

## Original Article

# Correlation Of Serum Cardiac Troponin I With Significant Left Ventricular Systolic Dysfunction In Patients With Chronic Heart Failure

Ali MA<sup>1</sup>, Alo D<sup>2</sup>, Molla AL<sup>3</sup>

### Abstract

**Objective:** The aim of the study was to observe the relationship between elevated levels of serum cardiac Troponin I (cTnI) and in-hospital morbidity & mortality in chronic heart failure with LV systolic dysfunction.

**Background:** Chronic heart failure is a public health problem in the United Kingdom and also in our country. Serum Cardiac troponin I (cTnI) has been validated as a sensitive and specific marker of cardiac myocyte damage and is elevated in some patients with chronic heart failure with LV systolic dysfunction and predicts adverse outcome.

**Materials and Methods:** This study was prospective, cross sectional and observational study. The study was carried out among chronic heart failure with LV systolic dysfunction patients in the Department of Cardiology, National Institute of Cardiovascular Diseases, Sher-E-Bangla Nagar, Dhaka, during the period of April 2004 to December 2004. In this Study, total 740 patients of heart failure were evaluated Among 740 patients, initially 100 patients were selected as chronic heart failure on the basis of inclusion & exclusion criteria, history, physical examination, biochemical, X-ray, ECG & other relevant investigations. Finally, 60 patients were selected by echocardiography who had ejection fraction of  $\leq 40\%$ . Cardiac troponin I was measured in each and every studied patient. In-hospital outcome was observed in terms of morbidity & mortality. So hospitalised patients were followed up clinically and by investigation.

**Results:** The results of this study revealed that serum cTnI was significantly elevated ( $cTnI \geq 0.04$  ng/ml) in serum of 29 patients (48.33%) and low or insignificant ( $cTnI \leq 0.04$  ng/ml) in serum of 31 patients (51.67%). Patients with significantly elevated serum cardiac troponin I (cTnI) level (group-A) had significantly higher in-hospital morbidity & mortality than patients who had insignificant serum cardiac troponin I (cTnI) level (group-B). In-hospital mortality was 15% (number of death 09) out of total 60 patients. All expired patients were in NYHA class-IV. On the other hand, there was no mortality in group-B. In-hospital morbidity was 2.75 times higher among the patients who had significantly elevated serum cTnI level. A significant correlation was found between the patients who had significantly elevated serum cTnI level ( $cTnI$  level  $> 0.04$  ng/ml) and the patients who had insignificant serum cTnI level ( $cTnI$  level  $< 0.04$  ng/ml) in consideration to in-hospital morbidity & mortality.

**Conclusion:** Conclusion of this study is that serum cardiac troponin I (cTnI) level is significant predictor of increased morbidity & mortality in chronic heart failure. with LV systolic dysfunction. Serum Cardiac troponin I (cTnI) level may be a useful tool for identification, selection of therapeutic strategies and assessment of prognosis in patients with chronic heart failure who are at increased risk of ventricular systolic dysfunction and death. So it is a message for the physician as well as patients.

**Key wards:** Cardiac troponin I, Heart failure, Mortality, Morbidity.

1. Dr. Md. Ashraf Ali, Assistant Professor, Department of Cardiology, Abdul Malek Ukil Medical College, Noakhali.

2. Dr. Dilara Alo, Associate Professor, Department of Neonatology, Abdul Malek Ukil Medical College, Noakhali.

3. Dr. Abdul Latif Molla, Assistant Professor, Department of Cardiology, Chittagong Medical College, Chittagong.

## Introduction

Heart failure is common in clinical practice and its incidence is increasing day by day. Heart failure is not a disease per se but a consequence of various cardiovascular disorders. It may be defined as "The pathophysiological state in which an abnormality of cardiac function is responsible with the requirements of the metabolizing tissues and/or can do so only from abnormally elevated ventricular diastolic volume"<sup>1</sup>.

In practice, heart failure is diagnosed whenever a patient with significant heart disease develops sign and symptoms of low cardiac output, pulmonary congestion or systemic venous congestion.

