

# ASSESSMENT OF SEPSIS INDUCED CARDIAC DYSFUNCTION IN NEONATAL SEPSIS BY SPECKLE TRACKING ECHOCARDIOGRAM AND TISSUE DOPPLER AND CORRELATION WITH SERUM CARDIAC TROPONIN -T AND PROCALCITONIN

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## Abstract

**Aim:** The aim of this work was assessment of sepsis induced cardiac dysfunction (SIMD) in neonates with sepsis by 2-dimensional speckle tracking echocardiography, tissue Doppler as well as other conventional echocardiographic methods and its correlation with serum procalcitonin (PCT) and, cardiac troponin -T (cTnT).

**Methods:** This study was prospective controlled cohort study that included 60 neonates with diagnosis of neonatal sepsis compared to 60 healthy newborns who were matching in age and sex. both groups was subjected to basic and advanced transthoracic echocardiography and some lab markers in order to assess sepsis induced cardiac dysfunction, and correlates the findings with serum procalcitonin, cardiac troponin -T.

**Results:** Out of the enrolled 60 patients and 60 controls. Mean age of cases was  $16.62 \pm 4.74$  days and  $14.85 \pm 5.88$  days for controls. blood culture was positive in 48.3%; 65.5% was gram positive and 34.4 % was gram negative, Median Procalcitonin among cases was 5.20 ng/ml compared to 0.22 among controls, median cTnT among cases was 0.27 compared to 0.03 among controls, LVGLS was  $-10.79 \pm 1.47$  among cases vs  $-14.68 \pm 1.13$  among controls, P value  $< 0.001$ . mean EF was  $46.03 \pm 6.93$  among cases versus  $62.58 \pm 5.69$  among controls, P value  $< 0.001$ , There was significant positive correlation between left ventricular global longitudinal strain (LV GLS) and PCT and cTnT levels. **Conclusion.** PCT is good markers of neonatal sepsis. cTnT is a good laboratory indicator for cardiac affection in neonatal sepsis. speckle tracking echocardiography is a promising tool in assessment of cardiac function PCT and cTnT were correlated with both LV and RV systolic dysfunction detected by tissue Doppler imaging (TDI) and STE, SIMD is very common comorbidity in neonatal sepsis,

**Keywords:** Neonatal sepsis; Procalcitonin; CRP; Cardiac Troponin T; Tissue Doppler; Speckle Tracking Echocardiography.

## Introduction

Neonatal sepsis refers to an infection involving the bloodstream in newborn infants less than 28 days old. Neonatal sepsis remains a leading cause of morbidity and mortality among neonates, especially in middle and low -income countries [1]

There is remarkable heterogeneity among studies regarding the case definition of neonatal sepsis. The presence of a positive blood culture historically constitutes the 'gold standard' for the presence of neonatal sepsis [2].

In 2016, the International Sepsis Definition Taskforce convened by the Society of Critical Care Medicine, and the European Society of Intensive Care Medicine, updated definitions and clinical criteria for sepsis. These should facilitate recognition, targeted management of patients with sepsis and also improve accurate characterization of the global sepsis burden. Sepsis-3 defines sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection, while the concept of septic shock incorporates profound circulatory, cellular and metabolic abnormalities associated with a greater risk of mortality [3] biomarkers for neonatal sepsis have been found to aid in the early detection of the condition before clinical symptoms appear ,none of the current markers meet all the necessary requirements [4].Sepsis-induced cardiac dysfunction (SIMD) refers to a wide spectrum of acute myocardial impairment caused by sepsis. The presence of myocardial dysfunction in sepsis is known to be associated with increased mortality from 20% to 50% [5].

Although numerous studies have demonstrated evidence of cardiovascular impairments in patients with sepsis over the last 50 years, there is no universally accepted definition of SIMD. The initial concept of SIMD came from the study by Parker, Shelhamer [6]. They observed that 50 % of septic patients had a decreased initial left ventricle ejection fraction (EF) despite normal or elevated cardiac index found in all septic patients.

Various biomarkers identify sepsis patients with heart damage or dysfunction. Serum levels of troponin I or T, both sensitive markers of cardiomyocyte damage [7].

