



Elevation of Troponin-I in Sepsis & Septic Shock

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Abstract

The study of Elevation of troponin I in sepsis and septic shock on 40 patients was conducted in KIMS Hospital and research centre ICU, Bangalore during the period from November 2012 to May 2014. Cases were selected according to the sepsis criteria and enrolled for study. Objective: To determine the association of elevated cTnI levels in patients with sepsis and septic shock.

Methodology & Results: *Data were analyzed between sepsis and septic shock groups and between troponin I positive and negative groups. The average age groups in sepsis were 47.7 and in septic shock were 53.8. Males were mostly affected in both sepsis and septic shock groups (67%) than females (32.5%). ECG was normal in majority of patients and sinus tachycardia seen in majority of patients with septic shock. ECHO showed normal in all patients expect in two patients in septic shock group who had global hypokinesia. Majority of Patients were diagnosed with Pneumonia (45%). Troponin I showed positive in 29(72.5%) patients and normal in 11(27.5%) patients which was statistically significant. Troponin I showed positive, more in septic shock group 19(95%) as compared to sepsis group 10(50%). In majority of cTnI positive patients CK (18(62.0%) and CK-MB 17(58.6%) was elevated which is not significant. Troponin I positive patients requiring ventilatory support (82.7%), dialysis (24.1%), ionotropic support (65.5%) were more than patients in negative group requiring ventilatory support (45%), dialysis 2(18.1%) and ionotropic support(9%). In troponin I positive group from all cultures gram positive isolated was 11(63.6%) and gram negative was 28(96.5%). In troponin I negative group from all culture gram positive isolated were 7(37.9%) and gram negative were 5(45.4%). Isolation of gram positive and gram negative organisms in troponin I positive group was 39(134.4%) compared to negative group which is 12(109.09%). Isolation of fungi and virus (H1N1) in troponin I positive group showed 6(20.6%) compared to negative group which is 1(90.9%) showing statistically significant.*

Conclusion: *Elevation of troponin I in sepsis and septic shock indicates inflammatory and toxic damage to heart apart from ischemic damage caused by myocardial Infarction.*

Introduction

Troponin I is a cardiac biomarker, it is elevated in Acute MI. It gives risk stratification and bad prognosis. It is also elevated in critically ill patients like sepsis and septic shock. It is also seen in pulmonary embolism, exacerbation of COPD, snake bite, Rhabdomyolysis.

In this study we have studied association of Trop I in sepsis and septic shock. It is observed in 31-80% of patients with SIRS, sepsis, septic shock. Its association in MI indicates irreversible ischemic damage. In sepsis the elevation is due to Inflammatory and reversible damage to the heart. The presence of cardiovascular dysfunction in

sepsis is associated with increased mortality rate of 70%-90% compared with 20% in septic patients without cardiovascular impairment. Thus myocardial dysfunction in sepsis has been the focus of intense research activity. Myocardial injury is common in patients without acute coronary syndrome.

Objective

- To determine the association of elevated cTnI levels in patients with sepsis and septic shock.
- To detect Myocardial damage in patients without Acute Coronary Syndrome.
- To determine cTnI values as an indicator for toxic and inflammatory damage to the heart apart from ischemic damage caused by MI.

Methodology

A total of 40 Patients aged >18years with a diagnosis of sepsis and septic shock admitted in KIMS Hospital and Research Centre from ICU were enrolled in the study. The study was conducted for a period of 18 months from November 2012 to May 2014, 40 Patients with prior history of heart disease and with ECG changes were excluded. Informed consent was obtained from patients relatives. Detailed history was taken in all the patients with respect to presenting complaints, Predisposing factors and accompanying illness. A thorough Clinical examination was carried out.

Investigations like CBC, Platelet Count, Serum electrolytes, RBS, ABG, RFT, LFT, PT, APTT, INR, Urine routine, ECG, ECHO, Cardiac Enzymes, Troponin I were done for all the patients on the day of admission. Troponin I were done by ELISA method. Chest X-ray, USG-Abdomen and Pelvis, Blood Culture, Urine Culture, Swab Culture and Sputum Culture were analyzed for all the patients.