Chronic heart failure is a public health problem in the UK and also in our country. Heart failure is a significant cause of morbidity and mortality. Approximately 50% of patients with severe heart failure due to Left ventricular dysfunction will die within 2 years<sup>2</sup>.

Cardiac Troponin I (cTnI) is an important investigation tool for identification of patients, selection of therapy and assessment of prognosis. Cardiac Troponin I (cTnI) inhibits the actin-myosin interaction<sup>3</sup>. Troponin I is not expressed in skeletal muscle. So Troponin I is more sensitive for detection of myocardial necrosis<sup>4</sup>. Low-level elevation of serum cTnI has been documented in a number of cardiovascular diseases, including heart failure. The pathology behind serum cTnI elevation in heart failure probably is distinct from that seen during myocardial infarction which is due to necrotic myocardium.

The mechanism of release of serum cTnI believed to be responsible for ongoing irreversible myocyte injury and/or apoptotic cell death in heart failure include activation of adrenergic, renin-angiotensin-aldosterone, or endothelin signaling pathways, calcium-handing abnormalities, inflammatory cytokines, nitric oxide, oxidative stress and mechanical stress<sup>5</sup>. Another possible mechanism of low level elevation cTnI is leakage of the cytosolic pool of cTnI during reversible injury as a result of loss of cell membrane integrity<sup>6</sup>.

Patients with advanced heart failure, detection of serum cTnI level is associated with impaired haemodynamics, elevated BNP levels and progressive ventricular dysfunction. Cardiac troponin I level is significant predictor of increased mortality and morbidity rates in patients with ischaemic and non-ischaemic heart failure. So, it is important to see the in-hospital morbidity and mortality in patients with chronic heart failure in relation to cardiac troponin I, as such type of study had

not been carried out previously in our country. Moreover, this study will create awareness of the physician. So that, they can take aggressive management strategies for these patients. Ultimately, knowledge from the study will give benefit to the individual patient as well as whole nation will be benefited.

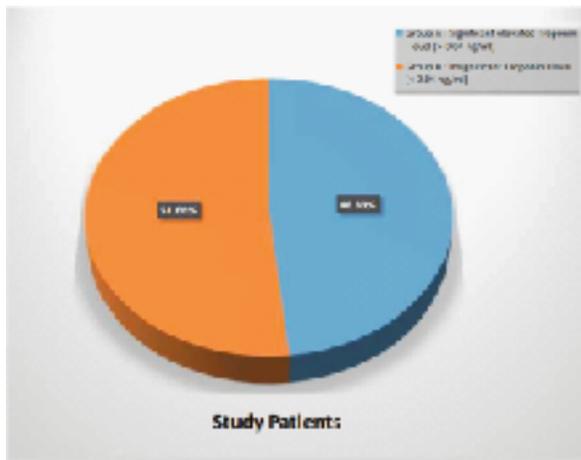
## Materials and Methods

This study was prospective, cross sectional and observational type. The study was conducted in the Department of Cardiology, National Institute of Cardiovascular Diseases, Sher-E-Bangla Nagar, Dhaka. The period was from April 2004 to December 2004. Among 740 patients, initially 100 patients were selected as chronic heart failure with the help of inclusion & exclusion criteria by taking meticulous history, physical examination and relevant investigations. Echocardiography was done for 100 patients. Among them, 60 patients were finally selected who had ejection fraction  $\leq 40\%$ . Ejection fraction was done by modified Simpsons method with the help of following formula:  $EF = \frac{(LVIDd)^3 - (LVIDs)^3}{(LVIDd)^3} \times 100$ . Epidemiological aspect (age, sex, occupation, housing status, socioeconomic status, pattern of heart failure and clinical characteristics of heart failure) were studied. serum Cardiac troponin I (cTnI) was done for the sixty (60) selected patients. On the basis of serum cardiac Troponin I level, patients were divided into two groups, group-A (cTnI level  $\geq 0.04\text{ng/ml}$ ) and group-B (cTnI level)  $< 0.04\text{ng/ml}$ ). The patients suffering from Chronic heart failure with ejection fraction (EF)  $\leq 40\%$  due to Ischaemic cardiomyopathy, Idiopathic dilated cardiomyopathy, Valvular heart diseases involving the left ventricle and Hypertensive heart failure were included in this study. On the other hand, the patients suffering from Acute coronary syndromes, Myocarditis, Cor pulmonale, Restrictive (Infiltrative) cardiomyopathy, Congenital heart disease, Heart failure associated with high metabolic demand and Pericardial diseases were excluded. Severe systemic disorders like chronic renal failure, hepatic failure and patients suffering from malignant disorder were also excluded from this study. Protocol was fully explained to the study group of patients and informed consent was taken. Clearance from ethical committee of the institution was obtained. All the information's were recorded in a standard case recording form. Data was processed and expressed in frequency, percentage, mean  $\pm$  standard deviation as applicable. Comparison between two groups were done by unpaired student's test and chi-square test.

