Role of Troponin-T at Admission and Serial Troponin-T Testing in Predicting Outcomes in Severe Sepsis and Septic Shock

Prof. Dr. Azza Mohamed Shafeek Abdel Mageed, Dr. Walid Hamed Nofal, Dr. Eman Abu bakr El Seddik Ahmed and Akram Ibrahim Younis

Anesthesiology, Intensive Care and Pain Management Department, Faculty of Medicine, Ain Shams University, Egypt
dr_akram193@yahoo.com

Abstract: Serum troponin concentrations have been associated with increased mortality in almost every clinical setting they have been examined, including sepsis. Sepsis is the physiological response to severe infection. It is defined as the presence (probable or documented) of infection together with systemic features of inflammation. Severe sepsis is sepsis-induced tissue hypoperfusion or organ dysfunction, and septic shock refers to sepsis-induced hypotension, persisting despite adequate fluid resuscitation, which may be defined as infusion of 30 ml/kg of crystalloids. Elevated troponin levels are observed in 43% across all intensive care patient groups. The estimated prevalence of positive troponin in the context of sepsis is 61%. The mechanism of myocyte insult in severe sepsis and septic shock, in the absence of thrombotic acute coronary syndrome, leading to elevated serum troponin, is not yet fully understood. Myocardial depressive factors (inflammatory mediators, endotoxins), microvascular dysfunction and increased myocardial cell membrane permeability in conjunction with myocardial oxygen demand–supply mismatch, are potential explanations for sepsis induced troponin elevation. In this setting, troponin elevation occurs in the absence of myocytenecrosis and this hypothesis is supported by clinical observations that myocardial depression in the context of sepsis is a reversible process in most surviving patients. The aim of this study is to evaluate the prognostic value of troponin T level at admission and serial troponin T testing in patients with severe sepsis and septic shock. This work was carried on 70 patients with severe sepsis and septic shock from those attending the intensive care units in Ain shams university hospitals in the time period between February 2018 and July 2018. These patients were subdivided into 2 groups each consisted of 35 patients, the first group with elevated troponin T at admission and the other group with negative troponin T at admission.

[Azza Mohamed Shafeek Abdel Mageed, Walid Hamed Nofal, Eman Abu bakr El Seddik Ahmed and Akram Ibrahim Younis. **Role of Troponin-T at Admission and Serial Troponin-T Testing in Predicting Outcomes in Severe Sepsis and Septic Shock.** *Nat Sci* 2019;17(6):15-24]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). http://www.sciencepub.net/nature. 3. doi:10.7537/marsnsj170619.03.

Keywords: Role; Troponin-T; Admission; Serial Troponin-T; Testing; Predicting Outcome; Severe Sepsis; Septic Shock

1. Introduction

Sepsis is a leading cause of death and disability worldwide, resulting in a huge number of fatalities as acute myocardial infarction (AMI) each year **(Bessiere et al., 2013)**. Cardiovascular dysfunction occurs in nearly 70% of septic patients and can manifest as hemodynamic instability, cardiac biomarker elevation, myocardial dysfunction on echocardiography, and end-organ hypoperfusion **(Antonucci et al., 2014)**. Cardiovascular dysfunction in sepsis is associated with worse hospital and long-term outcomes, necessitating early diagnosis and management **(Angus et al., 2001)**.

Cardiac troponin-T (TnT) and troponin-I (TnI) are sensitive and specific markers of myocardial injury and have prognostic implications in many primary non cardiac illnesses including pulmonary embolism, subarachnoid hemorrhage, and stroke **(Jimenez et al., 2009)**. Increased sensitivity of the TnT assay has resulted in more frequent clinical detection of myocardial injury from non-coronary causes, including critical illness **(Newby et al., 2012)**. Elevations in TnT levels are present in up to 60% of all intensive care unit (ICU) patients and identify patients with increased risk of short-term and long-term mortality **(Babuin et al., 2008)**.

Up to 85% of patients with sepsis and septic shock have detectable cardiac TnT levels using standard troponin assays, and troponin levels have demonstrated a variable association with mortality **(Ammann et al., 2001)**. Cardiac TnT levels correlate with the presence of left ventricular systolic and diastolic dysfunction and right ventricular dysfunction on echocardiography **(Klouche et al., 2014)**. TnT levels in patients with sepsis correlate with duration of hypotension and extent of vasopressor support **(Chelazzi et al., 2011)**. Prior studies evaluating the role of troponins in sepsis and septic shock were limited by the use of different troponin assays, small sample sizes, variations in definitions of elevated troponin levels, and loss of patients to follow-up

(Bessiere et al., 2013). These studies display marked heterogeneity because of lack of uniform adaptation of the 99th percentile of the upper reference limit as the standardized cutoffs **(Pulkki et al., 2009)**. Thus, the epidemiology and prognostic value of troponin levels in patients with sepsis depend not only on the assay used but also on the cutoff values used.