Echocardiographic assessment of Left and right ventricular function is traditionally being performed by M-mode estimation of fractional shortening (FS) and ejection fraction (EF), MAPSE and TAPSE. Tissue Doppler imaging (TDI) speckle tracking echocardiography (STE) are relatively new echocardiographic techniques, which measure the myocardial tissue functions both are superior to conventional echocardiography in terms of load independent assessment of global systolic function. Speckle tracking echocardiography (STE) is a promising tool (STE) proved to be similar to the cardiac magnetic resonance in reproducibility and accuracy [8].

## Materials and Methods:

### Study Design, Setting, and Patients:

- **The present study was** prospective controlled cohort study. conducted in the time from June 2021 to

September 2022 at neonatal intensive care unit -Aswan university hospital, Egypt. Full term-neonates (37 – 40 weeks) presented with clinical symptoms and signs of neonatal sepsis, and confirmed to have neonatal sepsis by positive blood culture and/or positive sepsis markers were included in the patients group, while normal healthy controls were assigned in the control group. On the other hand, those with congenital malformations, Infants with genetic syndromes, Infants with congenital heart diseases, premature neonates, Infants of diabetic mothers, Infants with hypoxic ischemic encephalopathy, Infants with intra-uterine growth retardation were excluded.

**Data collection:**

All included children was subjected to full history taking including demographic data, Complete physical examination and Laboratory investigations including ;Complete blood count. Blood culture. Serum levels of C reactive protein. Serum level procalcitonin. Cardiac troponin-T, Chest X Ray. Transthoracic Echocardiogram (Vingmed Vivid-T8, General Electric Vingmed, and Milwaukee, Wisconsin, USA). data acquisition was performed with a S6 probe at a depth of 16 cm in all the standard echocardiographic views according to the recommendation of the American Society of Echocardiography [9]. All neonates were examined in the right anterior oblique position if possible with breathing room air, or on oxygen supplement or mechanical ventilation according to the individual condition .integrated M-mode, two-dimensional (2-D) mode , pulsed and continuous wave Doppler were used to estimate left ventricle (LV) internal dimensions, fractional shortening, ejection fraction mitral and tricuspid inflow velocities. Using the same device and probe, tissue Doppler imaging (TDI) was carried out in the apical view at a depth of 16 cm (standard long-axis and two- and four-chamber images). The myocardial velocity curves of the lateral mitral valve annulus, and lateral tricuspid valve annulus were measured using pulsed-wave tissue Doppler from the apical four-chamber planes. To determine the timing of cardiac cycle events, the ECG were connected and traced. The beginning of the QRS complex was used as a reference point. 100 millimetres per second was used to record at least 10 cardiac cycles, and the photos were electronically saved. For the analysis, the mean values of three heartbeats were employed. The right or left ventricle's systolic function is reflected in the systolic wave (S). The diastolic function of the right ventricle is shown by the early/atrial (E'/A') ratio of the tricuspid valve annuli, the diastolic function of the left ventricle was assessed by PWD mitral inflow early/atrial (E/A) ratio.

For speckle tracking analysis of left ventricular chambers; standard gray scale 2-D images were acquired in 3-standard apical views, using a 6 MHz transducer at a depth of 16 cm with a stable electrocardiography (ECG) recording using acoustic tracking software (EchoPAC; allowing offline semi-automated analysis of speckle based strain) to study left ventricle deformation and to measure left ventricle global longitudinal systolic strain. For the speckle tracking imaging (STI) analysis, we used high frame (65 frames/s) with harmonic two-dimensional images and the software generated six corresponding time-strain curves. The peak of the average curve of all the segments was considered as peak global longitudinal strain (PGLS). The peak global longitudinal strain was automatically

calculated from the combined deformation of the myocardial segments in each imaging plane and used as a measure of LV function. For myocardial strain, regional thickening or lengthening was expressed as a positive value and thinning or shortening as negative values.

**Statistical analysis:**

Data was analyzed using Statistical Package for Social Science (SPSS), version 26.0 for Windows. Quantitative data tested for normality by Shapiro-Wilk test data, expressed as mean  $\pm$  SD or median and range according to normality of data, qualitative data were expressed as frequencies and percentages. Independent Sample T-test/ Mann Whitney U test were used to compare mean/median difference between two independent groups. The Chi square test was used to compare proportions between groups. One way ANOVA compare mean difference between groups, Post hoc test with pairwise comparison compare significance between each 2 groups. Spearman correlation was used to explore the correlation between quantitative variables. Univariate linear regression analysis to identify prediction ability of cTnT and procalcitonin to detect changes in GLS. The level of significance was considered at P value < 0.05.