Exclusion Criteria

Patients with Acute Coronary Syndrome, Clinical Evidence of Congestive Cradiac failure, cardiac pulmonary resuscitation/defibrillation before admission. History of Previous Cardiac disease and patients with ECG Changes were excluded.

Statistical Methods

Categorical data is presented as numbers (percents) and continuous data as mean and median. Pearson Chi-test was used to compare categorical and continuous variables.

Chi square test

$$\chi^2 = \frac{\sum(O_i - E_i)^2}{E_i}$$
 where O_i is observed frequently and E_i is expected frequency

P value of <0.01: very strong presumption against null hypothesis.

0.01 < p < 0.05: strong presumption against null hypothesis.

0.05 < p < 0.1: low presumption against null hypothesis.

p > 0.1: no presumption against null hypothesis.

Results

Out of 40 individuals, 20 patients were with sepsis and 20 patients with septic shock were included in the study. In sepsis group, 15 male (75%), 5 female (5%) were seen which was statistically not significant. In septic shock group 12 males (60%), 8 females (40%) were seen which was statistically not significant. Mean age observed in sepsis group were 47.7 and septic shock was 53.8. In sepsis group ECG was normal in 11(55%) Patients, LVH in 1(5%) patient and sinus Tachycardia in 8(40%) patients.

In septic Shock group ECG was normal in 2(10%) patients, sinus tachycardia in 18(90%) patients. In sepsis group ECHO was normal in all 20 patients, (Mean EF-58%, SD-0.047). In Septic shock group ECHO was normal in 18 patients, Global Hypokinesia was seen in 2 patients with EF of 48%, 42%. (Mean EF-57%, SD-0.036). Total Mean EF was 58% with SD 0.0427. There was no significant difference of ECHO in sepsis and septic shock group. In Sepsis group mean PR was

114.05 SD 7.990,mean RR 37.19 SD 4.106,mean SBP 121.70 SD 14.970,mean DBP 78.00 SD 8.944, Temperature 100.91 F, SD 0.701.

In septic shock group mean PR was 121.5 SD 9.942,RR 41.06 Sd 3.589,SBP 77.78 SD 20.452, DBP 54.38 SD 9.369, Temperature 100.53 SD 0.640. Out of 40 Patients 23 had Pre Existing Co-morbidities, 17 had no co-morbidities.

In Sepsis, COPD+ Hypothyroidism was seen in one patient, DM in 6 Patients, HTN in 2 Patients, DM+HTn in 2 Patients, HTN+OLDCVA in 1 patient,8 Patients without any co-morbidities. In septic Shock group, HTN was seen in 1 patient, COPD in 1 patient, DM in 3 Patients, DM+HTN

in 6 Patients and 9 patients without any co-morbidities.

In sepsis group 9 patients with pneumonia,4-cellulitis,1-urosepsis,1-cholecystitis,mixed infections like leptospirosis +urosepsis in 1 patient, Cellulitis+urosepsis in 1 patient, pneumonia+cellulitis in 1 patient, pneumonia+urosepsis in 2 patients were seen which was statistically not significant.

In septic shock group 9 patients with pneumonia, 3-cellulitis,2-urosepsis,1-dengue,mixed infections like cellulitis+urosepsis in 1 patient, pneumonia+urosepsis in 3 patients, dengue+urosepsis in 1 patient were seen which was statistically not significant.