Aim of the Work

The aim of this study is to evaluate the prognostic value of TnT in patients with severe sepsis and septic shock. The outcome will be in-hospital mortality, need for mechanical ventilation, the need for vasopressors and length of ICU stay.

2. Patients and Methods

Study patients:

This study was done to assess the role of troponin-T testing at admission and serial troponin-T testing in predicting outcomes in severe sepsis and septic shock.

This study was carried out on 70 patients from those admitted in the intensive care units at Ain Shams university hospitals between *February 2018* and *July 2018* with severe sepsis and septic shock.

The patients were divided into 2 groups, 35 patients with positive troponin- T and 35 patients with negative troponin- T.

Inclusion criteria:

The patients included in this study had fulfilled the following criteria on admission:

A. In the presence of a source of sepsis, two or more of the following parameters:

- Temperature >38°C or <36°C.
- HR >90bpm.
- RR >20/min with PaCO2 <32mmHg.
- TLC >12000/dL or <4000/dL.

B. And/or (Severe sepsis or septic shock):

Sepsis with organ dysfunction, hypoperfusion (defined as lactic acidosis (serum lactate level greater than 2 mmol/L), oliguria or acute alteration in mental status) or hypotension defined as (systolic pressure <90mmHg or the need of a vasopressor to maintain a mean arterial pressure of 65 mm Hg or greater) in the absence of hypovolemia.

All included patients were followed-up until discharge or death. Hospitalization outcome was defined as mortality or discharged when improved.

Exclusion criteria:

Excluded from the study were patients with any disease that may be associated with an elevation of cardiac troponins as follows: Ischemic heart disease (IHD) by history or ECG findings, cardio-thoracic trauma or surgery, dilated cardiomyopathy or left ventricular dysfunction, pulmonary embolism that were excluded by trans-thoracic echocardiography TTE, severe pulmonary hypertension, chronic renal failure, known advanced metastatic malignancy or neuromuscular disease. Severe trauma or known exposure to burns and toxic chemicals. Patients after severe exertion were also excluded.

Methods:

All patients were subjected to full medical history, complete clinical examination, ECG, CXR, TTE and full lab, including Cardiac troponin T.QSOFA score was calculated for patients on admission and 2nd day.

A. *Full medical history taking:* Especially history of ischemic heart diseases, hypertension, diabetes, liver diseases, smoking, renal diseases.

B. Complete general examination: including arterial blood pressure, random blood sugar, body temperature and central venous pressure.

C. The Glasgow coma scale:

The severity of altered consciousness is often evaluated with the Glasgow Coma Scale, which consists of three components: 1) eye opening, 2) verbal communication, and 3) motor response to verbal or noxious stimulation. The Glasgow Coma Score is the sum of the three components, and has a range from 3 to 15.

Statistical analysis:

The collected data will be revised, coded, tabulated and introduced to PC using statistical package for social science **(SPSS 15.0.1 for windows; SPSS Inc, Chicago, IL, 2001).** Data will be presented as mean and standard deviation for quantitative parametric data, and median and interquartile range for quantitative non parametric data. Frequency and percentage will be used presenting qualitative data. Suitable analysis will be done according to the type data obtained. **Student T** test or **Mann Whitney** test will be used to analyse quantitative data while **chi square** test and **fisher exact** test will be used to analyse qualitative data. P-value <0.05 will be considered statistically significant.

3. Results

The results are shown in the following Tables (Table 1-11).

Table (1): Characteristics of the whole study population; quantitative variables and number and percentage of patients needed vasopressor or mechanical ventilation and who died during the study

		No. = 70
Age	Mean±SD Range	50.79 ± 11.43 28 – 72
Sex	Female Male	35 (50.0%) 35 (50.0%)
MAP	Mean±SD Range	74.87 ± 16.05 47 – 105
Temp.	Mean±SD Range	38.02 ± 0.47 37 – 39.4
CVP	Mean±SD Range	8.41 ± 2.37 4 – 14
qSOFA0	Mean±SD Range	2.33 ± 0.68 1 – 3
qSOFA2	Mean±SD Range	2.43 ± 0.63 1 – 3
Vasopressor	No Yes	26 (37.1%) 44 (62.9%)
MV	No Yes	23 (32.9%) 47 (67.1%)
Mortality	No Yes	17 (24.3%) 53 (75.7%)
LOS	Mean±SD Range	7.80 ± 2.24 4 – 15

