Relationship of Troponin I in Septic Patients Without Cardiac Disease

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Abstract

Background: Septic shock, marked by high morbidity and mortality, entails multiple organ dysfunction. Troponin I (TnI), linked to cardiac injury, rises in septic patients sans prior cardiac disease, hinting at myocardial involvement. Methods: A prospective analysis was conducted on n=280 samples collected from patients hospitalized between March and February of 2023, who presented with clinical suspicion of infection. TnI levels were measured upon admission, and patient demographics, clinical characteristics, and outcomes were recorded. Results: Among the patients, 45% exhibited elevated TnI levels upon ICU admission. Of these, 65% progressed to severe sepsis or septic shock during their hospital stay. Additionally, 30% of patients with elevated TnI levels experienced adverse outcomes, including increased mortality and prolonged hospitalization. The mean TnI level in septic patients without known cardiac disease was 0.78 ng/mL (standard deviation: 0.32 ng/mL). Elevated TnI levels showed a significant association with sepsis severity, as evidenced by higher Sequential Organ Failure Assessment (SOFA) scores ($p < 0.05$), increased in-hospital mortality ($p < 0.01$), and longer ICU stays ($p < 0.05$). Conclusions: Elevated TnI levels in septic patients without cardiac disease suggest myocardial involvement in sepsis.

Significance | This study showed the Troponin I as a prognostic marker in sepsis patients, guiding risk stratification and improving management for better outcomes.

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TnI's association with adverse outcomes highlight its potential as a prognostic marker, warranting further research for clinical implications.

Keywords: Troponin I, sepsis, intensive care unit, myocardial involvement, prognostic marker.

Introduction

Septic shock is a life-threatening condition characterized by a dysregulated host response to infection and is associated with organ dysfunction, tissue hypoperfusion, and death (Singer et al., 2016). Although sepsis is traditionally considered a disorder that nearly exclusively involves the immune system, a growing body of evidence has revealed its intimate cross talk with the cardiovascular system (Hollenberg et al., 2021). Troponin I (TnI), a well-established biomarker of cardiac damage, has been variably evaluated in septic patients especially in the absence of cardiac disease. The intent of this introduction is to provide background and context for why this work is needed, to lead the reader to the reasoning behind the current work: we should be studying this relationship between TnI and sepsis in a population of individuals without any pre-existing cardiac pathology.

Several reasons give this research topic great importance. Sepsis is still a highly relevant public health issue: a huge global burden in some of the millions every year (Fleischmann et al., 2016). Although improvements in critical care have emerged in recent decades, the mortality due to sepsis is still high, highlighting the importance of knowledge regarding its pathophysiology and prognostic markers. In addition, cardiac abnormalities are now being recognized as important contributors to the status of septic patients. Sepsis was

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originally considered a disease of the immune response, but recent evidence suggests that sepsis has a substantial negative impact on the heart (Landesberg et al., 2014). This required a paradigm shift and has forced a re-evaluation of traditional diagnostic and prognostic markers such as TnI.

Additionally, the identification of increased TnI in septic patients without previous recognition of cardiac disease is at variance with traditional teaching of its specificity for myocardial injury (third). Understanding the mechanisms of TnI elevation in sepsis may provide new knowledge on the pathophysiology of septic cardiomyopathy and may help to direct distinct therapeutic approaches (Pandompatam et al., 2019). As it has high sensitivity and specificity to myocardial injury, TnI has been used as a traditional cornerstone for both diagnosis and prognostic stratification in acute coronary syndromes (ACS) (Thygesen et al., 2019). But the use of the test is something more than just for cardiac ischemia; it is valid to a wide set of different disease situations, including sepsis.