**Ethical Consideration:**

The study procedure was authorised by Aswan University's Faculty of Medicine's Institutional Ethics and Research Review Board. Before their children were enrolled in the trial, each parent of a newborn involved in the study provided a written informed agreement. The World Medical Association Declaration of Helsinki, which addresses the moral conduct of research involving human participants and/or animals, was followed by our team.

## Results

**This study included 60 neonates with diagnosis of neonatal sepsis compared to 60 healthy newborns who were matching in age and sex.**

**Table 1** show demographic and laboratory data of the studied groups .no statistically significant difference between cases and controls regarding age of neonates at time of examination, gender, mode of delivery and weight. Mean age of cases was  $16.62\pm 4.74$  days and  $14.85\pm 5.88$  days for controls,

Regarding laboratory data, blood culture was positive in 48.3% of cases group; of them 65.5% was gram positive and 34.4 % was gram negative. the most common gram positive organism was staphylococcus aureus,while the most common gram negative organism was klebsiella pneumoniae, Median serum Procalcitonin level among cases was 5.20 (ng/ml) compared to 0.22 (ng/ml) among controls, median cTnT among cases was 0.27(ng/ml) compared to 0.03(ng/ml) among controls.

**Table 2 shows** Cardiac function assessed by 2D- Speckle tracking echocardiography, Tissue Doppler and other conventional echocardiographic methods in patients and control group:

Left ventricular systolic function was impaired in neonates with sepsis as proved by significant higher mean (less negative value) in 2D- Speckle tracking echocardiography among cases compared to controls, ( $-10.79\pm 1.47$  among cases vs  $-14.68\pm 1.13$  among controls) P value  $<0.001$ . M-mode EF was lower among cases compared to controls. S wave TDI lateral mitral annulus (cm/S) was lower among cases compared to controls.

Left ventricular diastolic function was impaired in neonates with sepsis as showed by reduced mitral valve E/A ratio among cases compared to controls, ( $0.82\pm 0.13$ ) among cases vs ( $1.17\pm 0.17$ ) among controls, P value  $<0.001$ .

right ventricular systolic function was also impaired as There was statistically significant lower S wave TDI lateral tricuspid annulus (cm/S) among cases compared to controls ( $5.19\pm 1.54$ ) among cases vs ( $8.91\pm 1.04$ ) among controls, P value  $<0.001$ , On the other hand 'TV E/A' which represent RV diastolic function showed no difference between cases and control .TV E/A' among cases ( $1.06\pm 0.32$ ) vs ( $0.93\pm 0.14$ ) among controls) P value 0.813.

**Table (3):** showed Correlation between left and right ventricle systolic and diastolic function measured by transthoracic echocardiography and cTnT and Procalcitonin

Regarding correlation between LV function and cTnT .There was strong negative correlation between cTnT and EF ( $r=-0.777$ , P-value  $<0.001$ ), strong positive correlation between cTnT and LVGLS ( $r=0.760$ , P-value  $<0.001$ ), moderate negative correlation between cTnT and S wave TDI lateral mitral annulus ( $r=-0.670$ , P-value  $<0.001$ ).

Regarding correlation between LV function and procalcitonin There was statistically significant strong negative correlation between procalcitonin and EF ( $r=-0.781$ , P-value  $<0.001$ ), strong positive correlation with LVGLS ( $r=0.702$ , P-value  $<0.001$ ), moderate negative correlation with S wave mitral ( $r=-0.581$ , P-value  $<0.001$ ).

Regarding correlation between RV function and cTnT and procalcitonin, There was moderate negative correlation between cTnT, procalcitonin and S wave TDI lateral tricuspid annulus .however we did not find any correlation between cTnT, procalcitonin and TV E'/A'.

