

Cardiac Function Affection in Infants with Neonatal Sepsis

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Abstract

Objective: Neonatal sepsis is associated with the presence of the systemic inflammatory response syndrome (SIRS) in response to a culture-proven infection. It is known as one of the most frequent causes of mortality in the neonatal intensive care units. The study has aimed to investigate the effects of neonatal sepsis on cardiac function of the infants.

Methods: The study is based on prospective cohort research. It consists of two groups; control group and focus group. The focus group comprised of 30 full-term neonates with neonatal sepsis admitted to NICU; whereas, healthy neonates were included in the control group. Neonatal sepsis was diagnosed among the infants with the presence of at least two clinical signs of sepsis including feeding intolerance, temperature instability, apnea, poor reflexes, poor capillary refill > 2 seconds. The clinical examination of neonates including CBC, CRP, blood culture, and sensitivity was also conducted. Moreover, echocardiography was performed on participants of both groups.

Results: The results revealed that 50% of the patients from both the groups were male. The mean weight of the infants ranged from 2.2 to 3.5 kg with a mean of 2.9 ± 0.3 kg. Results showed that 63.3% patients had low platelet count, and 16.7% patients suffered from leukocytosis. 11 patients (36.7%), suffering from sepsis, were diagnosed with significant shift in their neutrophil count. There were significant changes in the echocardiogram of the patients suffering neonatal sepsis; whereas, dramatic improvement in cardiac function was observed by comparing the parameters before and after resolution of sepsis.

Conclusion: The septic neonates experienced significant cardiovascular changes that are revealed through the technique known as echocardiography.

Keywords: Cardiac function; Cardiomyopathy; Cardiovascular complications; Infants; Inflammatory response syndrome (SIRS); Neonatal sepsis; Septic shock

Introduction

Sepsis has been defined as the presence of the systemic inflammatory response syndrome (SIRS) in response to a culture-proven infection. Neonates conceive infections during the perinatal time period because of multiple exposures and comparatively conceded immune system. The pressure of the disease, recognized to neonatal infections, changes by neonatal and maternal risk factors and by geographic region [1]. Sepsis and septic shock are recognized as one of the most frequent causes of mortal complications in neonatal intensive care units worldwide. It has been observed that early-onset sepsis has become a serious and common issue among neonates, especially preterm infants [2]. Neonatal period is the most critical stage in the life of newborn babies, and neonatal sepsis is one of the most common causes for mortality at this age. Cardiovascular complications, myocyte damage, and modification of cardiac blood flow induced by inflammatory mediators are the consequences of neonatal sepsis among newborns [3]. There is variation in clinical signs and symptoms of sepsis among the newborns on the basis of their gestational age and severity of infection. The cardiac symptoms among

these infants include; poor perfusion, cyanosis, reduced capillary refill, desaturation, hypotension, and bradycardia [4].

Neonatal sepsis considerably causes neonatal morbidity and mortality, and it has become a global health challenge [5]. Neither the neurodevelopment outcomes nor treatment plans of neonatal sepsis in surviving neonates has transformed considerably in the last 30 years regardless of various failed attempts to decline the burden of sepsis [6]. Generally, sepsis is observed as a disease that is aggravated by inappropriate immune response, which is encountered into the afflicted individuals. The cardiovascular system is the most important system that is compromised by sepsis. Therefore, it has been studied in clinical and basic researches. The initial early phase after sepsis is characterized by pulmonary hypertension, hypoxemia, and decreased cardiac output. These disturbances are developed due to activated granulocyte-derived biochemical mediators. These mediators include hydroxyl radicals and thromboxane B₂, which are also considered as arachidonic acid metabolite. Pulmonary hypertension tends to develop because these mediators are vasoconstrictors when released in the pulmonary tissue [7].

Problem statement

The frequency of myocardial dysfunction remains unknown, despite of increased awareness about sepsis induced myocardial dysfunction.

Despite of moderate to severe myocardial depression, the cardiac output remains normal or increase among the neonates, suffering from sepsis. Moreover, sepsis is also known as systemic inflammation response syndrome and is characterized as the leading cause of death among the neonates.

