

# THE STUDY OF CARDIAC BIO-MARKERS AND 2-D ECHOCARDIOGRAPHY IN CASES OF SEPTICAEMIA

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## Medicine

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### Abstract:

**Background-** Myocardial dysfunction in septicemia leading to septic shock is a transient potentially reversible impairment of biventricular contractility associated with high mortality, if not timely intervened. The present concept of sepsis induced cardiomyopathy is based on the facts that exogenous toxins such as lipoteichoic acid, endotoxin and endogenous cytokines, reactive oxygen species, pro inflammatory mediators like TNF alpha, IL 1, IL 6 induce direct myocardial depression, microvascular thrombotic injury leading to impaired contractility and focal ischemia. This is reflected by non invasive studies such as 2D ECHO and cardiac biomarkers which can lead to early recognition and management.

**Aims-** This study was planned to assess the cardiac manifestations of septicemia using clinical criteria, ECG, 2D ECHO and cardiac biomarkers Troponin I, CPK MB in patients presenting as septicemia and to find out the correlation.

**Settings and Design-** A prospective observational study was conducted in 50 patients presenting with septicemia or septic shock to the General Medicine Department of Dr S N Medical College and Associated Hospitals to study cardiovascular manifestations of sepsis.

**Methods and Material-** It is a prospective study where in cases of septicemia clinical parameters with laboratory investigations with emphasis on cardiac biomarkers Troponin I, CPK MB with 2D echocardiography was done. Data obtained was statistically analysed.

**Results and Conclusions –** It was observed that out of 50 patients, 52% had trop I + status while 48% had trop I- status. In severe sepsis and septic shock, majority (78.26%) had trop I + status. In ECHO findings, hyperdynamic EF, moderate LVSD and LV global hypokinesia accounted for 47.83%, 47.82% and 21.74% respectively. Vasopressor and ventilator support were used in 82.61% and 52.17% of the cases with severe sepsis and septic shock. Majority of the patients (76%) had normal CPK MB levels with no significant correlation between elevated levels and severity of sepsis, ECHO findings, CVS involvement, morbidity and mortality. The troponin positive status was associated with increased need for vasopressor, ventilator support and mortality compared to troponin negative status. Thus 2D ECHO and troponin levels can be used as tools for detection of cardiovascular involvement in sepsis.

**Key Words:** Sepsis, Troponin, CPK -MB, 2-D Echocardiography

## Introduction

Severe sepsis and septicemic shock is one of the leading causes of morbidity and mortality in non cardiac critical care units with mortality rates as high as 70% due to cardiac dysfunction compared to 20% without cardiac involvement.<sup>1</sup> Cardiovascular manifestations in form of myocardial depression, elements of hypovolemic, distributive and cytotoxic shock are observed. Over the past few decades the concept of cardiovascular involvement in sepsis has revolutionized from organ specific changes such as myocarditis, endocarditis etc to the present concept of non specific sepsis induced myocardial dysfunction. It is characterized by transient, potentially reversible impairment of uni or biventricular contractility in varying combinations.<sup>2</sup> It is one of the complex organ failures in sepsis with dynamic adaptation to the causative organism, host response and resuscitation. Early diagnosis and management is critical in management of such patients for favorable outcome. Invasive monitoring such as central venous pressure or pulmonary artery catheterization for assessment and decision making in treatment algorithm is not feasible in many hospital setups all over India due to lack of expertise, infrastructure and economic factors. Bedside 2D transthoracic ECHO can be used as a substitute which's non invasive, easily available and can be performed easily after training for rapid assessment of cardiac function and hemodynamic status.<sup>3</sup>

Initial studies on cardiac markers such as troponin I, pro BNP etc in sepsis have shown to be elevated in sepsis. Further, increased troponin, relation to severity of sepsis and unfavourable outcome was observed.<sup>4</sup> The number of studies evaluating 2D ECHO and cardiac markers in sepsis are limited. Initiating a step in this direction, a study was planned to assess the cardiac manifestations of septicemia using clinical criteria, ECG, 2D ECHO and cardiac biomarkers Troponin I, CPK MB in patients presenting as septicemia and to find out the correlation.

## Method

A prospective observational study was conducted in 50 patients presenting with septicemia or septic shock to OPD or to the General Medicine Department of Dr S N Medical College and Associated Hospitals.

## Inclusion Criteria

Patients aged  $\geq 16$  years, both sexes and Septicaemia diagnosed according to criteria adapted from American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference Committee.

## Exclusion criteria

1. Patients meeting criteria of SIRS with non infectious etiology
2. Pre existing valvular/structural heart disease patients.
3. Pre existing IHD with no recent record of echocardiological assessment ( $\leq 1$  month)
4. Known case of chronic kidney disease, alcoholic liver disease, severe anemia
5. Pre existing chronic respiratory ailments such as COPD, ILD, bronchial asthma, pulmonary fibrosis, bronchiectasis etc.

