Original Article

Assessment of Positive Troponin I in Non-Acute Coronary Syndrome Critically ill Patients

Sarfraz Ali Mangi, Faisal Ahmed, Naveen Roy, Rubina Khan, Imran Khan Sandeelo and Sumayya Zaman

ABSTRACT

Objective: To determine the frequency of positive Troponin I in non-acute coronary syndrome critically ill patients, at a tertiary care hospital, Karachi.

Study Design: Descriptive / cross sectional study

Place and Duration of Study: This study was conducted at the Cardiology Unit at Liaquat National Hospital Karachi from June 2019 to Dec 2019.

Materials and Methods: Total 148 patients of either gender with age between 35 to 70 years, diagnosed as critical illness were included. Non-ACS was diagnosed through ECG and echocardiography findings. Blood sample was taken for a troponin I test. Outcome variable was diagnosis of elevated Troponin I level. SPSS version 21 used for data analysis. Mean±SD were calculated for quantitative variables. Qualitative variables presented as frequency and percentages. Chi square test was applied and p-value ≤0.05 was taken as significance.

Results: There were 111 male and 37 female patients. The mean age was 51.15±9.76 years. The mean troponin-I score was 3.08±7.47 ng/mL with range 50.7(0.3–51.0). The elevated troponin-I was observed in 84(56.8%) patients. The result showed that age was significantly association with elevated troponin but gender, duration of illness, hypertension, and smoking status were not significantly association.

Conclusion: In conclusion there was high prevalence of cardiac troponin-positive patients admitted with critical illness other than ACS. It increases with the increase in age, predominant in male gender but no significant association with risk factors was noted.

Key Words: Positive Troponin I, Non-Acute Coronary Syndrome, Critically Ill Patients

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INTRODUCTION

It is important to determine the extent of disease and outcome of critical patients as it affects management approaches. There are many individual risk factors that predict the intensive care unit (ICU) mortality and can be judged by multiple investigations such as highly elevated troponin-I in critically ill patients.[1]Several reports have shown that cardiac involvement is a significant factor in deciding the outcome of critical patients.[2,3] For critically sick patients the pathophysiology of myocardial injury is considered to be multi - factorial, including the underlying disease mechanism, hypoxemia, acidosis, and therapeutic maneuvers.[4]

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This is estimated that some degree of myocardial damage can complicates as many as 15 per cent of ICU admissions and as many as 85 per cent of patients with sepsis may have elevated cardiac troponin..[2,5] Multiple studies have measured the prognostic importance of elevated cTnI in chronically ill patients without ACS. While some have proposed that cTnI levels correlate with myocardial damage and bad outcomes, others were unable to validate this association.[1,3,6]

Troponin I and troponin T cardiac isoforms are highly active and are common indicators for myocardial damage, as the main Diagnostic biomarker of an acute myocardial injury.[7] Cardiac troponins are also important prognostic indicators in acute coronary syndrome[8]and other diseases such as sepsis, septic shock, acute stroke and pulmonary embolism.[9,10]The increased levels of troponin suggest a worse prognosis epically in SIRS, sepsis and/or septic shock.[11,12]

The elevations of the serum troponin aren't usually due to an acute coronary syndrome. Multiple ICU conditions such as cardiac failure, pulmonary embolism, atrial fibrillation, acute right heart overload, cardiopulmonary resuscitation trauma, myocarditis, pericarditis, sepsis, hypovolemia, electrical cardioversion, renal failure and myocardial

contusion may lead to serum troponin elevations. Therefore, the secretion and accumulation of troponin is not sufficient by itself to establish an ACS diagnosis. Troponin can be elevated in:

1) Sustained ischemia, with permanent damage to myocytes. The cell membrane degrades, followed by phasing out cytosolic complexes.

2) Conditions allowing increased permeability of the myocyte membrane.

3) Myocardial depressive factors generated during sepsis cause free troponin degradation to components of less molecular weight.

4) Wall stress can cause microinjury and microinfarction to the ventricles.