Statistical analysis of result was performed by using SPSS (Statistical package for social science). P' value of less than 0.05 was considered as significant.

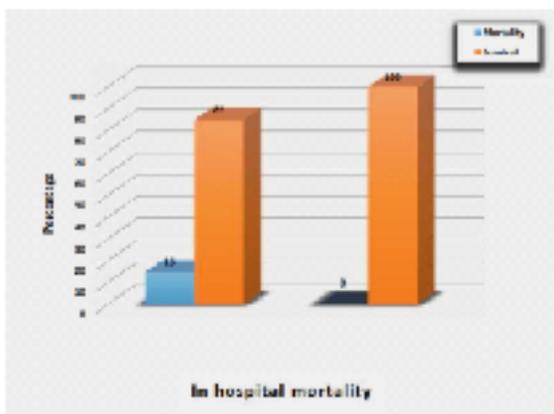
**Observation & Results**

Total 740 patients were screened during the period of April 2004 to December 2004 in cardiology department, NICVD. Among them 60 patients are finally selected for study. Studied patients were divided into two groups. Group-A (48.33%) : Significantly elevated cTnI level (cTnI ≥ 0.04ng/ml). Group-B (51.67%) shown in figure I.



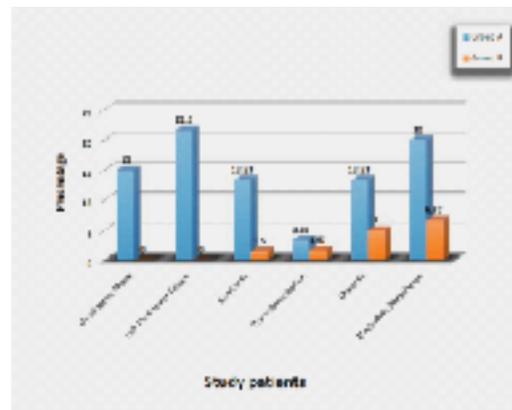
**Figure - I**

Insignificant cTnI level (cTnI ≤ 0.04ng/ml). In-hospital outcome was observed in terms of morbidity & mortality during hospital stay. The result of this study revealed that in-hospital morbidity was significantly higher in the patients of significantly elevated serum cTnI level than insignificant serum cTnI level. Regarding mortality, all expired patients (15%) had significantly elevated serum cTnI level. There was no mortality in insignificant serum cTnI level (Figure-II).