**Table 4** showed the Prevalence of left ventricular systolic impairment among neonatal sepsis was 87%..

**Table (1):** Demographic and laboratory data of the study participants

Data were expressed as mean  $\pm$  SD or frequency and %

	Cases (n=60)	Controls (n=60)	P- Value*
<b>Age at examination (days) Mean <math>\pm</math> SD</b>	16.62 $\pm$ 4.74	<b>14.85<math>\pm</math>5.88</b>	0.073
<b>Gender</b>			
▪ Male	36 (60.0%)	<b>31 (51.7%)</b>	0.358
▪ Female	24 (40.0%)	<b>29 (48.3%)</b>	0.358
<b>Weight Kg (Mean <math>\pm</math> SD)</b>	3.17 $\pm$ 0.38	<b>3.07<math>\pm</math>0.25</b>	0.081
▪ <b>Blood culture</b> Positivity	<b>Total</b>	29 (48.3%)	<b>0</b>
• <b>Blood culture</b> Positivity	<b>positive</b>	19 (65.5%)	<b>0</b> <0.001
	<b>negative</b>	10 (34.4%)	
	<b>Most common gram positive organism</b>	staphylococcus aureus	
	<b>Most common gram negative organism</b>	klebsiella pneumoniae	
<b>WBCs *10<sup>3</sup>: Mean <math>\pm</math> SD</b>	14.08 $\pm$ 7.77	7.70 $\pm$ 1.54	<0.001
<b>cTnT (ng/ml)</b>	0.27 (0.01-4.34)	0.03 (0.001-0.19)	<0.001
<b>Procalcitonin (ng/ml)</b>	5.20 (0.50-94.00)	0.22 (0.01-2.10)	

**Table (2):** Cardiac function assessed by 2D- Speckle tracking echocardiography, Tissue Doppler and other conventional echocardiographic methods in patients and the control group:

Variables	Cases (n=60)	Controls (n=60)	P-Value*
<b>Left ventricular systolic function</b>			
<b>GLS by Speckle tracking</b>	-10.79±1.47	-14.68±1.13	<b>&lt;0.001</b>
<b>EF (M-mode)</b>	46.03±6.93	62.58±5.69	<b>&lt;0.001</b>
<b>S wave TDI lateral mitral annulus (cm/S)</b>	3.96±1.03	7.65±1.23	<b>&lt;0.001</b>
<b>MAPSE (cm)</b>	0.48±0.11	0.89±0.13	<b>&lt;0.001</b>
<b>Left ventricular diastolic function</b>			
<b>MV E/A ratio</b>	0.82±0.13	1.17±0.17	<b>&lt;0.001</b>
<b>Right ventricular systolic function</b>			
<b>S wave TDI lateral tricuspid annulus (cm/S)</b>	5.19±1.54	8.91±1.04	<b>&lt;0.001</b>
<b>TAPSE</b>	0.53±0.12	0.87±0.18	<b>&lt;0.001</b>
<b>Right ventricular diastolic function</b>			
<b>TV E'/A'</b>	1.06±0.32	0.93±0.14	0.813

Data were expressed as mean ± SD.\*Independent Sample T test.

**Table (3):** Correlation between left and right ventricle systolic and diastolic function measured by transthoracic echocardiography and cTnT and Procalcitonin:

	LVEF		LV-GLS		S wave mitral Annulus		MAPSE		MV E/A		S wave tricuspid Annulus		TAPSE		TV E'/A'	
	r	p	r	p	r	p	r	p	r	P	r	p	r	p	r	p
<b>cTnT</b>	-0.777	<0.001	0.760	<0.001	0.670	<0.001	-0.633	<0.001	0.010	0.939	-0.655	<0.001	-0.694	<0.001	0.224	0.085
<b>Procalcitonin</b>	-0.781	<0.001	0.702	<0.001	0.581	<0.001	-0.544	<0.001	0.060	0.646	-0.572	<0.001	-0.565	<0.001	0.181	0.167

r (spearman correlation coefficient),P (P-value)

Negligible correlation r < 0.2, Mild correlation r = 0.2 to < 0.4, Moderate correlation r = 0.4 to < 0.7,

Strong correlation r = 0.7 to < 1, Perfect correlation r =1, No correlation r=0



**Table (4):** Prevalence of left ventricular systolic impairment among neonatal sepsis:

	<b>N=60</b>	<b>%</b>
<b>Cardiac dysfunction (EF &lt;55%)</b>	<b>47</b>	<b>78.0%</b>
<b>Normal (EF ≥55 %)</b>	<b>13</b>	<b>22.0%</b>

## Discussion

Sepsis has always been a curse for critically ill patients, and remains a high cause of mortality worldwide. Sepsis leads to haemodynamic alteration and profound hypovolaemia, which can induce myocardial depression or dysfunction. Echocardiographic assessment of Left and right ventricular function is traditionally being performed by estimation of fractional shortening (FS) and ejection fraction (EF), MAPSE and TAPSE. Tissue Doppler imaging (TDI) speckle tracking echocardiography (STE) are relatively new echocardiographic techniques, which measure the myocardial tissue functions[8].