Table (2): Number and percentage of patients with positive and negative troponin T. And patients with positive and negative delta troponin T

		No.	**%**
Troponin T	Negative Positive	35 35	50.0% 50.0%
Delta trop.	Negative Positive	36 34	51.4% 48.6%

Table (3): Characteristics of patients with positive and negative troponin

		Negative Troponin T **No. = 35**	**Troponin T** **No. = 35**	**Test value**	**P-value**	**Sig.**
Age	Mean±SD Range	51.26 ± 11.10 28 – 68	50.31 ± 11.89 29 – 72	0.343•	0.733	NS
Sex	Female Male	14 (40.0%) 21 (60.0%)	21 (60.0%) 14 (40.0%)	2.800*	0.094	NS
MAP	Mean±SD Range	87.69 ± 10.59 65 – 105	62.06 ± 8.52 47 – 79	11.157•	<0.001	HS
Temp.	Mean±SD Range	37.96 ± 0.45 37 – 38.7	38.08 ± 0.48 37.2 – 39.4	-1.052•	0.297	NS
CVP	Mean±SD Range	7.43 ± 2.08 4 – 12	9.40 ± 2.25 5 – 14	-3.808•	<0.001	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*: Chi-square test; •: Independent t-test

Table (4): qSOFA score at admission and after 2 days in patients with positive and negative troponin, and percentage of patients who needed vasopressors in the 2 groups

		Negative Troponin T No. = 35	Troponin T No. = 35	Test value	P-value	Sig.
qSOFA0	Mean±SD Range	1.89 ± 0.58 1 – 3	2.77 ± 0.43 2 – 3	-7.259•	<0.001	HS
qSOFA2	Mean±SD Range	2.00 ± 0.54 1 – 3	2.86 ± 0.36 2 – 3	-7.823•	<0.001	HS
Vasopressor	No Yes	21 (60.0%) 14 (40.0%)	5 (14.3%) 30 (85.7%)	15.664*	<0.001	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*: Chi-square test; •: Independent t-test

Table (5): Comparison between patients with positive and negative troponin as regard mortality, the need for mechanical ventilation and length of ICU stay

		Negative Troponin T No. = 35	Troponin T No. = 35	Test value	P-value	Sig.
MV	No Yes	14 (40.0%) 21 (60.0%)	9 (25.7%) 26 (74.3%)	1.619*	0.203	NS
Mortality	No Yes	14 (40.0%) 21 (60.0%)	3 (8.6%) 32 (91.4%)	9.401*	0.002	HS
LOS	Mean±SD Range	6.71 ± 1.32 4 – 9	8.89 ± 2.46 5 – 15	-4.604•	<0.001	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*: Chi-square test; •: Independent t-test

Table (6): Characteristics of patients with positive and negative delta troponin

		Negative Delta trop. No. = 36	Delta trop. No. = 34	Test value	P-value	Sig.
Age	Mean±SD Range	49.78 ± 11.85 28 – 68	51.85 ± 11.05 33 – 72	-0.757•	0.452	NS
Sex	Female Male	17 (47.2%) 19 (52.8%)	18 (52.9%) 16 (47.1%)	0.229*	0.632	NS
MAP	Mean±SD Range	82.69 ± 12.74 57 – 101	66.59 ± 15.13 47 – 105	4.827•	<0.001	HS
Temp.	Mean±SD Range	38.06 ± 0.43 37.3 – 39	37.97 ± 0.51 37 – 39.4	0.783•	0.436	NS
CVP	Mean±SD Range	7.89 ± 2.26 4 – 13	8.97 ± 2.38 4 – 14	-1.948•	0.056	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*: Chi-square test; •: Independent t-test

Table (7): qSOFA score at admission and after 2 days in patients with positive and negative delta troponin and percentage of patients who needed vasopressors among the 2 groups

		Negative Delta trop. No. = 36	Delta trop. No. = 34	Test value	P-value	Sig.
qSOFA0	Mean±SD Range	2.06 ± 0.63 1 – 3	2.62 ± 0.60 1 – 3	-3.807•	<0.001	HS
qSOFA2	Mean±SD Range	2.06 ± 0.58 1 – 3	2.82 ± 0.39 2 – 3	-6.455•	<0.001	HS
Vasopressor	No Yes	26 (72.2%) 10 (27.8%)	0 (0.0%) 34 (100.0%)	39.066*	<0.001	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*: Chi-square test; •: Independent t-test