Higher troponin levels in the absence of ACS will trigger an assessment of an alternative diseaselike pulmonary embolism, renal failure, pneumonia, and sepsis.[11,12] Regardless of the origin, elevated troponin levels are likely to have prognostic significance in critically ill patients.[13]Apart from having the diagnostic value in myocardial infarction the troponin I is found to have prognostic value in sepsis and critically ill patients. Though sepsis is common presentation in ICU patients with high mortality rate in Pakistan; therefore Troponin I can be used as to assess prognosis in local patients. There is no research study done on such patients locally. This is why the current study is proposed. The results of this study will provide statistics on magnitude of raised serum Troponin I in sepsis and critically ill patients. If serum Troponin I found significantly raised and associated with increased mortality, the study will suggest recommendations for routine screening and aggressive critical care of such patients.

MATERIALS AND METHODS

This single centre, cross-sectional, non probability consecutive study was performed between June 2019 and Dec 2019. The inclusion criterion research population was either gender of 35 to 70 years of age, diagnosed of cases of acute coronary syndrome and de novo lesion (> 70 percent lesion) in a native coronary artery after coronary angiography, in outpatient facilities and inpatients attending cardiology unit at Liaquat National Hospital Karachi.

The data were collected after taking permission from Ethical review committee of the Liaquat National Postgraduate Medical Centre Karachi. Approval of synopsis was taken from the College of Physicians and Surgeons of Pakistan. Patients who are brought to intensive care unit with suspicion of critically illness were approached. The patient whose immediate attendant provides the written consent was included in the study. The purpose and procedure of the study were explained and detailed history and physical examination (including pulse, BP, Temperature etc) were done before taking consent. Non-acute coronary syndrome was diagnosed through ECG & echocardiography findings as per operational definitions. It was followed by drawing blood sample, taken from the peripheral vein to perform a troponin I test.

Pre-approved proforma was used to collect and document data. Data were collected on demographic variables like gender, name, residence, age, GCS score, level of Troponin I and duration of illness. Outcome variable was diagnosis of elevated Troponin I level. Standard treatment protocols were followed for each patient. Participants in the study were enrolled in a way that confounding factors were controlled by strictly following the selection criteria.

Statistical analysis: Data were analyzed after entering into SPSS version 21. Continuous variables like age, duration of illness, GCS score, level of Troponin I were analyzed as mean ± Standard deviation. Categorical variable like gender, diagnosis of elevated Troponin I level were expressed in frequency & proportions. Age, gender, duration of illness, GCS score were stratified to analyze the effect of these variables on outcome. It was followed by applying the Chi-square test with a P value $\leq$0.05 was taken as significant.

RESULTS

Total 148 patients of either gender with age between 35 to 70 years, who were diagnosed as critically ill with duration >24 hours upto 7 days, were included in this study to determine frequency of positive Troponin-I in non-acute coronary syndrome. Stratification was accomplished, and post-stratification chi square testing was applied to observe the effect of modifiers on the result. The value of P $\leq$0.05 was considered to be substantial.

The results revealed that there were 111 male and 37 female patients. [Table-2].

The mean age of participants at study was 51,15±9,76 years, with a range of 35(35–70) years. The age distribution is given in Graph-1. The comprehensive descriptive age statistics are given in Table-1. The age in two classes was stratified. 71 patients were under 50 years of age and 77 patients were over 50 years of age.[Graph-1]

The mean duration of illness was 2.57±0.57 days, with range 2(2–4) days. [Table-1].

The mean GCS score was 3.64±1.25, with range 4(2–6). [Table-1]

The results showed that 41.9% patients were hypertensive and 55.4% patients were smokers. Table-2

The mean troponin-I level was 3.08±7.47 ng/mL with range 50.7(0.3–51.0). [Table-1]. With reference to the troponin-I levels it was revealed that elevated troponin was observed in 56.8% patients. [Graph-2]

The descriptive statistics for age, duration of illness, and GCS score according to elevated troponin-I was also calculated. The results showed that among patients with elevated troponin-I mean age was 49.65±9.33

years, mean duration of illness was 2.58±0.54 days, and mean GCS score was 3.86±1.30. The detailed descriptive statistics are presented in Table-13, Table-14 and Table-15 respectively.

