Original Article

Evaluation of Serum CK-MB Levels in Congestive Heart Failure

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Abstract

Context: The objective of this cross sectional study was to find out the relationship between the level of serum CK-MB and congestive cardiac failure. **Methods:** In total 72 subjects of different socioeconomic class were included randomly and was divided in to four groups, 36 subjects were apparently healthy and 36 subjects were divided in to three groups according to NYHA staging of heart failure. **Results:** The mean serum CK-MB was 0.897 ± 0.721 ng/ml among healthy subjects and 2.492 ± 2.535 ng/ml among the heart failure patients having significant difference ($p<0.001$) between two groups and the difference was more marked in NYHA class III group of heart failure patients. **Conclusions:** These findings show that there was a definite rise of serum CK-MB level as heart failure advances. The evaluation suggests the use of CK-MB as a marker for staging of heart failure.

Indexing wards: Serum CK-MB level, Congestive heart failure

Introduction:

Congestive heart failure (CHF) is defined as impairment of systolic and/or diastolic function of the heart, leading to failure of the heart to meet the demands of the peripheral tissues, or leading to maintenance of cardiac function under higher filling pressures[1]. In the mildest form of heart failure cardiac output is adequate at rest and becomes inadequate only when metabolic demand increases. The syndrome of heart failure in precise mechanistic and/or clinical terms is that the clinical syndrome of heart failure almost certainly represents the summation of multiple anatomic, functional and biological alterations that interact together in an exceedingly complex manner and in different genetic and environmental backgrounds over a sustained but variable period of time[2]. Heart failure is associated complex neurohormonal changes including activation of the renin angiotensin aldosteron axis and sympathetic nervous system[3]. At first these changes may help to optimize cardiac function by altering the after load or preload and by increasing myocardial contractility. The transition of asymptomatic cardiac dysfunction to symptomatic heart failure is associated with extensive remodeling of the muscular, collagenous, and vascular compartments of the myocardium[4].

Two mechanisms of cell death have been described in heart failure necrosis and apoptosis[5]. Apoptotic cells can be identified through histochemical visualization of nuclear DNA fragments or demonstration of a characteristic “ladder” of small DNA fragments[6].

The progression CHF results from a continuing loss of viable myocytes, dysfunction of viable myocyte, or both[6], with progressive chamber dilation and LV dysfunction[7]. If CHF progresses from a continuing loss of myocytes, then serum markers of myocardial necrosis might be

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identified in patients with progressive CHF. Reports from more than twenty years ago did not show an association between serum levels of creatine kinase (CK) or CK-MB and heart failure[8]. However, more sensitive assay techniques have been developed now. Furthermore with the development of more sensitive assays for detection of myocardial injury (cardiac troponins T and I & CK MB) has attracted recent interest about these markers.
CK-MB mass and myoglobin concentrations were in the normal reference range for all groups that is, healthy controls, hospitalized controls, and heart failure patients[4]. However congestive heart failure patients demonstrated an absolute increase in the CK-MB and myoglobin levels that paralleled the increase of cardiac troponin I[4]. Of the thirty five heart failure patients, eight had CK-MB level that exceeded the assay upper reference limit of 6ng/ml. importantly, when patients were stratified according to the CK-MB cut off, all markers of myocardial injury clearly tended to be increased in the group of CK-MB positive heart failure patients[4]. Serum concentrations of CK-MB and Tn-I may become elevated in severely symptomatic patients with CHF (particularly NYHA class III-IV), demonstrating a relationship between clinical severity of the disease and elevation of myocardial enzymes (CK-MB and Tn-I)[9]. The objective of this cross sectional study was to find out the relationship between the level of serum CK-MB and congestive cardiac failure.

Methods:
This cross sectional analytical study was carried out in the Department of Biochemistry Bangabandhu Sheikh Mujib Medical University (BSMMU) jointly with the Department of Cardiology of the same university between the period of July 2003 and June 2004. A total seventy two subjects were included in this study, among them thirty six from the inpatient division of cardiology department of BSMMU and thirty six healthy controls among the students and stuffs of the different departments of BSMMU, and were grouped as follows. Proper ethical permission was taken from the Ethical review board of BSMMU.