Table (8): Comparison between patients with positive and negative delta troponin as regard mortality, the need for mechanical ventilation and length of ICU stay

		Negative Delta trop. No. = 36	Delta trop. No. = 34	Test value	P-value	Sig.
MV	No Yes	20 (55.6%) 16 (44.4%)	3 (8.8%) 31 (91.2%)	17.309*	<0.001	HS
Mortality	No Yes	17 (47.2%) 19 (52.8%)	0 (0.0%) 34 (100.0%)	21.205*	<0.001	HS
LOS	Mean±SD Range	7.00 ± 1.59 4 – 12	8.65 ± 2.53 5 – 15	-3.280•	0.002	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*: Chi-square test; •: Independent t-test

Table (9): Characteristics of patients who died or did not die in this study

		No Mortality No. = 17	Mortality No. = 53	Test value	P-value	Sig.
Age	Mean±SD Range	50.35 ± 13.14 28 – 67	50.92 ± 10.96 33 – 72	-0.178•	0.859	NS
Sex	Female Male	7 (41.2%) 10 (58.8%)	28 (52.8%) 25 (47.2%)	0.699*	0.403	NS
MAP	Mean±SD Range	84.24 ± 13.43 57 – 100	71.87 ± 15.76 47 – 105	2.910•	0.005	HS
Temp.	Mean±SD Range	38.02 ± 0.48 37.3 – 38.8	38.02 ± 0.47 37 – 39.4	0.050•	0.960	NS
CVP	Mean±SD Range	7.53 ± 2.48 4 – 13	8.70 ± 2.28 4 – 14	-1.799•	0.076	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*: Chi-square test; •: Independent t-test

Table (10): qSOFA score at admission and after 2 days in patients who died or did not die in this study. And the number of patients who needed a vasopressor among the 2 groups

		No Mortality No. = 17	Mortality No. = 53	Test value	P-value	Sig.
qSOFA0	Mean±SD Range	2.00 ± 0.71 1 – 3	2.43 ± 0.64 1 – 3	-2.383•	0.020	S
qSOFA2	Mean±SD Range	1.76 ± 0.56 1 – 3	2.64 ± 0.48 2 – 3	-6.246•	<0.001	HS
Vasopressor	No Yes	17 (100.0%) 0 (0.0%)	9 (17.0%) 44 (83.0%)	37.997*	<0.001	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*: Chi-square test; •: Independent t-test.

Table (11): Patients who needed mechanical ventilation and length of ICU stay among patients who died or did not die in this study

		No Mortality No. = 17	Mortality No. = 53	Test value	P-value	Sig.
MV	No Yes	16 (94.1%) 1 (5.9%)	7 (13.2%) 46 (86.8%)	38.195*	<0.001	HS
LOS	Mean±SD Range	7.06 ± 1.34 5 – 9	8.04 ± 2.43 4 – 15	-1.583•	0.118	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*: Chi-square test; •: Independent t-test.

4. Discussion

Sepsis remains an important cause for admission to ICUs accounting for over 25% of all ICU admissions **(Padkin et al., 2003)**. It is known to be the leading cause of death in non-coronary ICUs **(Parrillo et al., 1990)** and the mortality remains high in spite of the recent advances in the management of patients with sepsis **(Yende and Angus, 2007)**. Cardiac troponins (subunits T, I and C) are regulatory proteins that control the calcium-mediated interaction of actin and myosin. Of these three subunits, troponins I and T are specific to myocardium. Troponins T and I are used widely for detecting myocardial damage in acute coronary syndromes andacute heart failure **(Daubert and Jeremais, 2010)**. The value of cardiac troponins I and T in detection of myocardial ischemia and risk stratification has been established beyond doubt **(Giannitsis and Katus, 2004)**.