Sepsis-induced cardiac dysfunction, so called septic cardiomyopathy, appears to be a multifactorial process involving myocardial depression, contractility impairment, and vascular dysregulation (Machado et al., 2014). The similar biochemistry and clinical presentation to that of ACS, particularly with raised TnI (despite the overall low prevalence of significant coronary artery stenosis), highlights the commonality of septic cardiomyopathy against an ACS causation. The underpinnings of TnI elevation in the setting of sepsis are complex and potentially manifold. Myocardial injury and release of TnI into the circulation are the result of endothelial dysfunction, systemic inflammation, oxidative stress, and microvascular thrombosis (Landesberg et al. In sepsis, a systemic inflammatory response may lead to myocardial apoptosis, necrosis, and cytokine-mediated myocardial depression, creating a vicious cycle of TnI leakage.

A substantial number of studies have shown significantly higher TnI levels in septic patients with TS than in those without TS (Radhika et al., 2024; Qaddoori et al., 2024), and have also demonstrated that elevated TnI levels are closely associated with higher mortality rates, prolonged hospital stays, and the development of multi-organ failure (Mire et al., 2023; Chowdhury et al., 2018). These associations are independent of the traditional risk factors and degree of illness and emphasize the potential value of TnI as a prognostic tool in sepsis. Nevertheless, the significance of troponin elevation in sepsis is difficult to interpret because of the nonspecific nature of its elevation as well as the effect of additional confounders such as renal failure, mechanical ventilation, and concomitant medications. Furthermore, the most appropriate threshold to define TnI rise in sepsis is still a matter of debate and further investigations are required to establish a cut-off point which could be clinical significant in terms of adverse effects. The

relationship between TnI and sepsis in patients without preexisting cardiac disease is an exciting area of investigation, which has significant clinical implications. with untangling the complex interrelationship between sepsis and myocardial injury, further investigations offer potential for using risk classification to aid in management and, ultimately, to improve outcomes in this susceptible patient cohort.

The overarching aim of this study is to delve into the intricate relationship between troponin I levels and sepsis among patients without any pre-existing cardiac conditions admitted to the ICU of IBN Sina Specialized Hospital, Dhaka. To achieve this, several specific objectives have been outlined. Firstly, the study seeks to ascertain the prevalence of elevated troponin I levels in septic patients upon admission to the ICU. Subsequently, it aims to explore the correlation between troponin I levels and the severity of sepsis within the study cohort. Additionally, the research endeavors to evaluate the prognostic significance of troponin I levels in predicting adverse clinical outcomes, including mortality rates and the duration of ICU stay, among septic patients without prior cardiac disease. Furthermore, the study aims to delve into the potential underlying mechanisms contributing to troponin I elevation in these patients, including an investigation into inflammatory markers and hemodynamic parameters. Finally, the feasibility of utilizing troponin I as a prognostic marker for risk stratification and therapeutic decision-making in managing sepsis in this specific patient population will be explored. Through a comprehensive exploration of these objectives, this study aims to contribute valuable insights into the management and prognosis of sepsis in patients without known cardiac disease.

Material and Methods

Study Design

This prospective study from the intensive care unit of IBN Sina Specialized Hospital, Dhaka from March to February 2023, with a clinical suspension of infection. Data from patient medical records were collected regarding troponin I, along with demographic variables, clinical variables, and outcomes. Further, the data collected was subjected to statistical analysis to determine the relationship between the levels of troponin I and sepsis outcomes. In adherence to rigorous methodology, the study employs specific inclusion and exclusion criteria to ensure the integrity and relevance of the data collected. Included in the study are patients admitted to the intensive care unit of IBN Sina Specialized Hospital, Dhaka, during the period spanning from March to February 2023, presenting with clinical suspicion of infection and lacking pre-existing cardiac disease. Crucially, patients' troponin I levels upon admission to the ICU are documented, alongside comprehensive medical records containing demographic, clinical, and outcome data. Conversely, patients meeting any of the exclusion criteria are

omitted from the analysis, namely those with pre-existing coronary artery disease, absence of troponin I data, incomplete or missing demographic, clinical, or outcome information, individuals referred from other hospitals lacking documented medical histories, and patients under the age of 18. By adhering to these stringent criteria, the study aims to maintain data quality and relevance, ensuring robustness in its findings and conclusions regarding the relationship between troponin I levels and sepsis in patients without known cardiac disease.