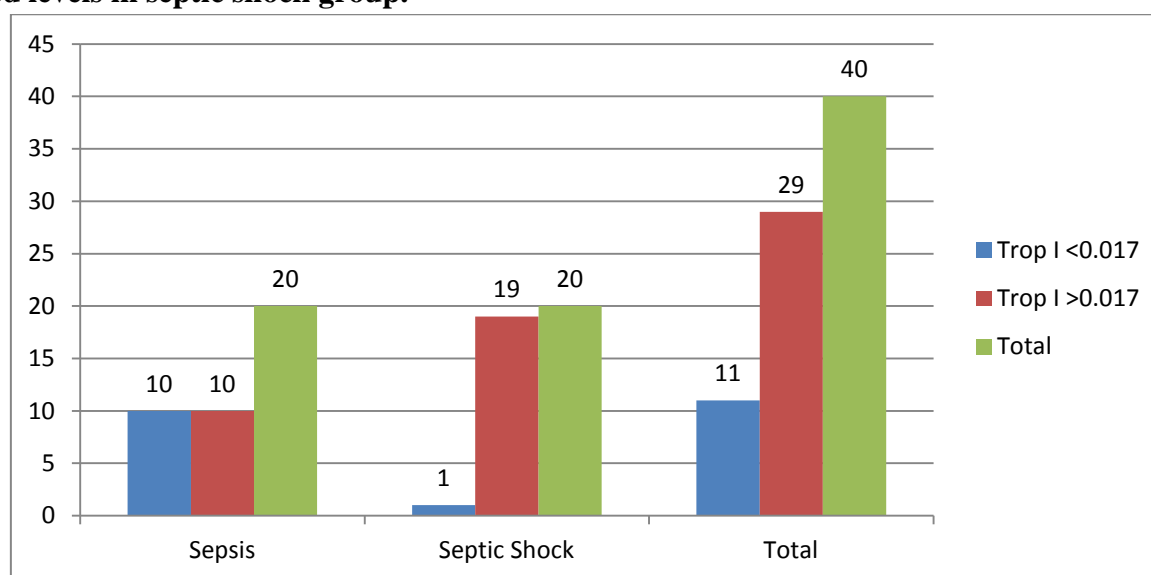
Troponin I category in sepsis and septic shock patients

DIAGNOSIS	TROP I		TOTAL
	<0.017 microgm/I	>0.017microgm/I	
Sepsis	10(50%)	10(50%)	20
			50.0%
Septic shock	1(5%)	19(95%)	20
	11	29	50.0%
Total	27.5%	72.5%	40
P Value			0.001438

Troponin I value of 0.017 micrograms/I is taken as cutoff value from our lab. In Sepsis group, Troponin I was positive in 10(50%) patients and normal in 10(50%) Patients. In septic shock group Troponin I was positive in 19(95%) patients and

normal in 1(5%) patient. Elevation of Troponin I was statistically significant with a P value of 0.001438 showing a trend of increased levels in septic shock group.

No. of patients with elevated and normal value of troponin I in sepsis and septic shock with a trend of increased levels in septic shock group.



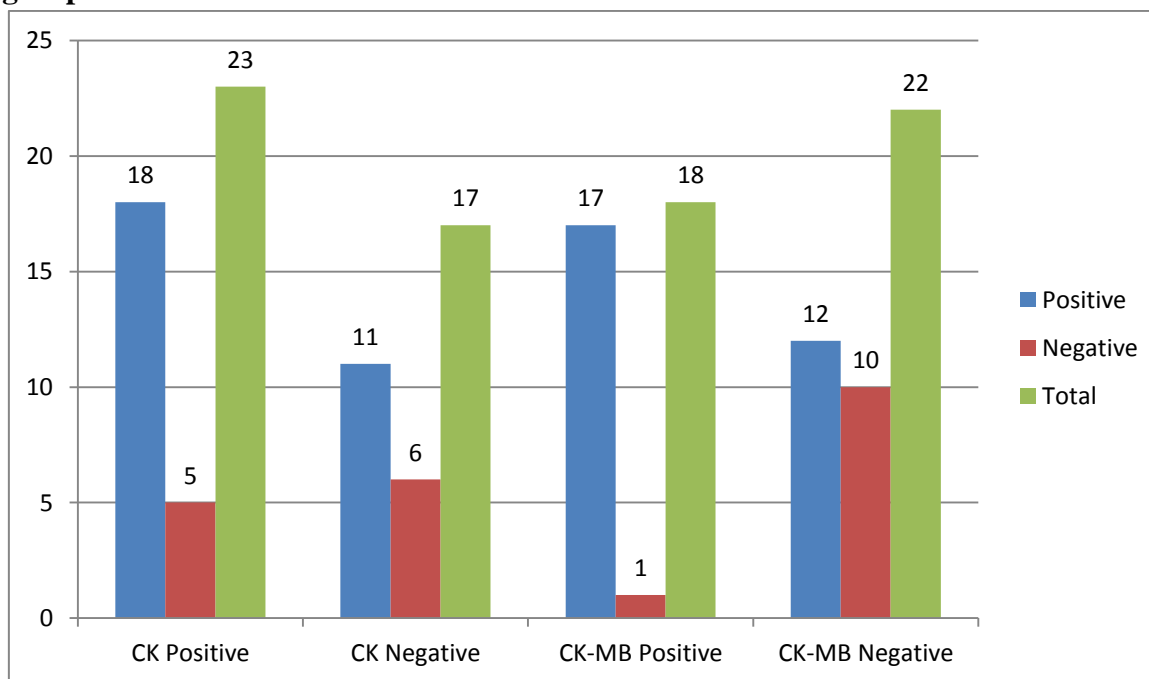
Troponin I in comparison with Elevated Cardiac C enzymes