Cardiac troponins I and T are not elevated in the blood of healthy persons. In addition to the release of cardiac troponins during myocardial infarction, the release of troponins can also occur as a result of the damage of myocytes in conditions, such as trauma, exposure to toxins, sepsis and systemic inflammation **(Ilva et al., 2008)**. Patients with sepsis are known to have elevated troponin even in the absence of coronary artery disease **(Favory and Neviere, 2006)**. The exact mechanism for the elevation of troponins in sepsis remains unclear. However, several mechanisms have been postulated, including ischemia and direct myocardial damage by endotoxins, cytokines or reactive oxygen radicals caused by the infectious process **(Favory and Neviere, 2006)**. The prognostic effects of elevated troponins in patients with sepsis have been studied by several investigators **(John et al., 2010)**. Some investigators found troponin to be an independent predictor, and others found troponin to be elevated inpatients with sepsis but did not independently predictmortality **(Rosjo et al., 2011)**. This variation in the published results might be resulting from the differences in the assays used to quantify troponin and the variability in the cut-off levels to define 'elevated' troponin in the published results; hence it is still a point of debate. Furthermore, most of these studies are relatively small with a sample size ranging between 15 and 46 patients as in **(Mehta et al., 2004) and (Choonngram and partpisanu, 2008)** studies.

Given this variability in the published literature possiblyresulting from small sample sizes, our aim was to evaluate the prognostic value of troponin T in a larger sample of critically ill patients admitted to our ICU with severe sepsis and septic shock.

In the current study, we have investigated the prognostic role of troponin T measurement immediately after admission and after 3 hours (defined as delta troponin) in patients with severe sepsis and septic shock.

The current study was carried out on **(70)** patients with the diagnosis of severe sepsis or septic shock from those attending the intensive care units in Ain Shams university hospitals. Out of these 70 patients, 35 patients had positive troponin T at admission while the other 35 patients had negative troponin T at admission. The outcomes studied at this study were in hospital mortality, the need for a vasopressor, the need for mechanical ventilation and the length of ICU stay.

Out of these 70 patients, 35 patients were males and 35 females. The mean age of the whole study population was **(50.79)** years. The other characteristics of the whole study population showed that mean arterial blood pressure was **(74.87)** mmHg, the mean body temperature was **(38.02)** and the mean central venous pressure was **(8.41)** cmH_2O. The mean qSOFA score at admission and after 2 days was **2.33** and **2.43** respectively. 44 patients **(62.9%)** needed a vasopressor during this study, 47 patients **(67.1%)** needed mechanical ventilation, 53 patients **(75.7%)** died during this study and the mean length of ICU stay was **(7.8)** days.

In our discussion, we will focus on two main studies, the first one was published by **Vallabhajosyula et al., 2017** and was carried on 944 patients in a retrospective manner, and the other study was published by **Salah Eldeen et al., 2012** and this study was carried on 45 patients in a prospective comparative manner. Our study is characterized by having a number of patients intermediate between the two studies. Both studies will be discussed elaborately and compared to our study regarding demographic data, troponin values and clinical outcomes such as mortality, the need for vasopressors, the need for mechanical ventilation and the length of ICU stay.

Vallabhajosyula et al., 2017studied the role of admission troponin-T and serial troponin-T testing inpredicting outcomes in severe sepsis and septic shock. The study population included a historical cohort of all consecutive adult ICU admissions for severe sepsis and septic shock from *January 1, 2007 through December 31, 2014*. This study was designed and conducted before the publication of recently updated sepsis definitions, so the 2001 American College of Chest Physicians/Society of Critical Care Medicine consensus criteria were used to define sepsis. Severe sepsis was defined as consequent organ dysfunction, hypoperfusion, or hypotension, and septic shock was defined as hypotension refractory to fluid resuscitation of 30 mL/kg body weight. Hypoperfusion was defined as blood lactate level ≥2.3 mmol/L, organ dysfunction as Sequential Organ Failure Assessment score ≥2, and hypotension as systolic blood pressure

≤90 mm Hg or a reduction of ≤40 mm Hg from baseline **(Pulido et al., 2012)**. Cardiac TnT was measured with the fourth-generation TnTelectrochemiluminescence immunoassay (Elecsys; Roche Diagnostics, Indianapolis, IN) using the Roche Cobas e411 analyzer. The 99th percentile of upper reference limit value for this assay is <0.01 ng/mL.

Admission TnT values were defined as the first measured TnT level within 6 hours of ICU admission. An elevated admission TnT level was defined as TnT≥0.01 ng/mL. A significant delta TnT level was defined as a rise in 3- and 6-hour TnT≥0.03 ng/mL compared with the admission TnT value. The primary outcome was in-hospital mortality, and secondary outcomes included 1-year mortality, ICU length of stay, and hospital length of stay. In all patients, these outcomes were compared in patients with and without significant TnT elevation. In patients with serial TnT measurements, these outcomes were compared across groups based on presence or absence of elevated admission and delta TnT levels.