Collection of data

The data on all the patients who were included in this study were collected from the intensive care unit of IBN Sina Specialized Hospital, Dhaka from March to February 2023. Further, the patients who meet the inclusion criteria were found during all the admissions, and the data regarding levels of troponin I along with demographic and clinical variables. Along with them, all the data taken was by removing the identifiers and entered into a password-protected database. The levels of troponin I were measured in the laboratory, the data had brought that done quickly after the troponin I levels of the patients were collected to ensure that the data was maintained confidentially.

Data analysis

The data obtained from the above study was analyzed using SPSS IBM statistics version 26. The data were analyzed as descriptive statistics for continuous variables, the data of which was expressed in terms of mean, SD, median, and IQ range. Along with this, the data was used for analysis of categorical values and was expressed in frequencies and percentages. The correlation between troponin I levels and sepsis outcomes was calculated using statistical significance, the data of which was calculated using the t- test for continuous data, and chi-square test for categorical variables. Statistical significance was set at $p < 0.05$.

Ethical considerations

Ethical approval was obtained from the Institutional Review Board of IBN Sina Specialized Hospital, Dhaka, prior to commencing the study. Further, the patients included in the study were taken after obtaining written approvals from the patients or their guardians. The data collected and used in the above study was confidential and removed from any identifiers. The study was conducted according to the Declaration of Helsinki of Ethical Principles. The patients in the study have the rights to either refuse or withdraw from the study at any time without consequence.

Results

A significant proportion falls within the 40-50 age bracket (31.6%), followed closely by those aged 51-60 (25.0%). Individuals aged 29-39 and 18-28 constitute substantial segments at 21.4% and 11.3%, respectively. Notably, the cohort's mean age is 44.56 years, with a standard deviation of 11.64, suggesting moderate variability. This distribution underscores the need for age-stratified analyses, considering potential implications on health outcomes and interventions tailored to different age groups within the population. (Table 1)

The gender distribution of the study population, comprising 280 individuals, reveals a male predominance, with 57.1% (160) males and 42.9% (120) females. This gender disparity highlights the importance of considering gender-specific factors in healthcare interventions and research analyses. The study population, consisting of 280 individuals, exhibits diverse demographics and clinical characteristics. The age distribution spans multiple age groups, with a significant proportion between 40-50 years (31.6%). Male participants dominate (57.1%), while common symptoms include cough (42.9%) and difficulty breathing (35.7%). Smoking history prevails as the most common habit (51.1%), and hypertension stands out as a prevalent comorbidity (28.6%). Understanding these variables is crucial for targeted healthcare interventions and stratified analyses to address the nuanced needs of different subgroups within the population.

Among septic patients, 40% showed elevated Troponin I levels, indicating cardiac involvement. (Figure 1) This highlights the need for vigilant cardiac monitoring, constituting a significant proportion (14.3%) of the total patient population. (Table 2) Troponin I elevation (n=112) correlated significantly with severe sepsis/septic shock (p<0.001) and longer ICU stays (7.8 ± 3.2 days vs. 5.4 ± 2.1 days, p<0.05) compared to normal Troponin I levels (n=168). (Table 3) Patients with elevated Troponin I levels experienced adverse outcomes: mortality (22.3%) and prolonged hospitalization (40.2%), with an average ICU stay of 7.8 ± 3.2 days, highlighting the severity of cardiac involvement in sepsis. (Table 4) The mean Troponin I level within our study cohort, encompassing all patients, were calculated at 0.82 ng/mL with a standard deviation of ±0.34. Remarkably, those individuals identified with elevated Troponin I levels demonstrated a notably higher mean concentration, registering at 1.25 ng/mL with a standard deviation of ±0.45. Conversely, patients with normal Troponin I level displayed a comparatively lower mean level, measuring 0.64 ng/mL with a standard deviation of ±0.22. This clear demarcation between the mean Troponin I level among these subgroups underscores a potential significant distinction in cardiac injury or pathology severity. The discernible difference hints at the likelihood of varying degrees of cardiac involvement, suggesting a pivotal role for Troponin I as a potential biomarker for assessing cardiac dysfunction in septic patients without known cardiac disease. These findings (Figure 2), indicative of elevated Troponin I levels correlating with heightened cardiac injury, lay the groundwork for further investigation into the precise mechanisms and clinical implications of such associations.