Aim of the study

The study has aimed to assess the dimensions and functions of left and right ventricles to determine the myocardial performance during neonatal sepsis by echocardiography. These procedures have been carried out among the septic neonates after their admission and are compared with non-septic normal newborns after assuming resolution of systemic inflammatory response.

Methodology

The research has been based on prospective cohort study that included 30 full-term neonates with neonatal sepsis admitted to NICU in the focus group. However, thirty healthy neonates were included in the control group, excluding neonates with congenital heart disease, infants of diabetic mothers, asphyxiated newborns, and neonates with chromosomal anomalies or metabolic errors. Only 30 neonates were included in the study due to lack of informed consents from their parents.

Neonatal sepsis was diagnosed with the presence of at least two clinical signs of sepsis (feeding intolerance, temperature instability, apnea, poor reflexes, poor capillary refill>2 seconds). It was also diagnosed on the basis of two of the following laboratory findings, which include; leucopenia <5.000/mm³, leukocytosis >20.000/mm³, thrombocytopenia <100.000/mm³, elevated C-reactive protein>10 mg/dl and bandemia>0.2. The infants were also checked for recovery of bacterial pathogen in blood-culture [8]. Full history of the patients was collected and clinical examination was conducted to investigate CBC, CRP, blood culture, and sensitivity.

Echocardiography

Echocardiography was done for both control and focus groups. The participants of focus group were diagnosed with sepsis, and follow up was taken after the resolution. M-Mode and 2-D (2-dimensional) echocardiography were employed to determine the cardiac dimensions. Later, fractional shortening (FS %) and ejection fraction (EF) were calculated as they are the indicators of left ventricular systolic function. The procedure was carried according to the recommendations of the American Society of Echocardiography [9]. Tei index & MAPSE were also calculated for the left ventricle. Tricuspid annular plane systolic excursion (TAPSE) and Tei index need to be taken for the assessment of RV function [10].

Myocardial performance index (MPI) (an index of ventricular function independent of ventricular geometry) was calculated as the ratio of the sum of iso-volumetric contraction and relaxation times over the ejection time. MPI was calculated for the left and right ventricles by obtaining the “a” value, i.e., the time from closure to opening of the corresponding AV valves and the “b” value, which is the ejection time of ventricle. An average of three recorded cycles for the “a” and “b” has been obtained and MPI is calculated according to the formula [11];

$$MPI=a-b/b$$

M-Mode was also used for measurement of tricuspid annular plan systolic excursion (TAPSE) at tricuspid annulus, as well as MAPSE at lateral mitral annulus and basal part of septum in apical 4 chamber view [12].

Results

Both patients and control groups were comparable in gestational age and weight. Concerning male to female ration, males represented 50% of both focus and control groups; whereas, patient’s weights ranged from 2.2 to 3.5 kg with a mean of 2.9 ± 0.3 kg (Table 1). Table 2 shows the level of CRP, relevant CBC findings, and results of bacteriological culture in cases during sepsis.

Variable	Controls (n=30)	Cases (n=30)	p-value	Significance
Weight (kg)	3.0 ± 0.5	2.9 ± 0.3	0.174	Insignificant

Table 1: Body weight in cases with sepsis and controls.

Variable	Value
CRP (mg/l)	57.5 (24 to 128)
CBC	-
Low platelets	19 (63.3%)
Leukocytosis	5 (16.7%)
Neutrophil shift	11 (36.7%)
Bacterial culture	-
<i>Klebsiella</i>	15 (50.0%)
<i>Pseudomonas</i>	4 (13.3%)
MRSA	3 (10.0%)
CONS	6 (20.0%)
Anthracoids	1 (3.3%)
<i>Acinetobacter</i>	2 (6.7%)
<i>E. coli</i>	3 (10.0%)

Table 2: Laboratory results for patients with neonatal sepsis.

63.3% patients were reported with low platelet count; while, patients with leukocytosis represent only 16.7%. Neutrophil shift was present in 11 patients, representing 36.7% of septic cases. Table 3 has shown that MAPSE, TAPSE, ESD, ESV, EF, and FS are significantly affected among septic patients (P<0.05). The confidence level taken for the study is 95%. Therefore, the p-values obtained less than the level of significance (α=0.05) are considered significant.