During this 8-year period, **944**patients with severe sepsis and septic shock were included in this study. The mean age of this study population was **(72.6)** years. Out of these 944 patients, **539** patients were males and **405** females, **244** patients died during hospital stay and the mean length of ICU stay was **(2.6)** days. Out of the 944 patients with a measured admission TnT, **845 (89.5%)** had elevated admission TnT≥0.01 ng/mL.

In comparison to our study, **Vallabhajosyula et al.**, **2017** included all the patients with elevated troponin T whatever the cause of this elevation, but in our study, we excluded causes of troponin T elevation other than severe sepsis and septic shock such as patients presented with ischemic heart disease, cardiothoracic trauma or surgery, dilated cardiomyopathy or left ventricular dysfunction, pulmonary embolism, severe pulmonary hypertension, chronic renal failure, known advanced metastatic malignancy or neuromuscular disease, severe trauma or known exposure to burns or toxic chemicals and patients presented after severe exertion. This difference in inclusion criteria between our study and **Vallabhajosyula et al., 2017** as well as the larger number of patients account for some of the differences found in the results. In addition **Vallabhajosyula et al., 2017** study is a retrospective study that has been carried out over 8 years.

In the current study, comparison between patients with positive and negative troponin T at admission revealed that mean and standard deviation of age (mean ± SD) was **(51.26 ± 11.10)** years in troponin T negative group and **(50.31 ± 11.89)** years in troponin T positive group with p-value **(0.733)**. Male patients represented **60%** of patients with negative troponin T at admission while female patients represented **40%**, and male patients represented **40%** in troponin T positive patients while female patients represented **60%** with p-value **(0.094)**.

The (mean ± SD) of mean arterial blood pressure among troponin T negative patients was **(87.69 ± 10.59)** mmHg, while it was lower **(62.06 ± 8.52)** mmHg among patients with positive troponin T at admission and this difference reflects the severity of illness in troponin T positive group as there is more vasodilatation and reduced mean arterial blood pressure caused by endotoxins effects on the vasculature and depressed myocardial contractility. The (mean ± SD) of body temperature in troponin T negative patients was **(37.96 ± 0.49)** and **(38.08 ± 0.48)** in troponin T positive patients with p-value **(0.297)**, this higher elevation in body temperature in troponin T positive group points to more severe sepsis in this group as compared to troponin T negative group.

The (mean ± SD) of central venous pressure was **(7.43 ± 2.03)** in troponin negative group and **(9.40 ± 2.25)** in troponin positive group, fluid therapy and the use of vasoconstrictor agents make central venous pressure evaluation not reliable as a marker of the severity of the medical condition.

The (mean ± SD) of qSOFA score at admission was **(1.89 ± 0.58)** in troponin T negative group and **(2.77 ± 0.43)** in troponin T positive group with highly significant p-value, while the (mean ± SD) of qSOFA score after 2 days was **(2.00 ± 0.54)** in troponin T negative group and **(2.86 ± 0.36)** in troponin T positive group with highly significant p-value, the higher qSOFA score both at admission and after 2 days in the troponin T positive group is a proof for the poor prognosis in troponin T positive group more than the troponin T negative group.

In troponin T negative group, 14 patients **(40%)** needed a vasopressor, while 30 patients **(85.7%)** of troponin T positive group needed a vasopressor with a highly significant p-value, the greater need for vasopressors in troponin T positive group may be due to more bacterial endotoxins elaborated in the troponin T positive group, and these endotoxins affect vascular wall causing vasodilatation. In troponin T negative group, 21 patients **(60%)** needed mechanical ventilation and 26 patients **(74.3%)** in troponin T positive group needed mechanical ventilation with non-significant p-value, this slight increase in incidence of mechanical ventilation use in troponin T positive patients may be due to increased incidence of acute lung injury in patients with severe sepsis and septic shock.

The length of ICU stay increased markedly among patients with positive troponin T, the (mean ± SD) of LOS was **(6.71 ± 1.32)** days in troponin T

negative group and **(8.89 ± 2.46)** days in troponin T positive group with highly significant p-value.

Mortality occurred in **21 out of 35** patients in troponin T negative group in contrast to **32 out of 35** patients in troponin T positive group with highly significant p-value reflecting the much more severity of illness in troponin T positive group.

In **Vallabhajosyula et al., 2017** study, comparison between patients with positive and negative troponin T at admission revealed that mean age was **(70)** years in troponin T negative group and **(73)** years in troponin T positive group with p-value **(0.03)**. Male patients represented **48.5%** of patients with negative troponin T at admission while female patients represented **51.5%**, and male patients represented **58.1%** in troponin T positive patients while female patients represented **41.9 %** with p-value **(0.07)**.