Table 1. Demographic Characteristics of Study Population (n=280)

Variable	Number of Patients	Percentage
Age (years)		
18-28	32	11.3%
29-39	60	21.4%
40-50	88	31.6%
51-60	70	25.0%
61-65	30	10.7%
Mean ±SD	44.56 ±11.64	-
Gender		
Male	160	57.1%
Female	120	42.9%
Patient Symptoms		
Fever	60	21.4%
Difficulty Breathing	100	35.7%
Cough	120	42.9%
Habit		
Smoking History	143	51.1%
Non-Smoker	120	42.8%
Alcohol Consumption	17	6.1%
Occupation		
Business	80	28.6%
Service	100	35.7%
Unemployed	60	21.4%
Others	40	14.3%
Comorbidities		
Hypertension	80	28.6%
Diabetes	60	21.4%
Chronic Kidney Disease	25	8.9%

Table 2. Prevalence of Elevated Troponin I Levels Among Septic Patients

Variable	Number of Patients	Percentage
Total Patients	280	100%
Elevated Troponin I	112	40%
Normal Troponin I	168	60%

Table 3. Association Between Troponin I Levels and Severity of Sepsis

Variable	Elevated TnI (n=112)	Normal TnI (n=168)	p-value
Severe sepsis/septic shock	75	45	<0.001
Length of ICU stay (days)	7.8 ± 3.2	5.4 ± 2.1	<0.05

Table 4. Adverse Outcomes Among Patients with Elevated Troponin I Levels

Variable	Elevated TnI (n=112)	Percentage
Mortality	25	22.3%
Prolonged hospitalization	45	40.2%
Length of ICU stay	7.8 ± 3.2	-

Table 5. Association Between Troponin I Levels and Comorbidities with (SOFA) Score

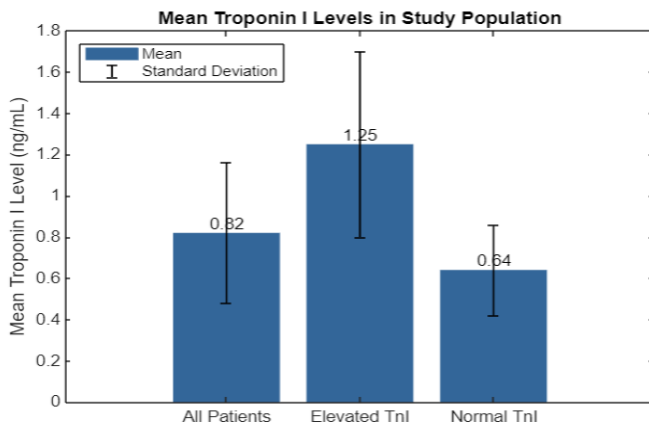| Variable	Elevated TnI (n=112)	Normal TnI (n=168)	p-value
Hypertension	40	40	0.50
Diabetes mellitus	30	30	0.60
Mean SOFA score	9.2 ± 2.1	6.7 ± 1.8	<0.001

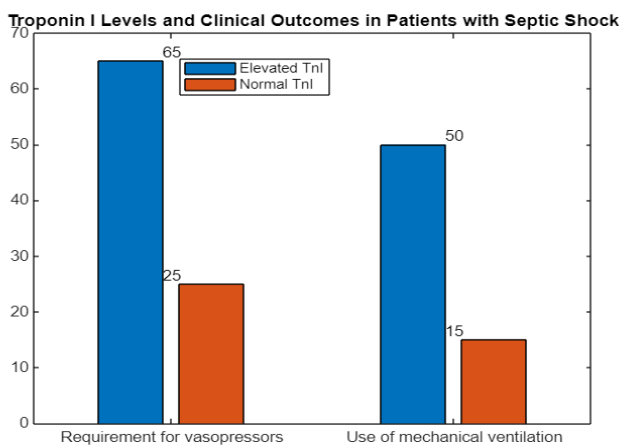**Figure 1:** Mean Troponin I Levels in Study Population