## Note-

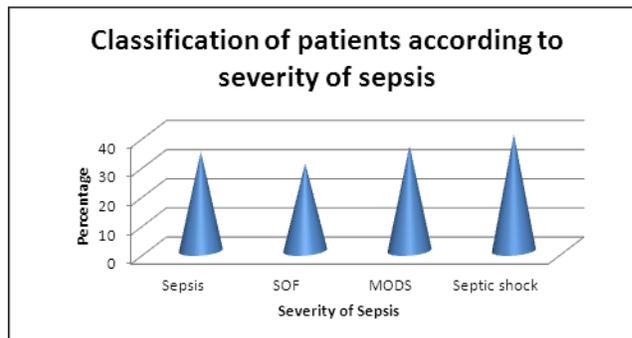
1. CPK MB and qualitative troponin I determination were performed on the same serum sample drawn for other biochemical tests.
2. A transthoracic 2D echocardiography were performed and following parameters were recorded.
  - Ejection fraction- Modified Simpson's method (disk summation method)
  - Valves- leaflet mobility, calcification and function were noted in various views.
  - Contractility- Right ventricular, Left ventricular contractility were noted with importance to any regional wall motion abnormality and global hypokinesia.
  - Systolic/diastolic dysfunction
  - Pericardial space
3. Statistically analyzed using the software SPSS version 16.

## Statistical Method

All data was statistically analyzed using SPSS software.

Parametric data were expressed as mean value ± standard deviation (SD) and categorical variables as percentage. The chi-square test was used for the comparison of dichotomous variables and the Fisher exact test for smaller variables. p value <0.05 was considered significant.

**Results**



- Respiratory and cardiovascular systems were the most common organ dysfunction accounting for 28% of the cases each .
- Majority of patients had septic shock (40%) followed by severe sepsis (36%).
- Most of the ECG findings were non specific such as sinus tachycardia (42.62%), T wave inversions (11.48%), ventricular premature contractions (6.56%) and few cases with ST changes.
- Out of 50 patients, 52% had trop I + status while 48% had trop I- status. In trop I+ patients with sepsis, majority (53.85%) had LV systolic dysfunction with moderate LVSD being most common followed by hyperdynamic EF accounting for 46.15%. 80% and 85.7% of Trop I + patients needed Vasopressor and ventilator support respectively while in Trop I – patients, only 20% and 14.3 % of patients needed Vasopressor and ventilator support respectively with statistically significant difference between two groups.

Ejection Fraction (%) (n=50)	Survivor (n=42)				Expired (n=8)				Total (%)	
	Trop I+ (n=18)	Trop I- (n=24)	Vasopressor (TropI+/- Trop I-)	Ventilator (TropI+/- Trop I-)	Trop I+ (n=8)	Trop I- (n=0)	Vasopressor (TropI+/- Trop I-)	Ventilator (TropI+/- Trop I-)	Trop I+ (n=26)	Trop I- (n=24)
Normal (51-54) (n=6)	00	06	00	00	00	00	00	00	0	25.00
Mild LVSD (41-50) (n=5)	03	01	01/01	01/0	01	00	00	01	15.38	4.17
Moderate LVSD (31-40) (n=9)	04	00	03	03	05	00	05	05	34.62	0
Severe LVSD (<= 30) (n=1)	01	00	01	00	00	00	00	00	3.85	0
Hyperdynamic EF (>=55) (n=29)	10	17	05/03	01/02	02	00	01	01	46.15	70.83

**Comparison of Ejection Fraction with troponin levels and complications in study group**

- In trop I + patients, LVDD was found in 38.46% while trop I – pts. had in 41.67% of the cases.

LV Diastolic dysfunction	Survivor (n=42)				Expired (n=8)				Total (%)	
	Trop I+ (n=18)	Trop I- (n=24)	Vasopressor (+/-)	Ventilator (+/-)	Trop I+ (n=8)	Trop I- (n=0)	Vasopressor (+/-)	Ventilator (+/-)	Trop I+ (n=26)	Trop I- (n=24)
LVDD I (n=16)	05	09	2/01	1/01	02	0	02	02	26.92	37.50
LVDD II (n=4)	01	01	1/0	1/0	02	0	00	01	11.54	4.17

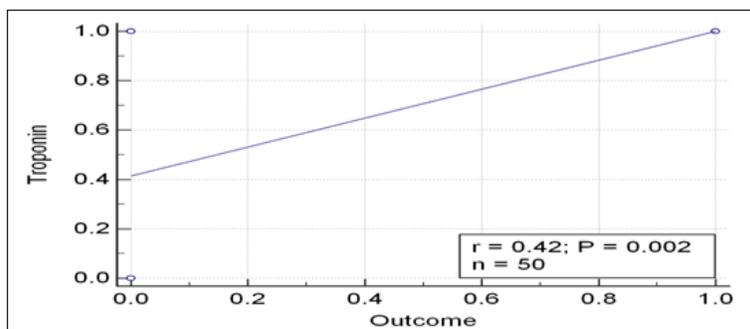
**Comparison of LV diastolic dysfunction with troponin levels and complications in sepsis**

- Overall LV global hypokinesia, RWMA and jerky IVS were more common in Trop I + patients compared to Trop I – patients.