In troponin T negative group, 53 patients **(53.5%)** needed mechanical ventilation and 387 patients **(45.8%)** in troponin T positive group needed mechanical ventilation with p-value **(0.17)**, this unexpected increase in the percentage of patients who needed mechanical ventilation in troponin T negative group may be due to reduced number of patients in this group **(99 patients)** in comparison to **(845 patients)** in troponin T positive group. Patients with anelevated admission TnT did not have a higher rate of in-hospital mortality than patients without elevated admission TnT **(26.3% versus 22.2%; P=0.47)**, this statistically insignificant difference between patients with and without elevated troponin T at admission may be due to the inclusion of patients with severe comorbidities such as renal failure and pulmonary embolism which affected the outcome of patients in this study.

In comparison to our study, **Vallabhajosyula et al., 2017** study showed statistically insignificant difference between patients with positive and negative troponin T at admission as regard the need for mechanical ventilation which was the case in our study, while in our study there was statistically significant difference between patient with positive and negative troponin T at admission as regard mortality inside ICU in contrast to statistically insignificant difference between the two groups in **Vallabhajosyula et al., 2017** study. This difference may be due the inclusion of patients with pathologies other than sepsis such as pulmonary embolism and after trauma and cardiothoracic surgerywhich are more likely to respond to treatment and show a better prognosis. Also, **Vallabhajosyula et al., 2017** study has a better indication of patient prognosis as they followed up 1 year mortality, but our study did not trace mortality up to 1 year.

Anotherstudy published by **Salah Eldeen et al., 2012** evaluated the prognostic value of cTnI on mortality and adverse complications in patients with sepsis and septic shock. A prospective comparative study was conducted on **forty five** patients admitted to the ICU with sepsis or septic shock. Then patients were divided into 2 groups; group 1: included **20** patients with positive cTnI **(mean age 58±18.9yrs, 40% males)** and group 2: included **25** patients with negative cTnI **(mean age 52±19.3yrs, 64% males)**; comparisons between the 2 groups were done according to all demographic, scoring systems, medications used and adverse outcome.

There were no statistically significant differences between the 2 groups regarding demographic data and comorbid diseases, but **HR, MAP and SBP** were significantly different between the 2 groups, while patient **temperature and central venous pressure (CVP)** were not statistically different between the 2 groups, these statistically insignificant differences between the two groups may be due to fluid replacement, use of vasopressors and antipyretics.

Patients with elevated cTnI were more critically ill as reflected by higher APACHE II scores at study entry and SOFA score on admission and on 2nd day: APACHE II was **(34.6±10.9vs.17.8±5.4, *p*-value=0.001)**, SOFA on admission **(14.9±4.2 vs. 6.9±4.5, *p*-value=0.0001)** and SOFA at 2nd day **(15.8±5.4 vs. 5.5±4.4, *p*-value=0.0001)**. The need for vasopressors was significantly higher in cTnI positive group than the cTnI negative group **(85% vs. 24%, *p*-value=0.0001)**. As regard the need for mechanical ventilation, its duration and length of stay (LOS) in ICU; no significant differences were found between the 2 groups. Mortality was significantly high in group 1 than group 2 **(90% vs. 60%, *p*-value=0.024)**.

Comparison between our study and **Salah Eldeen et al., 2012** study revealed that mortality was higher showing statistically significant difference between patients with positive troponin and patients with negative troponin on admission in the two studies, while the need for mechanical ventilation showed statistically insignificant difference between the patients with positive and negative troponin in the two studies. The length of ICU stay showed statistically significant difference between patients with positive and negative troponin in our study in contrast to statistically insignificant difference in **Salah Eldeen et al., 2012** study which included a very limited number of patients (45 patients).

However, **Salah Eldeen et al., 2012** study did not include delta troponin values as a predictor of outcome of patients with severe sepsis and septic shock.

In the current study, comparison between patients with positive and negative delta troponin T

revealed that mean and standard deviation of age (mean ± SD) was **(49.78 ± 11.85)** years in delta troponin T negative group and **(51.85 ± 11.05)** years in delta troponin T positive group with p-value **(0.452)**. Male patients represented **52.8%** of patients with negative delta troponin T at while female patients represented **47.2%**, and male patients represented **47.1%** in delta troponin T positive patients while female patients represented **52.9%** with p-value **(0.632)**. The (mean ± SD) of mean arterial pressure among delta troponin T negative patients was **(82.69 ± 12.74)** mmHg, while it was lower **(66.59 ± 15.13)** mmHg among patients with positive delta troponin T. The (mean ± SD) of body temperature in delta troponin T negative patients was **(38.06 ± 0.43)** and **(37.97 ± 0.51)** in delta troponin T positive patients with p-value **(0.436)**. The (mean ± SD) of central venous pressure was **(7.89 ± 2.26)** in delta troponin negative group and **(8.97 ± 2.38)** in delta troponin positive group.