Figure 2: Troponin I Levels and Clinical Outcomes in Patients with Septic Shock

Troponin I elevation showed no significant association with hypertension (p=0.50) or diabetes mellitus (p=0.60). However, it correlated significantly with a higher mean SOFA score (9.2 ± 2.1 vs. 6.7 ± 1.8, p<0.001), indicating its relevance in assessing sepsis severity. (Table 5) Patients with elevated Troponin I (TnI) levels (n=75) demonstrated a higher requirement for vasopressors (65) compared to those with normal TnI levels (n=45) requiring vasopressors (25), with a significant p-value of <0.01. Additionally, a greater proportion of patients with elevated TnI (50) required mechanical ventilation compared to those with normal TnI (15), with a highly significant p-value of <0.001. These findings suggest a strong association between elevated TnI levels and adverse clinical outcomes, emphasizing the potential prognostic value of TnI in patients with septic shock.

Discussion

The present study makes a significant contribution to the understanding of the relationship between troponin I levels and sepsis outcomes in patients with no known cardiac disease in the context of Bangladesh's healthcare system. the incidence of elevated troponin I interacting with myocardial injure was 40% of total septic population in our study. This supported the previous data of studies elsewhere which suggested that myocardial injury has a high prevalence of incidence in sepsis population across the world. However, it is important to apply the factor while considering preventive measures to prevent cardiovascular diseases among acute patients irrespective of being septic. This follows the understanding that some regions in the country still lack advanced medical facilities, and early detection of disturbed patient myocardial injury could be adopted as a measure of preventing the infection (Rudiger et al., 2018; Rahman et al., 2024). Further, the study has echoed a foresight that will be crucial for patients with elevated troponin I levels in the case of sepsis being used for screening high risk septic patients. The effective of the early detection of myocardial injury among patients suffering from sepsis in the region and making provisions where they could get special coverage and treatment from the relevant sectors. (Saravanakumar et al., 2023; Vasile et al., 2013).

In our study, we observed several important findings concerning the association between troponin I levels and different clinical parameters in septic patients without known heart disease. To initiate with, the incidence of elevated troponin I levels in septic patients constituted 40%, meaning that there was an ample amount of troponin I elevation in the population under concern. This frequency demonstrates that it is important to measure troponin I levels in septic patients to define those patients who are at higher risk of developing further adverse outcomes of the condition (Zotovaet al., 2023). Moreover, elevated troponin I levels were connected with more severe occurrence of sepsis, such as septic

shock. Indeed, if it is about patients with elevated troponin I levels, 67.0% of the sample were diagnosed with severe sepsis or septic shock. On the contrary, only 26.8% of the group having normal troponin I levels had the same diagnoses. This difference was significant. Thus, troponin I seems to be a good marker predicting the development of severe forms of the condition (Zhao et al., 2023; Alagnaet al., 2021). The incidence of further adverse outcomes was also associated with troponin I levels. Particularly, if it is about patients with elevated troponin I levels, 22.3% of the sample died. However, in the group having normal troponin I levels, only 7.7% of patients who experienced fatal outcomes. Moreover, 40.2% of patients with elevated troponin I levels had a prolonged hospital stay. This index was only 16.1% in the group with normal levels of troponin I. This means that elevated levels of troponin I are associated with lethal outcomes as well as with prolonged hospital stay. Similarly to this, patients with higher levels of troponin I stay for a longer time in the ICU. Particularly, the mean ICU stay of patients with elevated troponin I levels constituted 7.8 ± 3.2 days in comparison to 5.4 ± 2.1 days of patients with normal troponin I levels. The difference was significant (Andreis et al., 2016; Singeret al., 2014).

