	1151	<0.001

There was a significant difference in serum H-FABP level on patients' admission regarding four different presenting classes of Ross classification, as the level increased gradually from class I to reach the maximum level among patients of group IV (Table 5).

Table (5): Serum levels of H-FABP in relation to Ross classification of HF on admission.

Ross classification	H-FABP level (ng/ml)	F test	P-value
	Mean ± SD		
Class I (N=0)	-----		
Class II (N=14)	1.589 ± 0.282	8.49	<0.001
Class III (N=10)	2.086 ± 0.952		
Class IV (N=6)	3.68 ± 1.723		

There was non-significant increase in the serum level of H-FABP among died than survived patients (Table 6).

Table (6): Prognostic value of H-FABP according to the outcome of patients with HF.

	Survived patients (N=26)	Died patients (N=4)	MW*	P-value
	Mean ± SD	Mean ± SD		
H-FABP levels (ng/ml)	1.996 ± 0.14	2.795 ± 1.14	355	0.407

This study showed that at cut-off value 2.08 ng/mL, the diagnostic performance of H-FABP as a diagnostic predictor for congestive heart failure had a sensitivity of 84.6% and specificity of 87.41% with 0.995 area under ROC curve (Figure 1).
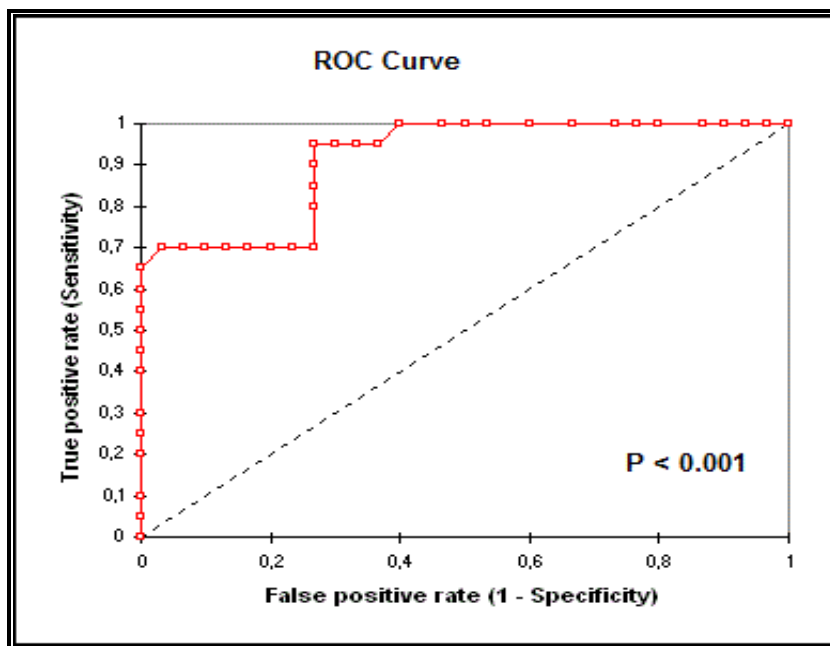
Figure (1): Receiver operating curve (ROC) analysis for the H-FABP levels as a diagnostic predictor in patients before treatment.

DISCUSSION

Heart failure is a major threat to global public health, affecting about 26 million people worldwide. The global epidemiology of HF in pediatric populations remained largely unknown[2].

In our study the most common age group was (2-12 m) represented 43.3% and that agreed with **Hussain et al.** [6] as their cases represented (63.1%) of this age and agreed also with **Rossano et al.** [7] who reported that most patients were infants and represented 63%.

In our study the number of male patients in all age groups were 13 with percentage 43.3%, number of female patients were 17 with percentage 56.7%. This agreed with **Webster et al.** [8] who reported that female represented 52.2% were more common than male represented 48.8% in HF patients and that was against **Hussain et al.** [6] who reported that HF was more common in males, with a male to female ratio of 1.45:1.

The most frequent heart defect among the patients in our study were VSD, DCM then VSD with ASD and this agreed with **Zoair et al.** [9] who reported that CHD was the most common cause of HF and represented 73.33%, then cardiomyopathy 16.67%, and also agreed with **EL Amrousy et al.** [10] who reported that 75% had congenital heart disease and 25% of patient had DCM.

In our study there was significance difference in H-FABP before and after treatment of heart failure in children and this agreed with **Zoair et al.** [9] who reported that serum level of H-FABP

before treatment was 5.278 ±3.253 ng/ml and after treatment was 2.089±0.160 ng/ml.

In our study there was high significant difference in serum level of H-FABP in patients on admission according to Ross classification. This did not agree with **Zhou et al.** [11] who reported that there was no significant difference between H-FABP at different classes of heart failure, they reported that H-FABP is up regulated during the early stage of heart failure and can be used in early stage of heart failure.

In **Zoair et al.** [9] the H-FABP level in patient with grade IV was significantly higher (9.744±1.67 ng/ml) than those in grade III (3.743±1.208 ng/ml) and grade II (2.418±0.07 ng/ml).

In our study there was no significant increase in serum level of H-FABP among died patient than survival patients and this was against **Zoair et al.** [9] who reported that significant increase in H-FABP was associated with adverse outcome; either death or hospitalization.

In our study the mean value of serum H-FABP among patient groups before treatment ranged from 1.2 to 6 ng/ml with mean 0.882 and cuff off point <2.08, specificity 87.41% and sensitivity 84.6%.

Glatz and Mohren [12] reported that sensitivity of H-FABP was explained by high concentration of H-FABP in myocardium compared to other tissue, the stability and solubility of H-FABP and it is molecular weight 15 kda compared to 18, 80 and 37 kda for Myo, CK-MB and cTnT.

Liu *et al.* [13] reported that H-FABP is an early sensitive and specific biomarker for evaluation of ischemic reperfusion injury postoperative in children with CHF.

Hasegawa *et al.* [14] during studying of myocardial damage in pediatric heart surgery, they found that H-FABP reached peak level scientifically earlier than CK-MB and TnT, after reach peak level, it decreased quickly while CK and TnT did not, they remained at high level. This suggest that H-FABP is expected to be a sensitive and specific marker to be used in early detection of myocardial damage although it currently takes approximately 1 hour to measure serum H-FABP level with the sandwich enzyme immunoassay kit. Hayabuchi *et al.* [15] reported that elevated circulating H-FABP level is considered a highly sensitive marker for ongoing myocardial damage in patient with CHF.

CONCLUSION AND RECOMMENDATIONS

H-FABP may be used as diagnostic and prognostic predictor of adverse outcome in children with heart failure.

Limitations of our study:

Further studies on large scale are required to confirm the role of H-FABP as a diagnostic marker of heart failure in children. Long-term follow-up is needed to correlate the serum level of H-FABP with the prognosis of heart failure as regards death or readmission.

Conflict of interest:

The authors declare no conflict of interest.

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