A dramatic improvement in cardiac function parameters has been observed by comparing the echocardiographic parameters during and after resolution of sepsis (Table 4).

Discussion

The hemodynamic response to sepsis is not characterized well among the neonates as compared with children and adults. The

hemodynamic abnormalities among the neonates are significantly more variable [13]. Early recognition and aggressive supportive therapy of sepsis-associated myocardial dysfunction are important to reduce morbidity and mortality among the neonates [14]. The present study has shown that the right ventricular function is represented by TAPSE and left ventricular function is represented by MAPSE, EF and FS. However, these functions are significantly affected in septic patients; whereas, myocardial performance index (Tei index) for both LV & RV were not different significantly. A study conducted by Abtahi and Jafari [3] found that right ventricular and left ventricular Tei indexes were significantly higher in septic neonates as compared to non-septic neonates.

Variable	Controls (n=30)	Cases (n=30)	p-value	Significance
SA (m2)	0.21 ± 0.02	0.20 ± 0.01	0.177	Insignificant
RV Tei	0.31 ± 0.03	0.30 ± 0.03	0.240	Insignificant
LV Tei	0.36 ± 0.03	0.36 ± 0.03	0.695	Insignificant
TAPSE (cm)	1.98 ± 0.34	1.71 ± 0.33	0.004	Significant
MAPSE (cm)	2.09 ± 0.36	1.82 ± 0.35	0.005	Significant
EDD (cm)	2.32 ± 0.07	2.31 ± 0.05	0.230	Insignificant
EDV (ml)	12.57 ± 1.12	12.21 ± 0.78	0.146	Insignificant
ESD (cm)	1.54 ± 0.03	1.62 ± 0.04	<0.001	Significant
ESV (ml)	3.62 ± 0.22	4.18 ± 0.19	<0.001	Significant
EF (%)	71.11 ± 0.79	65.74 ± 0.64	<0.001	Significant
FS (%)	33.90 ± 0.60	30.14 ± 0.59	<0.001	Significant

Table 3: Echocardiographic measures in cases during sepsis and controls.

Variable	During sepsis	After resolution of sepsis	p-value	Significance
RV Tei	0.30 ± 0.03	0.28 ± 0.02	<0.001	Significant
LV Tei	0.36 ± 0.03	0.32 ± 0.03	<0.001	Significant
TAPSE (cm)	1.71 ± 0.33	1.99 ± 0.40	<0.001	Significant
MAPSE (cm)	1.82 ± 0.35	2.11 ± 0.42	<0.001	Significant
EDD (cm)	2.31 ± 0.05	2.32 ± 0.05		
EDV (ml)	12.21 ± 0.78	12.49 ± 0.79	<0.001	Significant
ESD (cm)	1.62 ± 0.04	1.42 ± 0.06	<0.001	Significant
ESV (ml)	4.18 ± 0.19	2.86 ± 0.40	<0.001	Significant
EF (%)	65.74 ± 0.64	77.11 ± 2.96	<0.001	Significant
FS	30.14 ± 0.59	38.92 ± 2.48	<0.001	Significant

Table 4: Comparison of echocardiographic measures in cases before and after resolution of sepsis.

Tomerak et al. [15] stated significant difference in left ventricular diastolic dysfunction (lower E/A ratio in the septic than the non-septic newborns), while no difference was noticed in the LV systolic function

(EF and FS) between septic and non-septic neonates. Abdel-Hady et al. [16] stated that the TDI (Tissue Doppler Imaging) indexes of global myocardial function (RV and LV Tei indexes) were significantly higher. Whereas, the atrio-ventricular annular systolic velocities were significantly lower in septic infants as compared to the controls. This indicated that both LV and RV systolic and diastolic dysfunction in these infants were more sensitive to detect myocardial dysfunction through conventional echocardiography. A study conducted by Nguyen et al. [17] examined the variability in heart rate of the infants that is associated with early onset of neonatal sepsis. The results revealed that early onset of neonatal sepsis have been associated with increased heart rate that is measured during randomly selected stationary periods. Cardiac depression is probably multi-factorial during sepsis [18]. Figure 1 shows the synopsis of the underlying mechanism in septic myocardial dysfunction.