Group-I (n=12) Patients with congestive cardiac failure and belongs to the group of NYHA (New York Heart Association) class I patients of congestive cardiac failure. **Group-II** (n=12) Patients with congestive cardiac failure and belongs to the group of NYHA class II patients of congestive cardiac failure. **Group-III** (n=12) Patients with congestive cardiac failure and belongs to the group of NYHA class III patients of congestive cardiac failure and **Group-IV** (n=36) normal healthy adults with no history of any disease living in the same geographical area. Diagnosis was based on clinical history, examinations and echocardiography. Blood samples were collected from the subjects.

Serum CK-MB measurement was based on Microparticle enzyme Immunoassay (MEIA) principle[10]. Serum creatinine was estimated by alkaline picrate method[11]. Serum ALT was estimated by single vial Method[12]. Echocardiography was done by ALOKA prosound SD 5000 echocardiography machine. Twelve lead ECG was performed to exclude acute myocardial infarction and unstable angina.

Analysis of variance (ANOVA) test, independent samples 't' test (unpaired 't' test) and Pearson correlation test were done using computer based SPSS 12.0 for windows software. Mean values of the different parameters were compared for difference between groups and 95% confidence limit was taken as level of significance.

Results:

Serum CK- MB
The mean concentration of serum CK-MB in control subjects and CHF patients were 0.897 ± 0.721 ng/ml and 2.492 ± 2.535 ng/ml (Table 1) respectively having significant difference between two groups (p<0.001). The mean concentration of serum CK-MB in group I was 1.742 ± 2.339 ng/ml, in group II was 1.233 ± 1.182 ng/ml, in group III was 4.5 ± 2.614 ng/ml (Table 2) respectively having significant difference among the groups (p<0.001). Independent "t" test was done between the groups shows significant difference (p <0.001) between group III and any other groups.

Table 1: Serum CK-MB level of the congestive heart failure patients and the control subjects

Parameter	Control (n=36)		CHF (n=36)		p Value
	Mean	Range	Mean	Range	
CK-MB (ng/ml)	.897 ± .721	0.0-2.5	2.492 ± 2.535	0.5-9.6	< 0.001

Table 2: Comparison of CK-MB conc. between different groups

Comparison	Mean ± SD	p Value
Gr I vs Gr II	1.742 ± 2.339 vs 1.233 ± 1.182	> 0.05
Gr I vs Gr III	1.742 ± 2.339 vs 4.5 ± 2.614	< 0.001
Gr I vs Gr IV	1.742 ± 2.339 vs 0.897 ± .721	> 0.05
Gr II vs Gr III	1.233 ± 1.182 vs4.5 ± 2.614	< 0.001
Gr II vs Gr IV	1.233 ± 1.182 vs 897 ± .721	> 0.05
Gr III vs Gr IV	4.5 ± 2.614 vs 897 ± .721	< 0.001

Ejection fraction

The mean ejection fraction of congestive cardiac failure patients and control subjects were 34.22 ± 11.090 % and 67.89 ± 3.276 % (Table 3) respectively having significant difference (p<0.001) between the two groups. Among the congestive cardiac failure patients mean ejection fraction of group I were 46.92 ± 4.379 %, group II were 32.75 ± 7.073 %, group III were 23.00 ± 2.558 % and healthy subjects were 67.89 ± 3.278 (Table 4) respectively having significant difference (p<0.001) among the groups (Table 5).

Table 3: Ejection fraction of the patients of CHF and the control subjects

Parameter	CHF (n=36)		Control (n=36)		p Value
	Mean	Range	Mean	Range	
Ejection fraction (%)	34.22± 11.09	62-76	67.89 ± 3.276	20-52	< 0.001

Table 4: Ejection fraction of the different groups of the study subjects

Group	Ejection fraction (%)	
	Mean ± SD	Range
Group I (n=12)	46.92 ± 4.379	35 - 52
Group II (n=12)	32.75 ± 7.073	20 - 40
Group III (n=12)	23 ±2.558	20 - 28
Group IV (n=36)	67.89 ± 3.278	62 - 76

Table 5: Comparison of ejection fraction among different groups

Parameter	G - I	G - II	G - III	G - IV	F value	P value
Ejection fraction (%)	46.92 ± 4.379	32.75 ± 7.073	23 ± 2.558	67.89 ± 3.278	447.682	< 0.001

Table 6: Blood pressure, serum creatinine and serum ALT concentration of control subjects and CHF patients

Parameters	Study subjects		P value
	Control (36)	CHF (36)	
Serum creatinine (µ mol/L)	1.0306±0.1635	0.9667 ± 0.2084	> 0.05
Serum ALT (IU/L)	22.3167±9.4236	25.4361±11.7639	> 0.05

Figure 1 shows significant negative correlation between the levels of CK-MB with ejection fraction which is the indication of increase in release of CK-MB from damaged myocardium with the progression of heart failure.