Troponin I (<0.017)	C K Positive	C K Negative	Median of CK in relation to Trop I	CK-MB Positive	CK-MB Negative	Median of CK-MB in relation to Trop I
Positive(29)	18(62.0%)	11(37.9%)	402,32	17(58.6%)	12(41.3%)	32,3.5
Negative(11)	5(45.4%)	6(54.5%)	172,25	1(9.09%)	10(90.9%)	5
Total(40)	23(57.5%)	17(42.5%)		18(45%)	22(55%)	
P Value		0.342558			0.004931	

In troponin I positive group CK was elevated in 18(62.0%) patients, normal in 11(37.9%) patients. In troponin I negative group CK was elevated in 5(45.4%) patients, normal in 6(54.5%) patients. Out of 40 patients CK was elevated in 23(57.5%) patients, negative in 17(42.5%) patients. Elevation of CK in relation to troponin I was statistically not significant with a P Value of 0.342558. Median Total CK elevation in troponin I Positive patients was 402 as compared to 172 in troponin I negative patients.

In troponin I positive group CK-MB was elevated in 17(58.6%) and normal in 12(41.3%) patients. In troponin I negative group CK-MB was elevated in 1(9.09%) and normal in 10(90.9%) patients. Out of 40 Patients CK-MB was elevated in 18(45%) and normal in 22(55%) patients. Elevation of CK-MB in relation to troponin I was statistically significant with a P value of 0.004931. Median total CK-MB elevation in troponin I positive patients was 32 as compared to 1 in troponin I negative patients.

Elevation of cardiac enzymes in relation to Troponin I showing increased elevation in troponin I positive group.



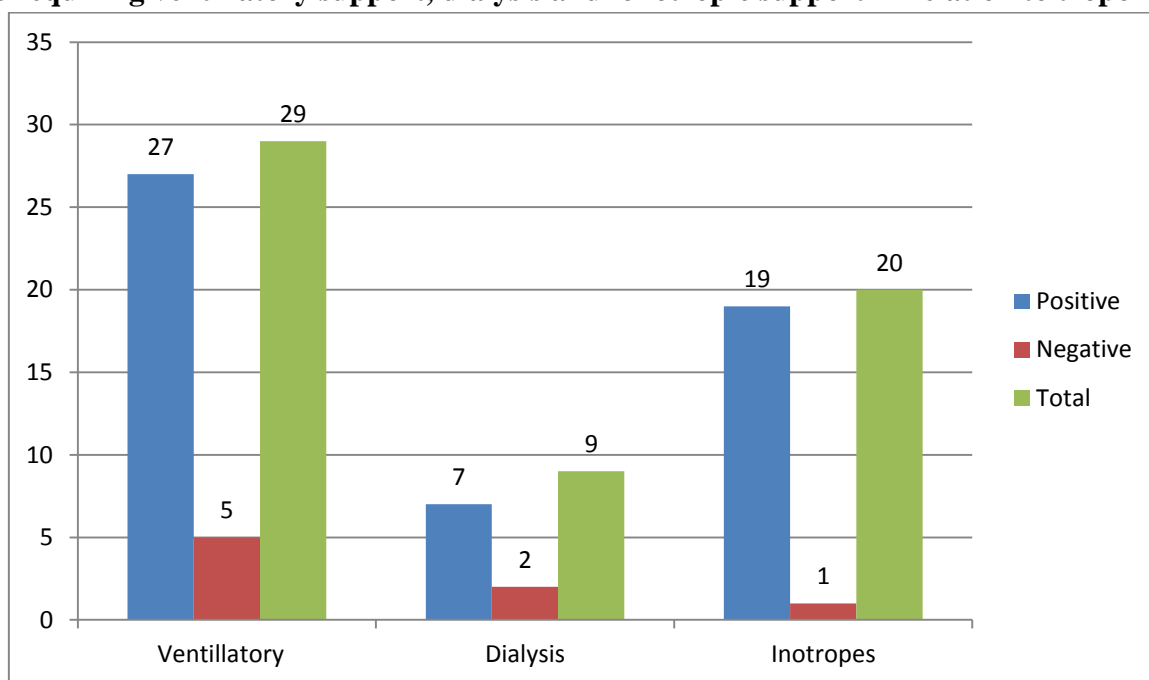
In troponin I positive group 24(82.7%) patients required ventilatory support, 7(24.1%) patients required dialysis and 19(65.5%) required ionotropic support. In troponin I negative group 5(45%) patients required ventilatory support, 2(18.1%) patients required dialysis and 1(19%) required ionotropic support. Out of 40