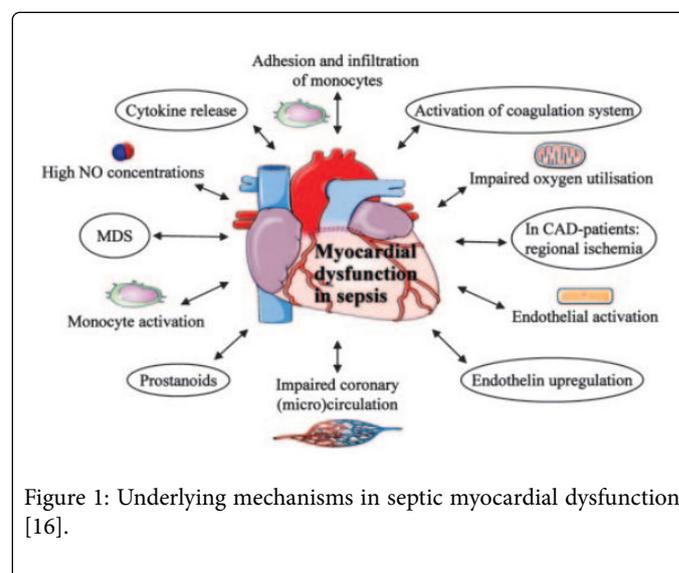


Figure 1: Underlying mechanisms in septic myocardial dysfunction [16].

Neonates are likely to experience infections during the perinatal period because of multiple exposures and compromised immune system. CRP and pro-calcitonin are considered as the most common acute phase reactants in neonatal sepsis. The levels of CRP tend to rise within 6-8 hours and reach at peak after 24 hours. The increase in CRP concentration is increased as a result of inflammation that triggers the release of IL-6 [4]. Myocardial depression has been observed as an adaptive event that tends to reduce energy expenditure due to limited generation of energy. Eventually, this prevents the activation of cell death pathways and do not render potential for complete functional recovery [19]. The septic patients are likely to suffer with undiagnosed regional myocardial ischemia, coronary artery disease, and secondary infarction. The decreased systemic vascular resistance under the conditions of adequate volume resuscitation has been encountered in sepsis. This may lead to elevated cardiac index, which obscures myocardial infarction [20].

A study conducted by Merx and Weber [18] revealed that the patients suffering volume resuscitated sepsis experience myocardial dysfunction that results in increased end-diastolic volume index and decreased ejection fraction. The non-septic patients are capable of maintaining normal cardiac volume, unlike the septic patients. Although, the acute changes in the end-diastolic volume index and ejection fraction remain sustained for several days but these changes are reversible. The septic patients are likely to suffer impaired diastolic

and ventricular systolic function. It has also been suggested that dysfunction of left ventricle is closely parallel to dysfunction of right ventricle. Septic shock is considered as the most severe complication of sepsis that account for 10% of infants admission in NICU. Factors such as cytotoxic, hypovolaemic, and distributive shock are responsible for pronouncing and characterizing cardiovascular dysfunction [20]. The cardiomyopathy induced by sepsis has been characterized by biventricular impairment of intrinsic myocardial contractility. Subsequently, this results in reduced left ventricle ejection fraction and stroke work index. A study conducted by Cao et al. [21] stated that clinical diagnosis of neonatal sepsis is followed by detection of abnormal heart rate of transient decelerations. This appears to be non-stationary as compared to variability in normal heart rate.

Conclusion

The study has concluded that significant cardiovascular changes may occur in the septic neonates; whereas, echocardiography is a reliable and useful tool to evaluate the myocardial function during neonatal sepsis. TAPSE, MAPSE, ESD, ESV, EF, and FS have strong predictive value for sepsis. Moreover, there is a significant improvement in all cardiac functions after resolution of sepsis. The complex pathology of neonatal sepsis involves the stimulation of immune system along with subsequent inflammation and myocardial dysfunction. The present study was limited to 30 neonates only due to lack of informed consents and time as well. Future studies may consider larger sample size by surveying different hospitals to execute further analysis.

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Conflict of Interest

The research holds no conflict of interest.

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