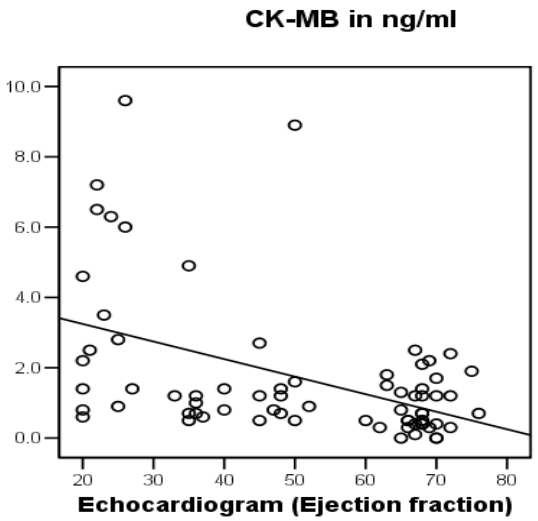


Figure 1: Correlation (p<0.05) between serum CK-MB and Ejection Fraction

Discussion:

Congestive cardiac failure is the only major cardiovascular disorder that is increasing in incidence prevalence and cause of death[13]. The incidence of heart failure has markedly increased over past two decades[14]. Elevated CK-MB level in the serum is an established diagnostic test for the patients of myocardial infarction. According to some the mean concentration of CK-MB in heart failure patients (4.8 ± 0.7ng/ml) significantly higher than in normal healthy donor and hospitalized control subjects (3.0 ± 0.4ng/ml)[4]. They also showed that among the 35 patients of congestive cardiac they studied, 8 have mean serum CK-MB level of 10.2 mg/ml. In this study it is found that the mean CK-MB concentration in heart failure patients was 2.492 ± 2.535 ng/ml tables and in control subjects was

0.897 ± 0.727ng/ml, significantly higher mean serum CK-MB concentration in the patients of congestive heart failure. Findings of this study and findings of the workers mentioned above are consistent but the mean concentration of CK-MB in any of the studies did not cross the upper reference range. In the literature provided with the AxSYM CK-MB reagent pack provided the information that the concentration of CK-MB in healthy subjects should be low or undetectable and the cut off value for myocardial infarction is 10ng/ml. In our study the mean CK-MB level was 0.897 ± 0.727 (Table I) in control subjects which was significantly lower than the mean CK-MB level of the control subjects of workers mentioned above. The difference of mean CK-MB level of the control subjects of them and us may be due to difference in the height, weight, food habit and physical activity of those subjects and Bangladeshi people. So is possible that mean serum CK-MB level of Bangladeshi people is much lower than American population and needs large number of study population for the fixation of normal serum CK-MB level of Bangladeshi people. In our study we also found significant difference of mean CK-MB level with NYHA class III patients of congestive heart failure with other three groups (control subjects, NYHA class I patients and NYHA class II patients $p<0.001$) Table. This finding suggests the associated release of CK-MB with cardiac troponin I from damaged myocardium. We also found strong positive correlation of CK-MB with cardiac troponin I ($p<0.01$). The positive correlation between CK-MB and cardiac troponin I was also showed by some warkers[4]. Which means that cardiac troponin I and CK-MB may simultaneously released from damaged myocardium. So it can be assumed that the rate of release CK-MB from myocardium increases as heart failure progresses. The level of CK-MB with ejection fraction showed significant negative correlation (Fig I) which is the indication of increase in release of CK-MB from damaged myocardium with the progression of heart failure.

Conclusion:

The result of the study showed that serum CK-MB level was significantly higher in patients of congestive cardiac failure especially in NYHA class III patients but, did not exceeded upper reference limit. So it can be assumed that though serum CK-MB level is not exceeding the upper reference limit but the increase positively correlates as heart failure progresses to advance stage. So it may be recommended for estimation of serum CK-MB for the diagnosis and staging of heart failure along with other markers such as serum cardiac troponin I concentration and ejection fraction. But further study should be carried out with the inclusion of large sample and designed as long term prospective is recommended.

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