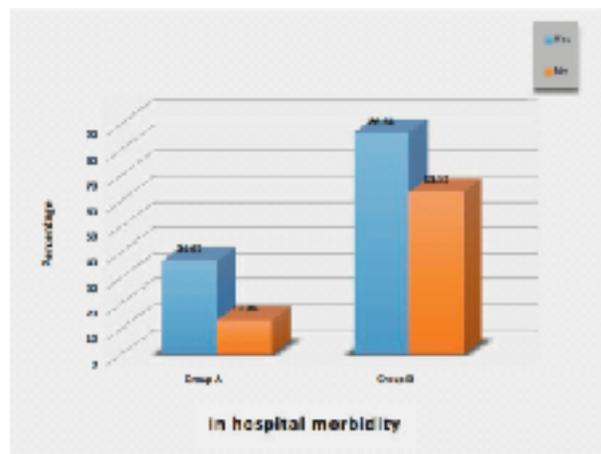
**Figure-II**

A significant correlation has been observed in chronic heart failure with significantly elevated serum cardiac Troponin I (cTnI) level and in-hospital morbidity & mortality. It has been shown in Figure-I that 48.33% of patients had significantly increased cTnI level (group-A) and 51.67% of patients had insignificant cTnI level (group-B). From Figure-III it is apparent that major morbidity like cardiogenic shock (15%) and acute left ventricular failure (21.67%) had significantly elevated cTnI level. But there was no major morbidity in Group-B. Morbidity like arrhythmias (13.33%), thromboembolism (3.33%), uraemia (13.33%) and electrolyte disturbances (20%) also had significantly elevated serum cTnI level. Morbidity like arrhythmia (1.5%), thromboembolism (1.67%), uraemia (5%) and electrolytes disturbances (6.67%) were much lower in Group-B than Group-A shown in Figure-III.



**Figure-III (In-hospital complications)**

This analysis revealed that significantly elevated cTnI level in advanced chronic heart failure had increased incidence of morbidity & mortality. Figure-IV.



**Figure-IV**

Figure-IV shows that in-hospital morbidity was significantly high among Group-A (36.67%) compared to Group-B (13.33%). The relative risk indicated that the in-hospital morbidity was 2.75 times higher in Group-A (Figure-VI).

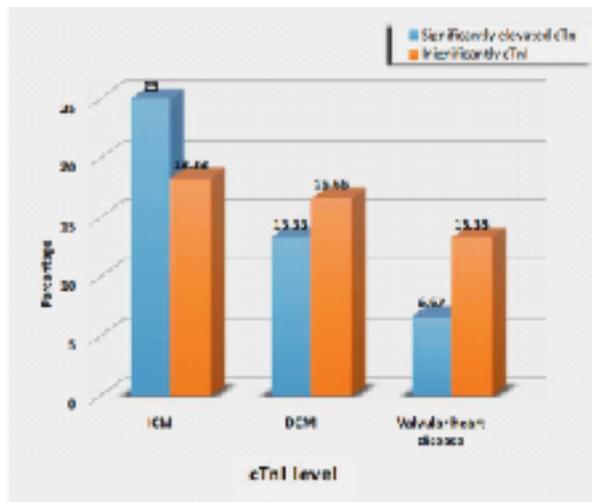


Figure-V

Study patients were clinically divided into four groups according to NYHA classification. Echocardiography and cTnI level was done for every patients. NYHA clinical class I, II, III & IV patients were 6.67%, 11.6%, 40% & 41.67% respectively and their mean serum cTnI level was 0.022 ng/ml, 0.033 ng/ml, 0.043 ng/ml and 0.367 ng/ml respectively. Ejection fraction was higher in NYHA-I clinical class (36.5%) and low in NYHA-IV clinical class (25.2%). Complications were more in NYHA clinical class IV groups than other class. All mortality were in NYHA class IV (15%) and their mean ejection fraction (25.2%) was lower than mean ejection fraction (29.13%) of other class. Their (NYHA-IV) mean serum cTnI level (0.367 ng/ml) was greater than mean serum cTnI level (0.1967 ng/ml) of other NYHA class. Among NYHA-IV patients, 3.33% patients had insignificant cTnI level and 38.33% patients had significantly elevated serum cTnI level, which was statically significant ( $P < 0.001$ ). Majority of the NYHA-III patients (30%) had insignificant serum cTnI level. Only 10% of NYHA-III patients had significantly elevated serum cTnI level. This difference was also statistically significant ( $P < 0.001$ ). All NYHA-I and NYHA-II patients had insignificant serum cTnI level. Analysis revealed that NYHA-IV group of patients was worse than other functional class. Mean left ventricular ejection fraction was  $29.13 \pm 9\%$ . Mean ejection fraction