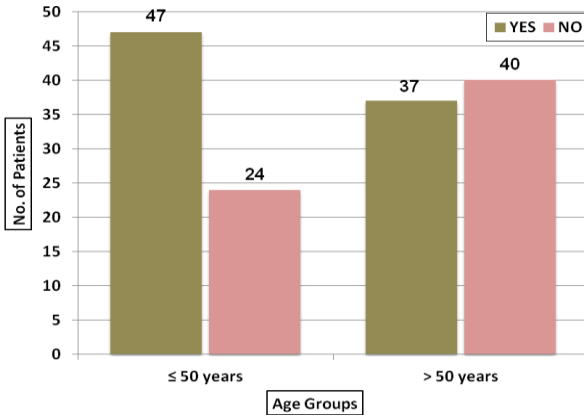
Stratification with respect to age, duration of illness, gender, GCS score, hypertension, and smoking status was done to check effect of these modifiers on outcome i.e. elevated troponin-I levels. Post stratification Chi square test was measured and p-value ≤0.05 was considered as significant. The result showed among total patients who were observed elevated troponin, 64 were male patients and 20 were female patients. [Graph-2]. The association was not significant with gender (p=0.702). There were 47 patients of age ≤50 years and 37 patients of age >50 years. [Graph-2] The association of age was found significant (p=0.026). Among these patients of elevated troponin-I, GCS score was ≤4 in 40 patients and it was >4 in 44 patients. The association of was found significant (p=0.017). Total 35 patients were hypertensive and 50 patients were smokers. The association was not found significant among hypertension (p=0.949) and also with smoking (p=0.248).

Table No.1: Descriptive statistics of age, duration of dyspepsia

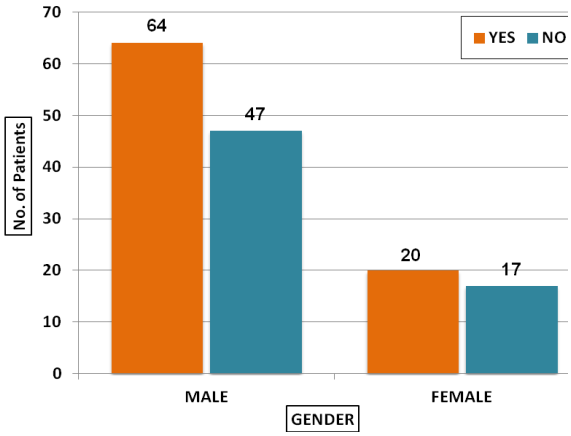
Statistics	Age (Years)	Duration of illness (days)	GCS Score	Troponin I level (ng/mL)
Minimum	35	2	2	0.3
Maximum	70	4	6	51.0
Mean	51.15	2.57	3.64	3.08
Std. Deviation	9.76	0.57	1.25	7.47

Table No. 2: Frequency distribution of gender, hypertension, smoking status, elevated Troponin I level(n=148)

Gender	Frequency(n)	Percentage (%)
Male	111	75.0%
Female	37	25.0%
Total	148	100%
Hypertension	Frequency(n)	Percentage(%)
YES	62	41.9%
NO	86	58.1%
Total	148	100%
Smoking status	Frequency (n)	Percentage(%)
YES	82	55.4%
NO	66	44.6%
Total	148	100%
Elevated Troponin I level	Frequency (n)	Percentage (%)
YES	84	56.8%
NO	64	43.2%
Total	148	100%



Graph No. I: Percentage of elevated troponin level according to age groups(n=148)



Graph No.2: Percentage of elevated troponin level according to gender(n=148)

DISCUSSION

For critically ill patients with mechanical ventilation elevated cTnI is associated with higher mortality and longer duration. Cardiac troponin I and T are the most widely known and sensitive laboratory markers of myocardial tissue damage, and can increase in patients with many other diseases than acute coronary syndrome.[1,5]

In a study[14,17] (55 percent) of 58 patients admitted to two intensive medical care units as a result of serious diseases other than ACS, or 32 (63 percent) of 51 patients admitted for sepsis, SIRS, or septic shock, were troponin-positive. Mortality in troponin-positive patients was fourfold higher and LVEF considerably lower compared to troponin-negative patients. It is the first research in which the majority of troponin-positive patients attempted to systematically eliminate severe coronary artery disease by autopsy or stress echocardiography.[14]Our results showed that the elevation of troponin could be used as a potential risk factor for mortality for patients in intensive care without coronary artery disease. This is interesting that

there was no substantial difference in SAPS between troponin-positive and negative patients while a slightly higher percentage of shock-presenting patients were troponin-positive relative to those without shock.