patients 29(72.5%) patients required ventilatory support, 9(22.5%) patients required dialysis and 20(50%) required ionotropic support. Patients requiring ventilatory support in relation to troponin I elevation was statistically significant with a P value of 0.018309.

Patients requiring inotropic support in relation to troponin I elevation was statistically significant with a P value of 0.001438, Whereas patients

requiring dialysis in relation to troponin I elevation was statistically not significant with a P value of 0.687098.

Patients requiring ventilatory support, dialysis and inotropic support in relation to troponin I



Inotropes I in relation with type of Pathogen Isolated in Sputum Culture

TROPONIN I	GRAM POSITIVE	GRAM NEGATIVE	VIRAL (H1N1)	FUNGAL	TOTAL
POSITIVE	4(13.7%)	15(51.7%)	1(3.4%)	1(3.4%)	21(72.4%)
NEGATIVE	1(9.09%)	2(18.1%)	0	1(9.09%)	4(36.3%)
TOTAL	5(12.5%)	17(42.5%)	1(2.5%)	2(5%)	25(62.5%)
P VALUE					1.2777

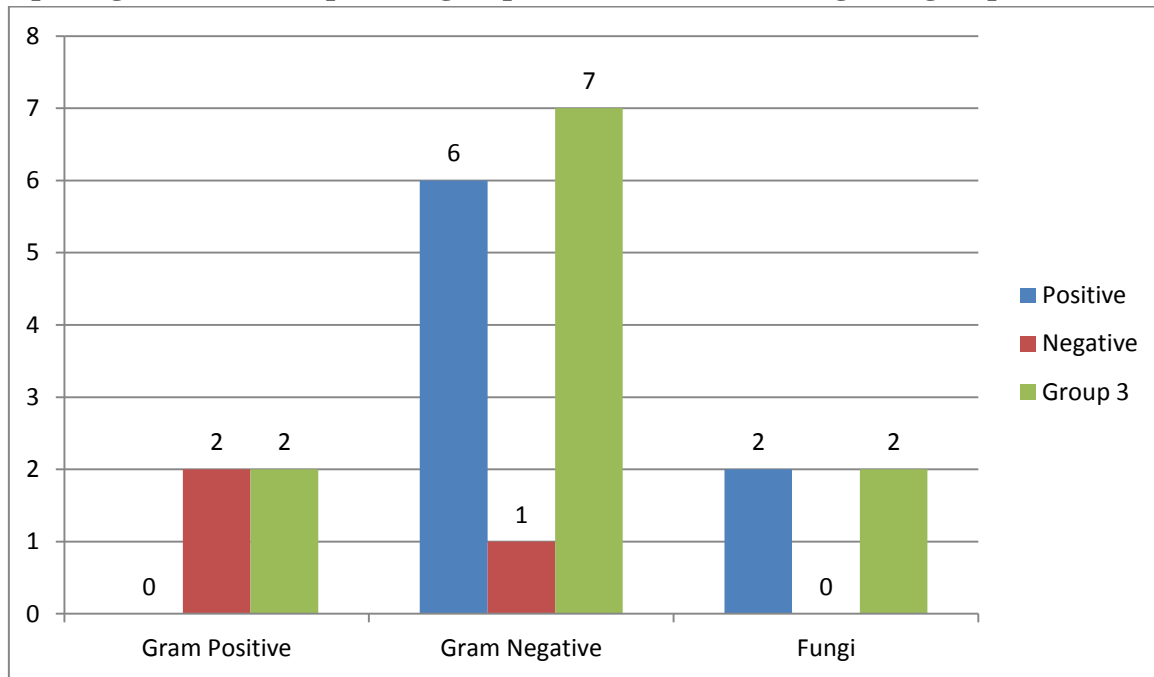
In Troponin I positive group gram positive isolated was 4(13.7%), gram negative 15(51.7%),viral (H1N1) 1(3.4%) and fungi 1(3.4%). In troponin I negative group gram positive was isolated in 1(9.09%), gram negative in 2(18.1%), fungal in 1(9.09%) patients. In troponin I Positive group total no. of pathogens isolated were 21(72.4%) as compared to 4(36.3%) in troponin I negative group which was not statistically significant with a P value of 1.2777.