ECHO findings	Survivor (n=42)		Expired (n=8)		Percentage (%)	
	Trop I+ (n=18)	Trop I- (n=24)	Trop I+ (n=8)	Trop I- (n=0)	Trop I+	Trop I-
LV Global Hypokinesia	4	1	2	0	23.08	4.17
Jerky IVS	1	1	1	0	7.69	4.17
RWMA	2	0	0	0	7.69	0
PAH	4	3	3	0	26.92	12.50

#### Comparison of ECHO parameters with troponin levels

7. The troponin status was compared with outcome in terms of discharge/expiry and the results are as shown in the graph with p value of 0.0024 which is statistically significant



#### Relation of troponin status with outcome of patients in study group

8. Majority of the patients (76%) had normal CPK MB levels with no significant correlation between elevated levels and severity of sepsis, ECHO findings, CVS involvement, morbidity and mortality.
9. In severe sepsis and septic shock, majority (78.26%) had trop I + status. In ECHO findings, hyperdynamic EF, moderate LVSD and LV global hypokinesia accounted for 47.83%, 47.82% and 21.74% respectively. Vasopressor and ventilator support were used in 82.61% and 52.17% of the cases with severe sepsis and septic shock.

Parameters		Discharge (n=16)	%	Expired (n=7)	%	Total % (n=23)
TROP I	Positive	11	47.83	7	30.43	78.26
	Negative	5	21.74	0	0.00	21.74
CPKMB	Normal	10	43.48	5	21.74	65.22
	Elevated	6	26.09	2	8.70	34.78
LVDD-1		3	13.04	2	8.70	21.74
LVDD-II		1	4.35	2	8.70	13.04
LV Global Hypokinesia		4	17.39	1	4.35	21.74
Jerky IVS		1	4.35	1	4.35	8.70
Mild PAH		3	13.04	3	13.04	26.09
Vasopressor		14	60.87	5	21.74	82.61
Ventilator		6	26.09	6	26.09	52.17
<b>Ejection Fraction</b>						
Normal		1	4.35	0	0	4.35
Hyperdynamic EF		9	39.13	2	8.70	47.83
Mild LVSD		2	8.70	1	4.35	13.04
Moderate LVSD		3	13.04	4	17.39	30.43
Severe LVSD		1	4.35	0	0.00	4.35

## Discussion

Sepsis is generally viewed as a disease aggravated by an inappropriate immune response encountered in the affected individual affecting various organs including heart causing multi organ dysfunction, failure and consequently death. Cardiovascular changes are important in septic shock; peripheral vascular dysfunction, which can result in heterogeneous microcirculatory flow, can frequently induce myocardial depression. In this population, cardiovascular collapse can increase the risk of death in sepsis as much as two times, and myocardial depression occurs in almost 40% of septic patients which can be prevented by early diagnosis and management.<sup>5</sup> Hence we planned to assess it by the clinical parameters, laboratory investigations specifically cardiac biomarkers CPK MB and troponin I with 2 D Echocardiography in 50 patients admitted to our hospital meeting criteria of sepsis of infectious etiology and the following findings were obtained. ECG findings were sinus tachycardia (42.62%) followed by t-wave inversions (11.48%), ventricular premature contractions (6.56%) and ST changes (4.87%) in study population. In patients with infectious diseases, abnormalities of ECG seen are heart blocks, sinus tachycardia, ST segment and T wave abnormalities, premature ventricular contractions according to paper by Sandhya Nalmas et al.<sup>6</sup>

Majority of study population (60%) had CPK MB levels in the range of 1-20 U/l thereby normal CPK MB levels. 24% of the patients had levels ranging from 21-30 U/l.

Out of 50 patients in our study, 52% had trop I + status while 48% had trop I- status. In trop I+ patients with sepsis, majority (53.85%) had LV systolic dysfunction with moderate LVSD being most common followed by hyperdynamic EF accounting for 46.15%. (Table 1) In Trop I + patients, LVDD was found in 38.46% while Trop I – patients had in 41.67% of the cases. (Table 2) Overall LV global hypokinesia, RWMA and jerky IVS were more common in Trop I + patients compared to Trop I – patients. (Table 3)

In study by Verelst KM et al, 46 patients of septic shock, increased levels of trop I and trop T was found in 50% and 36% of patients respectively. LV function assessment indicated that both elevated levels were associated with LV dysfunction ( $p < 0.0001$ ).<sup>7</sup>

In study by Mehta et al, out of 37 patients with septic

shock, 43% had elevated troponin I levels.<sup>8</sup> In a study by Spies et al, out of 26 patients with sepsis, 69% had elevated Troponin levels.<sup>9</sup> Near similar results were found by Juan N Pulido et al and Bouhemad B et al.