Many laboratory markers as PCT and cTn-T are used to detect and predict the severity of neonatal sepsis. Therefore, we performed this study to assess cardiac dysfunction in neonates with sepsis by 2-dimensional speckle tracking echocardiography, tissue Doppler as well as other conventional echocardiographic methods and its correlation with serum procalcitonin, cardiac troponin –T.

In our study; there was no statistically significant difference between cases and controls regarding demographic characteristics ,In our study Blood culture was positive in 29 (48%) of cases ,of them there was (65.5%) Gram positive with predominant organism was staphylococcus aureus, on the other hand (34.4%) of cases was gram negative . the most common organism was klebsiella pneumoniae this align with **Joseph, Lian [10]** how reported that Regarding the causative organism in neonatal sepsis, gram-positive bacteria were found to be the most prevalent isolated organisms in late onset sepsis, while, gram-negative pathogens were more common among underweight infants with early onset sepsis [11].

Many laboratory markers are used to detect and to monitor neonatal sepsis, in our study we find that, mean WBC count was ( $14.08 \pm 7.77$ ), which was significantly higher compared to control ( $7.70 \pm 1.54$ ) (p-value  $< 0.001$ ) , our results was in disagreement with **Worku, Aynalem [12]** whom study included 250 patients with neonatal sepsis and was made in Ethiopia. They reported that The WBC was significantly lower in cases than in control groups. our present study also disagreed with **Abdel-Hakim, Shehata [13]** whom study included 50 patients with neonatal sepsis and was made in Al-Minia University, Egypt. They reported that there was no significant difference between WBCS count in sepsis and control group (p-value

>0.05 These data highlight the fact that The usefulness of WBCS count as biomarker of neonatal sepsis has not been proven yet, as it have poor positive predictive value (PPV) and negative predictive value (NPV) but studies have shown that serial normal WBC count helps in safely ruling out of neonatal sepsis [14].

Biomarkers for diagnosis of neonatal sepsis have been proposed for decades The most common biomarker used for this purpose in the neonatal intensive care unit is C-reactive protein (CRP), several studies advocate for procalcitonin (PCT) as a more sensitive and specific marker. In our study there were statistically higher median level of Procalcitonin, among cases in comparison to controls, P-Value <0.001. Our results was in agreement with **Morad, Rabie [15]** whom study included 50 neonates suspected with sepsis enrolled from the neonatal intensive care unit (NICU) of Zagazig University Hospitals, Egypt. they reported that PCT has high sensitivity and specificity in diagnosis of neonatal sepsis. [16].

Although cTnT is not used as a sepsis marker its usully increased in patients with neonatal sepsis, and indicates cardiac affection [17]. In our study the median cTnT (ng/mL) among cases was 0.27 compared to 0.03 among controls, which was significantly higher in neonates with sepsis than in control neonates. Possible reasons for elevation of cTnT in neonates with sepsis is decrease of myocardial perfusion or, microscopic tissue damage secondary to microvascular thrombosis, and due to the accelerated apoptosis in response to release of pro-inflammatory cytokines [17].

Speckle tracking echocardiography is relatively new echocardiographic techniques, which measure the myocardial tissue function. It has been successfully used in adult population. However, only a limited number of studies have been performed to investigate myocardial dysfunction in neonatal sepsis using Speckle tracking echocardiography. Data about echocardiographic changes in heart of neonates with sepsis are still needed regarding Left Ventricle and Right Ventricle systolic and diastolic function.