2(18.18%), gram negative 1(9.09%), fungi was not isolated. In troponin I positive group total no. of pathogens isolated were 8(27.5%) as compared to 3(27.2%) in troponin I negative group which was statistically significant with a P value of 0.035462.

Troponin I in relation with Type of Pathogen isolated in urine culture

In troponin I positive group gram positive was not isolated, gram negative isolated was 6(20.6%), and fungi was 2(6.89%) patients. In troponin I negative group gram positive isolated was

Type of pathogens isolated from urine culture in relation to troponin I positive and negative groups where the pathogens isolated in positive group were more than the negative group.



Troponin I in relation with type of pathogens isolated in Blood Culture

TROP I	GRAM POSITIVE	GRAM NEGATIVE	FUNGAL	TOTAL
POSITIVE	4(13.7%)	4(13.7%)	2(6.89%)	10(34.4%)
NEGATIVE	1(9.09%)	1(9.09%)	0	2(18.1%)
TOTAL	5(12.5%)	5(12.5%)	2(5%)	12(30%)
P VALUE				0.000395

In troponin I positive group gram positive isolated was 4(13.7%), gram negative 4(13.7%), and fungi 2(6.89%). In troponin I negative group gram positive isolated was 1(9.09%), gram negative 1(9.09%), fungi was not isolated. In troponin I positive group total no. of pathogens isolated were 10(34.4%) as compared to 2(18.1%) in troponin I negative group which was statistically significant with a P value of 0.000395.