in insignificant serum cTnI group was  $33 \pm 5\%$  and significant group  $25 \pm 5\%$  which was also statistically significant ( $P < 0.001$ ). Their mean cTnI level (0.367ng/ml) was greater than mean cTnI level (0.1907ng/ml) of the other NYHA group. Figure-V shows that highest percentage of patients (43.33%) had ischaemic cardiomyopathy. Among them, 25% had significantly elevated serum cTnI level and 18.33% had insignificant cTnI level which was statistically significant ( $P < 0.001$ ). Among idiopathic dilated cardiomyopathy (30%) & valvular heart disease (20%), majority had insignificant cTnI level (16.67%, 13.33% respectively) in comparison to significantly elevated cTnI level group (13.33% and 6.67% respectively) which was also statistically significant. So, it was found that Idiopathic dilated cardiomyopathy and valvular heart diseases patients were prognostically better than ischaemic cardiomyopathy.

## Discussion

Serum Cardiac Troponin I (cTnI) with significant left ventricular systolic dysfunction in patients with chronic heart failure is commonly seen in CCU, PCCU and general medical wards. It is associated with increased short and long term morbidity & mortality. Many studies have been done in home and abroad. All the studies showed the increased morbidity & mortality in chronic heart failure with LV systolic dysfunction with elevated cardiac Troponin I (cTnI) level. In the context of our country this study was done to observe the relationship between elevated levels of cTnI and in-hospital morbidity & mortality in chronic heart failure with LV systolic dysfunction.

In this study, 48.33% patients had increased serum cTnI level and 51.67% patients had insignificant serum cTnI level. In the study of Horwich<sup>7</sup> et. al. 2003 49.1% patients had increased serum cTnI level and 50.84% patients had insignificant serum cTnI level which is similar to this study.

In this study, most common symptoms of heart failure were fatigue and weakness (93.33%), exercise intolerance (90%), dyspnoea (81.67%), palpitation (66.67%), peripheral oedema (45%), abdominal fullness (40%), orthopnoea (36.67%) and others are less common. Most common signs were bilateral basal crepitation (46.67%), raised jugular venous pressure, dependent oedema (45%) and hepatomegaly (43.33%). Musfiqur Rahman<sup>8</sup>, 2001 reported in his study that most common symptoms of heart failure were dyspnoea (84%), fatigue (80%),

cough (48%), chest pain (32%), right upper abdominal pain (26%) and palpitation (22%). In his study, majority of the symptoms were near similar to my study. Signs of chronic heart failure in the study of Musfiqur Rahman<sup>8</sup> 2001 were, oedema (84%), raised Jugular venous pressure (88%), congestive hepatomegaly (88%) and basal crepitation (80%) which was much greater than my study. This dissimilarity was due to inclusion of all forms of heart failure in his study. In this study isolated right heart failure, corpulmonale and other forms of heart failure where EF more than 40% were not included.

In this study, ischaemic cardiomyopathy was the most common cause of heart failure (43.33%), followed by idiopathic dilated cardiomyopathy 30%, valvular heart diseases, which involve the left ventricle 20% and hypertensive heart failure was 6.66%. In one western study hypertensive heart failure was (41%), ischaemic cardiomyopathy 33%, valvular heart diseases 17%, idiopathic dilated cardiomyopathy 5% and mixed 9%, Horwich<sup>7</sup> et. al. 2003, found that ischaemic cardiomyopathy patients were 50% and idiopathic dilated cardiomyopathy patients were 33%.

In my study, some forms of heart failure were similar and some were dissimilar to those studies. Hypertensive heart failure was only 6.67% in comparison to western study (41%). Hypertension cause both systolic and diastolic dysfunction but in my study, hypertensive patients of only systolic dysfunction and whose ejection fraction was  $\leq 40\%$  were included. The western study included all form of congestive heart failure, irrespective of ejection fraction. This is why, some form of heart failure was quiet dissimilar to my study.