In the current study Global longitudinal strain (GLS) by speckle tracking echocardiography was significantly worse (less negative) among cases in compare to control (**-10.79±1.47 and -14.68±1.13** respectively) p-value <0.0001 this indicated that left ventricular systolic function is seriously impired in neonates with sepsis, GLS provides an angle-independent assessment of regional myocardial deformation and

does not rely on geometrical assumptions with the ability to measure the motion in any direction within the image plane. Our work agreed with Sumbaraju, Nayak [18] whom study included 68 patients with neonatal sepsis and was made in Kasturba Medical College, India. They reported that GLS was worse (less negative) in cases in compare to control. In addition **Awany, Tolba [19]** whom study included included 50 neonates with the diagnosis of sepsis and 50 healthy controls and was made in Tanta University, Egypt. they reported that GLS was worse (less negative) in cases in compare to control ( $-10 \pm 2.3$  and  $-18.3 \pm 2.7$  respectively) p-value  $< 0.0001$ .

As regard assessment of LV systolic function by TDI and other conventional echocardiographic methods; Our study revealed that the mean LV EF by M-mode was significantly lower among cases compared to controls, these findings are consistent with **Alzahrani [20]** in his study which included 30 patient and 30 control and was done in Taif University, KSA. he found that Mean EF was lower in cases ( $65.74 \pm 0.64$ ), compared to control ( $71.11 \pm 0.79$ ) and P value  $< 0.001$ . our study agreed with an adult study by **Machado, F., et al [21]** who reported that LVEF was lower in septic patients compared to control, Our study disagreed with a previous neonatal study done by **Awany, Tolba [19]** in Tanta university –Egypt, they found that among 50 neonates with sepsis and their matched control the LV-EF had no significant difference. **Tomerak, El-Badawy [22]** conducted a study in Cairo University Children's Hospital, Cairo, Egypt. They assessed the LV-EF in 30 septic and 30 non septic newborns they concluded that there was no significant difference in LV-EF among neonates with sepsis compared with control.

Our study revealed that S wave TDI lateral mitral annulus (cm/s) was significantly lower in septic neonates ( $3.96 \pm 1.03$ ) when compared to control ( $7.65 \pm 1.23$ ), P value  $< 0.001$ . it also revealed that that mean MAPSE (cm) was significantly lower in septic neonates ( $0.48 \pm 0.11$ ) when compared to control ( $0.89 \pm 0.13$ ), P value  $< 0.001$ . our finding findings are consistent with **Awany, Tolba [19]** who stated that LV systolic function assessed by TDI and MAPSE were significantly depressed in septic neonates in compare to control. Our study disagreed with **Fahmey, Hodeib [23]** whom study included 50 neonates fulfilling the diagnostic criteria for sepsis and 25 healthy neonates, and was made in Beni Suef University Hospital, they concluded that Left ventricular systolic function (S wave mitral annulus and MAPSE) was not significantly different between septic and healthy neonates.

As regard LV diastolic function; Our study revealed that neonates with sepsis were associated with LV diastolic dysfunction suggested by low MV E/A ratio in cases in compare to controls. This agreed with **Tomerak, El-Badawy [22]** they detected LV diastolic dysfunction by the reduced E/A ratio in the septic premature and full-term neonates in comparison to the controlled non-septic newborns ,however, **Abdel-Hady, Matter [24]** demonstrated that there is no significant difference between case and control as regard LV diastolic function.

As regard RV systolic function; Our study revealed that S wave TDI lateral tricuspid annulus (cm/s) was significantly lower in septic neonates when compared to control. TAPSE was significantly lower in septic neonates when compared to control, these findings are consistent with **Awany, Tolba [19]** whom study included 40 sepsis Patient, and was made in Tanta university hospital, again our result agreed with **Lanspa, Cirulis [25]** whom study included 393 adult patients with septic shock, and was made in United States ,they found that right ventricular dysfunction is present in nearly half of studied septic patients

As regard RV diastolic function; in our study we did not find any echocardiographic evidence of impaired diastolic function, there was no significant difference regarding TV E/A' ratio between septic and healthy neonates.echocardiographic changes in heart of neonates with sepsis are still needed especially regarding RV performance. This is especially important as the cardiac effects of sepsis in not limited to the left side of the heart but mostly include the RV as well,**Levy, Holland [26]**.