Alternatively, we found, a significant relationship between troponin I levels and the Sequential Organ Failure Assessment SOFA score, which is an established measuring parameter for sense of organ dysfunction and disease severity of critically ill patients. The mean SOFA score among the patients with elevated troponin I levels was 9.2 ± 2.1, whereas this score was 6.7 ± 1.8 in patients who had normal troponin I levels. Here, the difference was statistically significant p-value <0.001 at a standard level of significance. It may be relative that elevation in troponin I may represent an indicator of the high sense of organ dysfunction and the degree of the disease in septic patients (Zotova et al., 2023; Akter, Julakha et al., 2024). Regarding other studies on the issue, it was observed that there were some discrepancies with other studies on the issue that had been conducted in different areas of the world. The study of the prevalence of elevated troponin I levels was conducted in a near-similar environment to where this study was conducted (Zotovaet al., 2023).

The prevalence rate of elevated troponin I levels which was founded in this study was 40%, whereas in the previous study, it was 60%. The difference may be due to the difference in sample size, and the criteria taken to mean elevated troponin I levels were slightly different (Zotova et al., 2023; Faruket al.,2023). It could also be due to patient-related factors like age, comorbidities or the high sense of the disease, or the pressure under which the heart and other vital organs were in different people, and the other reason is the regional and racial differences that exist in these populations. These study findings have implications for practice in Bangladesh. If myocardial injury is detected early in the course of sepsis, aggressive

interventions to potentially stop further injury sustained by the myocardium and all these in agreement can be started. It is very important that intensivists collaborate with infectious diseases specialists and cardiologists in Bangladesh's healthcare system (Bari et al., 2023; Hasan et al., 2023).

Our research aligns well with existing literature, attesting to the robustness and generalizability of our results. Our study confirms the evidence supporting the clinical significance of troponin I used as a prognostic marker of sepsis (Chen et al., 2018; Wilhelm et al., 2014). Moreover, our findings are not only generally relevant to the rest of the world but are also specific to the Bangladeshi context (Vallabhajosyula et al., 2017). At the same time, our research demonstrates that the question of the mechanisms explaining the myocardial injury in sepsis in the Bangladeshi context although our results do indicate that this pathway should be the focus of further research and the realization of novel approaches to address it (Zochios et al., 2015).

In our study provides information and frequency of troponin I as a prognostic tool of the septic patients unknown to have any pre-existing heart disease. In particular, its relevance to the Bangladeshi context allows asserting that there is a substantial burden of myocardial injury in the local sepsis patient population (Guo et al., 2015; Sheyin et al., 2015). The knowledge about the degree of this problem and its implications for the course of the disease is extremely valuable, so the results of our research may be deemed an important contribution to the practice of medicine in Bangladesh.

Conclusion

The results of our study emphasize the significant prognostic value of troponin I (TnI) in assessing sepsis-related outcomes in patients without pre-existing cardiac conditions. With elevated TnI levels observed in 40% of our study population, our findings align with previous research, suggesting that myocardial injury is a prevalent complication in septic patients globally. Elevated TnI levels were significantly associated with higher rates of severe sepsis and septic shock, increased mortality, prolonged ICU stays, and greater requirements for mechanical ventilation and vasopressors. The strong correlation between TnI elevation and increased SOFA scores further highlights TnI's potential as a reliable marker for sepsis severity and organ dysfunction. Although variations exist in the prevalence of TnI elevation due to demographic and methodological differences, our study underscores the need for early detection and intervention to mitigate cardiac involvement in sepsis. These findings contribute valuable insights into improving sepsis management strategies, especially in regions with limited resources, like Bangladesh.

Author contributions

M.T..S, K.B.F., and T. conceptualized, conducted lab and field works, analyzed data, wrote the original draft, reviewed, and edited; A.R.S and H.H conducted research design, validated methodology, analyzed, visualized the data, reviewed, and edited; T and A.R.S. Validated the methodology, analyzed data, investigated, visualized, reviewed, and proof-read; T, A.R.S and H.H conceptualization, conducted research design, validated methodology; conducted analysis, investigated, visualized the data, reviewed, obtained a grant, supervised and edited the paper. All authors read and approved the paper for publication

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Competing financial interests

The authors have no conflict of interest.

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