In my study, morbidity in the form of acute left ventricular failure (21.67%), cardiogenic shock (15%), arrhythmias (15%), thromboembolism (5%), mild uraemia (18.33%) and mild to moderate electrolyte disturbances (26.67%) were noted. It was also observed that highest number of patients developed mild to moderate electrolyte disturbances and lowest number of patient developed thromboembolism. In western as well as home study, it was found higher morbidity in their study but they did not mention the frequency of individual morbidity as percentage. In my study, overall mortality was 15%, whereas Horwich<sup>7</sup> et. al. 2003 found 12.18% mortality in their study. Mortality is little bit more in my study possibly due to advanced and more complicated patients were admitted in the hospital. Lack of advanced health care facilities and cardiac

transplantation were also other causes. Moreover most of the patients (53.33%) had poor socioeconomic status. In this study group-A (48.33%) patients had increased or significant cardiac troponin-I level ( $\geq 0.04\text{ng/ml}$ ) and group-B (51.67%) had insignificant cardiac troponin-I level ( $< 0.04\text{ng/ml}$ ). Mortality and morbidity varied greatly between the two groups of patients).

In my study, all expired patients had increased serum cTnI level. Serum Cardiac troponin-I level in expired patients were 1.005ng/ml. Mean serum cardiac troponin-I level was 0.03ng/ml in survive patients (Group-B). This revealed that serum troponin-I level in expired patients were much greater then Group-B, which was statistically significant ( $p < 0.001$ ).

Horwich<sup>7</sup> et. al. 2003 found significantly detectable levels of serum cardiac troponin-I with death in advanced heart failure. They also reported that serum cardiac troponin-I level was significantly higher in patients who died compared with those who survived. The mean serum cardiac torponin-I level in mortality group was  $0.5 \pm 1.9\text{ng/ml}$  whereas in survival group, mean level was  $0.1 \pm 0.5\text{ng/ml}$  ( $p < 0.01$ ). Relationship of increased serum cardiac troponin-I level in advanced heart failure with higher mortality in the study of Horwich<sup>7</sup> et al. 2003 were similar to my study.

Study patients were clinically divided into four groups according to NYHA classification. NYHA-I group was 6.67%, NYHA-II was 11.67%, NYHA-III was 40% and NYHA-IV was 41.67% patients. Horwich<sup>7</sup> et. al. 2003, showed that 50.42% patients were NYHA-IV, which was near similar to this study. No available data was found in home or abroad to compare the other NYHA group of patients. Mean serum cTnI level of the study patients was 0.1907ng/ml.

Mean serum cTnI level of group-A was 0.361ng/ml and mean serum cTnI level of group-B was 0.03ng/ml. No such available data are mentioned in any home and abroad study.

Mean ejection fraction of my study was 29.13%, average ejection fraction of group-A was 25% and group-B was 33%. Horwich<sup>7</sup> et. al. 2003 showed that, mean EF of their study in group-A ( $25 \pm 10\%$ ) and group-B ( $25 \pm 9\%$ ) which was similar to group-A but greater than group-B patients of my study. In my study, among the NYHA-IV group, 38.33% of patients had increased serum cTnI level and only 3.33% of patients had insignificant cTnI level. Among NYHA-III group 10% patients had increased cTnI level and 30% patients

had insignificant serum cTnI level. All the patients of NYHA-I and NYHA-II were under insignificant serum cTnI level group. All the mortality was NYHA-IV group of patients. In hospital morbidity and mortality were much more greater in NYHA- clinical class III and IV groups of patients who had increased serum cTnI level and lower ejection fraction than NYHA-I and NYHA-II who had insignificant serum cTnI level and relatively greater ejection fraction.

## Conclusion

Conclusion of this study is that serum cardiac troponin I (cTnI) level is significant predictor of increased morbidity & mortality in chronic heart failure with LV systolic dysfunction. Serum Cardiac troponin I (cTnI) level may be a useful tool for identification of patients, selection of therapeutic strategies and assessment of prognosis in patients with chronic heart failure who are at increased risk of ventricular systolic dysfunction and death. So it is a message for the physician as well as patients.

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