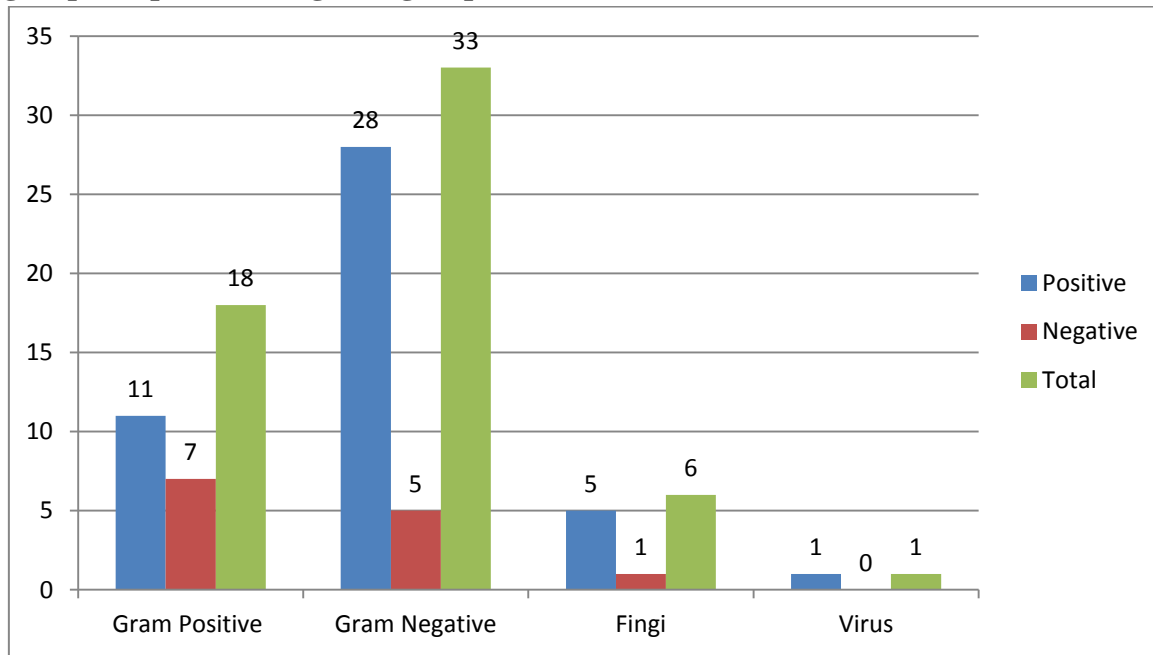
In troponin I positive group gram positive isolated weres 3(10.3%) and gram negative was 3(10.3%). In troponin I negative group gram positive was isolated in 3(27.2%) and gram negative was 1(9.09%). In troponin I positive group total no. of pathogens isolated were 6(20.6%) as compared to 4(36.3%) in troponin I negative group which was statistically not significant with a P value of 0.429195.

Type of Pathogen isolated in All Culture

In troponin I positive group from all culture gram positive isolated was 11(63.6%) and gram negative was 28(96.5%). In troponin I negative group from all culture gram positive isolated was 7(37.9%) and gram negative was 5(45.4%). Isolation of gram positive and gram negative organisms in troponin I positive group was 39(134.4%) compared to negative group which was 12(109.09%) which was statistically significant with a P Value of 0.05

In troponin I positive group from all cultures fungi isolated was 5(17.2%) and Virus(H1N1) was 1(3.4%). In troponin I negative group from all culture fungi isolated was 1(9.09%) and virus (H1N1) was not isolated. Isolation of fungi and virus (H1N1) in troponin I positive group was 6(20.6%) compared to negative group which was 1(9.09%) which was statistically significant with a P Value of 0.021161.

Type of Pathogen isolated in all culture where more number of pathogens are isolated in Troponin I Positive group compared to Negative group.



Discussion

In AMMAN et al Study. Troponin I in sepsis and septic shock were positive in 85% patients with a p value 0.0001 which showed majority of patients with sepsis and septic shock had elevated cTnI levels indicating inflammatory myocardial damage to heart in sepsis.⁸ In present study Troponin I is positive in 72.5% of patients with a p value of 0.001438 which is significant.⁸

In AMMAN et al study among cTnI positive patients gram positive pathogens isolated were 53% and gram negative pathogens isolated were 25 % whereas in present study gram positive pathogens isolated were 63.6% and gram negative pathogens isolated were 96.5%.⁸

In AMMAN et al, median total CK elevation in troponin I positive patients was 411U/L, median total CK-MB elevation in troponin I positive patients was 33U/L. In present study median total CK elevation in troponin I positive patients was 402U/L, median total CK-MB elevation in troponin I positive patients was 32 U/L.

In David R. Altmann et al study pneumonia was seen in 14(37%) patients, Cholecystitis in 3(8%) pts, Urosepsis in 1(3%) pts whereas in present study pneumonia was seen in 18(45%) patients, Cholecystitis in 1(5%) patients, Urosepsis in 3