In our study, cTnT and procalcitonin (PCT) is correlated to LV and RV systolic function ,on the other hand, we did not find any correlation between cTnT or procalcitonin (PCT) and LV or RV diastolic function .This finding agreed with **Al-Biltagi, Issa [27]** they studied the correlation between cardiac Troponins blood levels and degrees of cardiac dysfunction in 50 children with impaired LV and RV systolic function due to acute fulminant viral myocarditis, they concluded that The levels of cTnT were significantly higher in patients with fulminant myocarditis than in controls. This finding agreed with the work of **Kim et al** who found significant correlation between the serum level of cTnT and the reduction in EF [28].In a previous study done by Hai, Binh [29] high plasma concentrations of cTnT were found in 36% and cTnT was absolutely related to LV dysfunction in multiple

regression analysis. our work was partially correlates with **Landesberg, Levin [30]** they showed also that patients with sepsis who have systolic, diastolic or combined dysfunction had significantly higher serum levels of high-sensitivity cTnT than those without cardiac dysfunction.

Our work is aligned with **Noori, Mahjoubifard [31]** their study was in Tehran IRAN, they studied the level of procalcitonin, in children with cardiomyopathy in comparison to controls and the association with echocardiographic findings. They found that PCT had strong correlation with echocardiographic data of both LV and RV in patients with dilated cardiomyopathy. The increased level of serum procalcitonin in our patients compared to controls would be due to the systemic inflammatory process associated with the sepsis.

Myocardial depression is a well-recognized manifestation of organ dysfunction in sepsis.[32].In our study the prevalence of sepsis induced cardiac dysfunction defined by LV EF by M-mode < 55% was 78% ,This was in agreement with Jain and Sankar whom study included 31 children with septic shock and 30 sepsis subjects and was done in India They reported that The prevalence of SIMD was 71% in 'septic shock' and 23% in sepsis.[33]

## **Conclusion**

PCT is good markers of neonatal sepsis and together with cTnT were correlated with both LV and RV systolic dysfunction detected by TDI and STE.

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### References

- 1.Singh, M., M. Alsaleem, and C.P. Gray, *Neonatal sepsis*. StatPearls [Internet], 2022. **9**(2): p. 84-86.

2. Eichberger, J., E. Resch, and B. Resch, *Diagnosis of Neonatal Sepsis: The Role of Inflammatory Markers*. *Front Pediatr*, 2022. **10**: p. 840288.
3. Singer, M., et al., *The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)*. *Jama*, 2016. **315**(8): p. 801-10.
4. Mudey, G. and A. Mudey, *Challenges in the Diagnosis of Neonatal Septicemia*. *Journal of Datta Meghe Institute of Medical Sciences University*, 2021. **16**(3): p. 579-582.
5. Habimana, R., et al., *Sepsis-induced cardiac dysfunction: a review of pathophysiology*. *Acute Crit Care*, 2020. **35**(2): p. 57-66.
6. Parker, M.M., et al., *Profound but reversible myocardial depression in patients with septic shock*. *Annals of internal medicine*, 1984. **100**(4): p. 483-490.
7. Xiao, T., et al., *The analysis of etiology and risk factors for 192 cases of neonatal sepsis*. *BioMed research international*, 2017. **2017**.
8. Dalla, K., et al., *Strain echocardiography identifies impaired longitudinal systolic function in patients with septic shock and preserved ejection fraction*. *Cardiovascular Ultrasound*, 2015. **13**(1): p. 1-10.
9. Othman, F., G. Abushahba, and A. Salustri, *Adherence to the American society of echocardiography and European association of cardiovascular imaging recommendations for the evaluation of left ventricular diastolic function by echocardiography: a quality improvement project*. *Journal of the American Society of Echocardiography*, 2019. **32**(12): p. 1619-1621.
10. Joseph, C.J., W.B. Lian, and C.L. Yeo, *Nosocomial infections (late onset sepsis) in the Neonatal Intensive Care Unit (NICU)*. *Proceedings of Singapore Healthcare*, 2012. **21**(4): p. 238-244.
11. Hornik, C.P., et al., *Use of the complete blood cell count in early-onset neonatal sepsis*. *Pediatr Infect Dis J*, 2012. **31**(8): p. 799-802.
12. Worku, M., et al., *Role of complete blood cell count parameters in the diagnosis of neonatal sepsis*. *BMC Pediatrics*, 2022. **22**(1): p. 411.
13. Abdel-Hakim, G., et al., *Cord Blood Interleukin-6 as a Predictor of Early Onset Sepsis in High Risk Neonates*. *Annals of Neonatology Journal*, 2019. **1**(2): p. 38-48.
14. Murphy, K. and J. Weiner, *White Blood Cell Counts in Neonatal Early-Onset Sepsis*. *The Pediatric Infectious Disease Journal*, 2012. **31**(5): p. 541.
15. Morad, E.A., et al., *Evaluation of procalcitonin, C-reactive protein, and interleukin-6 as early markers for diagnosis of neonatal sepsis*. *International Journal of Microbiology*, 2020. **2020**.
16. Henriquez-Camacho, C. and J. Losa, *Biomarkers for sepsis*. *Biomed Res Int*, 2014. **2014**: p. 547818.