Mehta et al from India in 2004 conducted a single centre prospective study with 37 patients with severe sepsis, noted that 16 (43%) had cTnI+ and that there were higher incidence of segmentary Abnormalities of wall motion on echocardiography ( $p = 0.002$ ). The highest incidence of segmentary wall motion abnormalities in patients with cTnI + not found in other studies.<sup>10</sup> The troponin status was compared with outcome in terms of discharge/expiry and was observed that troponin +ve status was associated with mortality compared to negative status. Correlation of abnormal cTn I with duration of hypotension was seen by Arlati et al<sup>11</sup> with weak co relation with outcome. ( $r=0.28$ ). VerElst et al showed correlation with ICU admission, higher APACHE score, LV dysfunction in troponin positive patients.<sup>7</sup> Turner et al showed correlation between maximum dose of Vasopressor and maximum cTnI ( $r=0.55$ ).<sup>12</sup> Ammann et al showed correlation between cTnI and lower LVEF and higher mortality in Trop I positive patients ( $p=0.018$ ).<sup>4</sup>

## Conclusion

Our study showed correlation between troponin I positive status and severity of sepsis, need for Vasopressor, ventilator support, lower LVEF and mortality. Hence Troponin I and 2D Echocardiography are simple, non-invasive and effective tools that can be used to predict cardiovascular involvement in sepsis and treat appropriately.

## References

1. Merx, M. W., & Weber, C. (2007). Sepsis and the heart. *Circulation*, 116(7), 793-802.
2. Maeder, M., Fehr, T., Rickli, H., & Ammann, P. (2006). Sepsis-Associated Myocardial Dysfunction Diagnostic and Prognostic Impact of Cardiac Troponin and Natriuretic Peptides. *CHEST Journal*, 129(5), 1349-1366.
3. Bouferrache, K., Amiel, J. B., Chimot, L., Caille, V., Charron, C., Vignon, P., & Vieillard-Baron, A. (2012). Initial resuscitation guided by the Surviving

- Sepsis Campaign recommendations and early echocardiographic assessment of hemodynamics in intensive care unit septic patients: A pilot study\*. *Critical care medicine*, 40(10), 2821-2827.
4. Tanarat Choon-ngarm , Pailin Partpisanu “Serum cardiac troponin t as prognostic marker in septic shock”. *J med assoc thai* 91.12 (2008): 1818-22. Print.
  5. Fernandes CJ, Akamine N, Knobel E. Cardiac troponin: A new serum marker of myocardial injury in sepsis. *Intensive Care Med* 1999; 25: 1165-1168.
  6. Nalmas, S., Nagarakanti, R., Slim, J., Abter, E., & Bishburg, E. (2007). Electrocardiographic changes in infectious diseases. *Hospital physician*, 43(9), 15.
  7. verElst KM, Spapen HD, Nyugen DN, Garbar C, Huyghens LP, Gorus FK. Cardiac Troponins I and T are biological markers of left ventricular dysfunction in septic shock. *Clin. Chem.* 2000; 46:650-657
  8. Mehta, N. J., Khan, I. A., Gupta, V., Jani, K., Gowda, R. M., & Smith, P. R. (2004). Cardiac troponin I predicts myocardial dysfunction and adverse outcome in septic shock. *International journal of cardiology*, 95(1), 13-17.
  9. Spies, C., Haude, V., Overbeck, M., Schaffartzik, W., Schröder, K., Fitzner, R., & Runkel, N. (1998). Serum cardiac troponin T as a prognostic marker in early sepsis. *CHEST Journal*, 113(4), 1055-1063.
  10. Mehta, N. J., Khan, I. A., Gupta, V., Jani, K., Gowda, R. M., & Smith, P. R. (2004). Cardiac troponin I predicts myocardial dysfunction and adverse outcome in septic shock. *International journal of cardiology*, 95(1), 13-17.
  11. Arlati, S., Brenna, S., Prencipe, L., Marocchi, A., Casella, G. P., Lanzani, M., & Gandini, C. (2000). Myocardial necrosis in ICU patients with acute non-cardiac disease: a prospective study. *Intensive care medicine*, 26(1), 31-37.
  12. Turner, A., Tsamitros, M., & Bellomo, R. (1999). Myocardial cell injury in septic shock. *Critical care medicine*, 27(9), 1775-1780.