(7.5%) pts⁴. In David R Altmann et.al study gram positive organisms isolated was 15(40%), gram negative organisms isolated was 11(29%), fungi was 2(5%)⁽⁴⁾ whereas in present study gram positive organisms isolated was 18(45%) gram negative was 33(82.5%) and fungi was 6(15%). In David R.Altmann et.al⁹ study cTnI positive patient requiring ventilator support was 14(64%) and troponin I negative group was 8(50%) with a P value 0.51. In David R.Altmann et.al study cTnI positive patients requiring dialysis was 10(45%) and negative group 6(38%) with a P value 0.74 In David R.Altmann et.al study the need for mechanical ventilation and dialysis did not differ in troponin I positive and negative groups. In present study cTnI positive patient requiring ventilator support was 24(82.7%) and negative group requiring was 5(45%) which was statistically significant with a P value 0.018309. In the present study cTnI positive patients requiring dialysis dialysis were 7(24.1%) and negative group was 2(18.1%) which was statistically not significant with a P value of 0.687098.

In Mehta NJ et.al study CTnI positive patients requiring inotropic support were 94% and in cTnI normal patients were 53% with a P Value of 0.018 indicating increased morbidity and

mortality. In Present Study cTnI positive patients requiring inotropic support was 65.5% and in cTnI normal patients was 9% with a P Value 0.001438 which is significant.

In this study, we have studied association of troponin I levels in sepsis and septic shock. Troponin I, a cardiac biomarker which is elevated in Acute Myocardial Infarction is also associated to be elevated in critically ill patients like sepsis and septic shock which is observed in 72.5% of patients in our study which was statistically significant (P Value 0.0014378). 95% of patients with septic shock had elevated troponin I levels which indicates ongoing severe myocardial depression caused by various mechanisms of sepsis, which indicates increased morbidity and close monitoring of these patients is required. 82.7% patients with elevated troponin I had ventilatory support (P Value 0.018309) which was statistically significant indicating increased morbidity. 65.5% patients had inotropic support which was statistically significant (P Value 0.001438), which indicates increased morbidity.

In troponin I Positive group CK was elevated in 18(62.0%) patients of patients. Elevation of CK in relation to Troponin I was statistically not significant with a P value of 0.342558. In troponin I Positive group CK-MB was elevated in 17(58.6%) patients. Elevation of CK-MB in relation to troponin I was statistically significant with a P value of 0.004931.

This shows that cardiac enzyme elevation is not independent of troponin I elevation but it is not specific and significant as it can be elevated in other conditions like muscle injury, trauma, renal failure etc. and also cardiac specificity compared to troponin I is less.

96.5% of patients with gram negative and gram positive bacteria were isolated in troponin I positive which was statistically significant (P Value 0.05) which indicates that there could be endotoxin associated myocardial depression as it is one of the significant exogenous myocardial depressant substance released by gram negative bacteria proposed to cause myocardial depression,

lower svr, lower mean EF by activating inflammatory mediators and inflammatory cascade and similar inflammatory damage by other mechanisms by gram positive bacteria.

Isolation of fungi and virus (H1N1) also contribute to elevation of troponin I by activating inflammatory mediators was also statistically significant (P Value 0.021161). It indicates that cTnI is not only associated in myocardial infarction which is an indicator of irreversible ischemic damage, it can be elevated in conditions that cause inflammatory, toxic reversible damage to heart. It also indicates increased morbidity. ECG, ECHO may be normal in early stage of sepsis and septic shock when the underlying myocardial damage is undergoing.

Troponin I had greater sensitivity for minor degree of myocardial injury and also its isoform encoded by specific genes unique to myocardium makes it, a more reliable indicator to detect myocardial damage seen in majority of patients in sepsis and septic shock. Diagnostic test is also quick, convenient and cost effective.

Abnormalities of Cardiac function are frequent in patients with sepsis. Approximately 50% of patients with severe sepsis and septic shock may develop impairment of ventricular performance. Whereas evaluation of myocardial performance during septic shock is of critical importance to select the best therapeutic options, several factors complicate the diagnosis of sepsis induced myocardial dysfunction. Recently, Plasma cardiac troponin has been proposed has a biomarker that accurately detects myocardial dysfunction and provides prognosis information in septic patients.

Conclusion

Elevation of troponin I in sepsis and septic shock indicates inflammatory and toxic damage to heart apart from ischemic damage caused by MI. Thus, it can be used as a marker for silent myocardial damage seen in sepsis and septic shock which may not be picked up by ECG and ECHO in early stages.

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