Elevated rates of cTnI also correlate with reduced left ventricular activity in both non-coronary and coronary patients.[1,6] Cardiac dysfunction in sepsis is relatively well known and has been associated with poor prognosis.[2] In addition, a small recent study indicated that 44 percent of patients with extreme sepsis had systolic dysfunctions.[20] Their data showed that there is a stronger association between elevated cTnI and mortality in patients over 65, which is likely to be due to the degree, and probably irreversibility, of myocardial injury in this age group.[9]An significant finding from this study was that the majority of deaths among younger patients occurred during the first five days, while the majority of deaths (60 percent) occurred in the elderly population during this time period.

Several non-coronary medical trials dealt with the prognostic significance of elevated cTnI. Elevated cTnI correlated with poor outcome in selected groups such as patients with COPD and hemodyalisis.21 A research in individuals with emergency department found that there is a significant correlation between elevation and outcome of cTnI. Relos et al22 evaluated ICU patients, suggesting that moderate serum troponin I levels below the threshold for diagnosing acute myocardial infarction, which is associated with recurrent myocardial damage in critically ill patients and higher mortality rates and longer hospital and duration of ICU stay.

A significant correlation between death rates and elevated cTnI was observed in studies involving critically ill medical patients without coronary disease.14 However, the sample size was very small (58 patients) and most patients had sepsis (88%), restricting the interpretation of these results. Like those research, Kollef et al[3] indicated that cTnI serial measurements do not contribute independently to predicting hospital mortality beyond that given by clinically recognised cardiac dysfunction. Nevertheless, as previously suggested, elevated cTnI was previously associated with left ventricular function [1]

The difficult interpretation of non-coronary troponin rises reflects the limited understanding of the etiology of myocardial cell injury. It is clear how an acute coronary event or an oxygen supply-demand imbalance can render heart cells ischemia and how the subsequent necrosis leads to troponin release into the plasma. It is less clear how a diverse group of disease processes can result in troponin leaks with no evidence of coronary disease, and why this should be such a consistent predictor of poor outcomes.[23]In Alatassiet al[24] study the association of increased mortality with increased troponin level was observed whether patients had underlying advanced heart failure or not.

Our study results are comparable with the above stated literature findings. In our study ratio of male patients was very high as with female patients. More patients were found with age > 50 years. The duration of illness before reporting was 2 to 4 days. The mean troponin-I was 3.08±7.47 ng/mL with range 50.7(0.3–51.0) hence by the criteria elevated troponin was observed in 84(56.8%) patients. As male patients are more in our study, elevated Troponin was also found more in males rather than females, but the difference was not significant. More patients were aged > 50 years in our study but the elevated Troponin I was observed more in patients with age ≤50 years and the association of age was found significant. Smoking status and hypertension was mot associated with elevated Troponin I among non ACS patients.

CONCLUSION

The study results showed high prevalence of cardiac troponin-positive patients admitted with critical illness other than ACS. It increases with the increase in age, predominant in male gender but no significant association with risk factors was noted. We conclude that troponin elevation may be used as an early marker of severity of illness and outcome, particularly in older patients, male gender and patients with low GCS score.

Author's Contribution:

Concept & Design of Study:	Sarfraz Ali Mangi
Drafting:	Faisal Ahmed, Naveen Roy
Data Analysis:	Rubina Khan, Imran Khan Sandeelo, Sumayya Zaman
Revisiting Critically:	Sarfraz Ali Mangi, Faisal Ahmed
Final Approval of version:	Sarfraz Ali Mangi

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Gajic O, Ahmad SR, Wilson ME, Kaufman DA. Outcomes of critical illness: what is meaningful? Current opinion in critical care 2018;24(5):394.
2. Guest TM, Ramanathan AV, Tuteur PG, Schechtman KB, Ladenson JH, Jaffe AS: Myocardial injury in critically ill patients. A frequentlyunrecognized complication. J Am Med Assoc 1995;273:1945-9.
3. Poe S, Vandivier-Pletsch RH, Clay M, Wong HR, Haynes E, Rothenberg FG. Cardiac troponin measurement in the critically ill: potential for guiding clinical management. JInvestigative Med2015;63(8):905-15.
4. Kakihana Y, Ito T, Nakahara M, Yamaguchi K, Yasuda T. Sepsis-induced myocardial dysfunction:

pathophysiology and management. J Intensive Care 2016;4(1):1-0.
5. Ammann P, Pfisterer M, Fehr T, Rickli H. Raised cardiac troponins. Bio Med J 2004;328:1028-9.
6. Fernandes CJ Jr, Akamine N, Knobel E. Cardiac troponin: a newserum marker of myocardial injury in sepsis. Intensive CareMed 1999;25:1165-8
7. Thygesen K, Alpert JS, White HD. Joint ESC/ ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. J Am CollCardiol 2007;50:2173-95.
8. Hamm CW, Ravkilde J, Gerhardt W, Jorgensen P, Peheim E, Ljungdahl L, et al. The prognostic value of serum troponin T in unstable angina. N Engl J Med 1992;327:146-50.
9. Ammann P, Fehr T, Minder EI, Gunter C, Bertel O. Elevation of troponin I in sepsis and septic shock. Intensive Care Med 2001;27: 965-9.
10. Mehta NJ, Khan IA, Gupta V, Jani K, Gowda RM, Smith PR. Cardiac troponin I predicts myocardial dysfunction and adverse outcome in septic shock. Int J Cardiol 2004; 95: 13-7.
11. Di Angelantonio E, Fiorelli M, Toni D, Sacchetti ML, Lorenzano S, Falcou A, et al. Prognostic significance of admission levels of troponin I in patients with acute ischaemic stroke. J NeurolNeurosurg Psychiatr 2005;76:76-81.
12. Sandoval Y, Jaffe AS. Type 2 myocardial infarction: JACC review topic of the week. JAm Coll Cardiol 2019;73(14):1846-60.
13. Choon-ngarm T, Partpisanu P. Serum cardiac troponin-T as a prognostic marker in septic shock. Med J Med Assoc Thailand 2008;1818.
14. Vasile VC, Chai HS, Khambatta S, Afessa B, Jaffe AS. of elevated cardiac troponin T levels in critically ill patients with acute respiratory disease. Am J Med 2010 ;123: 1049-58.
15. Keller T, Zeller T, Peetz D. Sensitive troponin I assay in early diagnosis of acute myocardial infarction. N Engl J Med 2009;361:868–77.
16. Ilva TJ, Eskola MJ, NikusKCl. The etiology and prognostic significance of cardiac troponin I elevation in unselected emergency department patients. J Emerg Med 2010; 38:1–5.
17. Fromm RE Jr. Cardiac troponins in the intensive care unit: common causes of increased levels and interpretation. Crit Care Med 2007; 35:584– 8
18. Ammann P, Maggiorini M, Bertel O, Haenseler E, Joller- Jemelka HI, Oechslin E et al. Troponin as a risk factor for mortality in critically ill patients without acute coronary syndromes. J Am CollCardiol 2003;41:2004-9.
19. Latini R, Masson S, Anand IS, Missov E, Carlson M, Vago T et al. Prognostic value of very low plasma concentrations of troponin T in patients with stable chronic heart failure. Circulation 2007;116:1242-9.
20. Charpentier J, Luyt CE, Fulla Y, Vinsonneau C, Cariou A, Grabar S, et al. Brain natriuretic peptide: A marker of myocardial dysfunction and prognosis during severe sepsis.Crit Care Med 2004;32:660-65.
21. Baillard C, Boussarsar M, Fosse JP, Girou E, Le Toumelin P, Cracco C, et al.Cardiac troponin I in patients with severe exacerbation of chronic obstructive pulmonary disease. Intensive Care Med 2003;29:584-89.
22. Relos RP, Hasinoff IK, Beilman GJ: Moderately elevated serum troponin concentrations are associated with increased morbidity and mortality rates in surgical intensive care unit patients. Crit Care Med 2003;31:2598-603.
23. Hamilton MA, Toner A, Cecconi M. Troponin in critically ill patients. Minerva Anestesiol 2012;1039-45.
24. Alatassi A, Habbal M, Tamim H, Sadat M, Al Qasim E, Arabi YM. Association between troponin-I levels and outcome in critically ill patients admitted to non-cardiac intensive care unit with high prevalence of cardiovascular risk factors. BMC Anesthesiol 2018;18(1):54.