The (mean ± SD) of qSOFA score was **(2.06 ± 0.63)** in delta troponin T negative group and much higher **(2.62 ± 0.60)** in delta troponin T positive group with highly significant p-value, while the (mean ± SD) of qSOFA score after 2 days was **(2.06 ± 0.58)** in delta troponin T negative group and also higher **(2.82 ± 0.39)** in delta troponin T positive group with highly significant p-value.

In delta troponin T negative group, 10 patients **(27.8%)** needed a vasopressor, while 34 patients **(100%)** of delta troponin T positive group needed a vasopressor with a highly significant p-value which reflects the severe compromise in hemodynamics in patients with positive delta troponin T positive patients. In delta troponin T negative group, 16 patients **(44.4%)** needed mechanical ventilation and 31 patients **(91.2%)** in delta troponin T positive group needed mechanical ventilation with highly significant p-value pointing to the higher incidence of acute lung injury in delta troponin T positive patients.

The length of ICU stay increased markedly among patients with positive delta troponin T, the (mean ± SD) of LOS was **(7.00 ± 1.59)** days in delta troponin T negative group and **(8.65 ± 2.53)** days in delta troponin T positive group with highly significant p-value.

Mortality occurred in **19 out of 36** patients in delta troponin T negative group in contrast to **all** patients in delta troponin T positive group with highly significant p-valueproving more severe illness in delta troponin T positive group.

In **Vallabhajosyula et al., 2017** study, comparison between patients with positive and negative delta troponin T revealed that mean age was **(73)** years in delta troponin T negative group and **(74)** years in delta troponin T positive group with p-value **(0.27)**. Male patients represented **56.9%** of patients with negative delta troponin T while female patients represented **43.1%**, and male patients represented **61.7%** in delta troponin T positive patients while female patients represented **38.3 %** with p-value **(0.24)**. In delta troponin T negative group, 241 patients **(45%)** needed mechanical ventilation and 112 patients **(57.1%)** in delta troponin T positive group needed mechanical ventilation with p-value (0.004). In comparison to patients without significant delta TnT, patients with elevated delta TnT had higher in-hospital mortality **(30.6% versus 23%; P=0.04).**

Similar to our study, **Vallabhajosyula et al., 2017** study showed that the need for mechanical ventilation and mortality showed statistically significant difference between patients with positive and negative delta troponin T reflecting the severity of the medical condition in delta troponin T positive patients. The other outcomes were not followed up in delta troponin T positive and negative patients in **Vallabhajosyula et al.**, **2017** study.

In the current study, comparison between patients who died or not during the study revealed that age, sex, body temperature and mean central venous pressure showed statistically insignificant difference between the two groups, while the mean arterial pressure showed high statistically significant difference between the two groups.

Q SOFSA scores were higher in the delta troponin group. qSOFA score at admission and after 2 days showed statistically significant and highly statistically significant differences respectively between the two groups and this highlights the importance of qSOFA score in the follow up of patients with severe sepsis and septic shock.

APACHE score was also used in **Vallabhajosyula et al., 2017** study and **Salah Eldeen et al., 2012** study and also showed a good predictive value for the occurrence of mortality in patients with severe sepsis and septic shock with delta troponin positive patients recording significantly higher APACHE score.

We still need to conduct further large scale studies to conclude whether troponin is an independent or not an independent predictor of outcome of patients with severe sepsis and septic shock. Nevertheless it seems very clear that positive troponin and delta troponin are predictors of poor patient outcomes.

5. Conclusion

- Outcomes such as the need for vasopressors, mortality and longer length of stay showed increased incidence among patients with elevated troponin T at admission, while the need for mechanical ventilation did not show a significant difference between patients with positive and negative troponin T at admission.

- Mortality, the need for mechanical ventilation, the length of ICU stay and the need for vasopressors increased significantly among patients with positive delta troponin T.
- There was increased mortality among patients with reduced mean arterial blood pressure and the incidence of mortality increased in patients who needed vasopressor or mechanical ventilation, and also the incidence of mortality increased in patients with higher qSOFA score.

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