17. Alvarado-Socarrás, J.L. and E.F. Manrique-Hernández, *Cardiac Troponin-T as a Marker of Myocardial Dysfunction in Term Neonates with Perinatal Asphyxia: Correspondence*. The Indian Journal of Pediatrics, 2019. **86**(8): p. 766-767.
18. Sumbaraju, S.L., et al., *Myocardial performance imaging for the early identification of cardiac dysfunction in neonates with sepsis*. 2023.
19. Awany, M., et al., *Cardiac functions by tissue doppler and speckle tracking echocardiography in neonatal sepsis and its correlation with sepsis markers and cardiac troponin-T*. J Pediatr Neonatal Care, 2016. **5**(3): p. 00184.
20. Alzahrani, A.K., *Cardiac function affection in infants with neonatal sepsis*. J Clin Trials, 2017. **7**(1): p. 2167-0870.1000329.
21. Reinhart, K., et al., *Recognizing sepsis as a global health priority—a WHO resolution*. New England Journal of Medicine, 2017. **377**(5): p. 414-417.
22. Tomerak, R.H., et al., *Echocardiogram done early in neonatal sepsis: what does it add?* J Investig Med, 2012. **60**(4): p. 680-4.
23. Fahmey, S.S., et al., *Evaluation of myocardial function in neonatal sepsis using tissue Doppler imaging*. The Journal of Maternal-Fetal & Neonatal Medicine, 2020. **33**(22): p. 3752-3756.
24. Abdel-Hady, H.E., M.K. Matter, and M.M. El-Arman, *Myocardial dysfunction in neonatal sepsis: a tissue Doppler imaging study*. Pediatr Crit Care Med, 2012. **13**(3): p. 318-23.
25. Lanspa, M.J., et al., *Right ventricular dysfunction in early sepsis and septic shock*. Chest, 2021. **159**(3): p. 1055-1063.
26. Levy, P.T., et al., *Feasibility and reproducibility of systolic right ventricular strain measurement by speckle-tracking echocardiography in premature infants*. J Am Soc Echocardiogr, 2013. **26**(10): p. 1201-1213.
27. Al-Biltagi, M., et al., *Circulating cardiac troponins levels and cardiac dysfunction in children with acute and fulminant viral myocarditis*. Acta Paediatr, 2010. **99**(10): p. 1510-6.
28. Kim, J.-S., et al., *Troponin testing for assessing sepsis-induced myocardial dysfunction in patients with septic shock*. Journal of clinical medicine, 2019. **8**(2): p. 239.
29. Hai, P.D., et al., *Diagnostic value of high-sensitivity troponin T for subclinical left ventricular systolic dysfunction in patients with sepsis*. Cardiology Research and Practice, 2021. **2021**.
30. Landesberg, G., et al., *Myocardial dysfunction in severe sepsis and septic shock*. Chest, 2015. **148**(1): p. 93-102.
31. Noori, N.M., et al., *Comparison between procalcitonin, brain natriuretic peptide, and uric acid in children with cardiomyopathy and controls*. BioMed research international, 2015. **2015**.



32. Rudiger, A. and M. Singer, *Mechanisms of sepsis-induced cardiac dysfunction*. *Critical Care Medicine*, 2007. **35**(6): p. 1599-1608.
33. Jain, A., et al., *Prevalence and outcome of sepsis-induced myocardial dysfunction in children with 'sepsis' 'with' and 'without shock'—a prospective observational study*. *Journal of tropical pediatrics*, 2018. **64**(6): p. 501-509.

