

Research Article

Comparison of Functional Echocardiographic Markers in Septic and Non-Septic Neonate

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Abstract

Background: Neonatal sepsis accounts for significant morbidity and mortality and its hemodynamics is complex. Functional echocardiography is emerging at a rapid pace and currently it is considered as a key tool for providing real time information on cardiovascular performance.

Objective: To assess and compare functional Echocardiographic markers in septic and non-septic neonate.

Methodology: This cross-sectional comparative study was conducted in the Department of Neonatology, BSMMU over an Eighteen-month period from March 2022 to August 2023. 25 neonates including term baby and preterm ≥ 34 weeks with early or late-onset sepsis satisfying the inclusion criteria were enrolled for the study and compared with same gestational age matched healthy control.

Result: Comparison of functional echocardiographic parameters between two groups were statistically significant in respect to right and left ventricular output and tricuspid annular plane systolic excursion. Cardiac output was increased (rt. ventricular output 277.4 ± 74.2 Vs 209 ± 70 , lt. ventricular output 339.5 ± 43.2 Vs 276 ± 74.9 , p-values were 0.002 and 0.001 respectively) and tricuspid annular plane systolic excursion (0.49 ± 0.13 Vs 0.74 ± 0.34 , p value 0.001) was decreased in septic neonate compared to healthy counterpart. The result was also statistically significant result in respect to right and left ventricular output and tricuspid annular plane systolic excursion (p-values were 0.039, 0.004 and 0.01) respectively in comparison between preterm septic and non-septic newborn. When compared between the term neonates (37 weeks to 40 weeks) of both groups, there were also statistically significant result in respect to right ventricular output, left ventricular output and tricuspid annular plane systolic excursion (p-values were 0.006, 0.03 and 0.025) respectively.

Conclusion: Significant cardiovascular changes like cardiac output and right ventricular systolic dysfunction evidenced by Functional Echocardiography, were common association of neonatal sepsis in comparison to non-septic neonate.

Keywords: Neonatal Sepsis; Functional Echocardiography

Introduction

The first 28 days of life, the neonatal period is the most vulnerable time for a child's survival. Neonate face the highest risk of dying at an average global rate of 18 deaths per 1,000 live births in 2021, down by 51 per cent from 37 deaths per 1,000 live births in 1990. Globally, 2.3 million children died in the first month of life in 2021- approximately 6,400 neonatal deaths every day [1]. Preterm birth, intrapartum-related complications (birth asphyxia or inability to breathe at birth), infections and birth defects are the leading causes of most neonatal deaths [2]. Despite a declining neonatal mortality rate globally, marked disparities in neonatal mortality exist across regions and countries. Across countries, the risk of dying in the first month of life was about 53 times higher in the country with highest mortality than in the lowest mortality country. In regions where under-five mortality rates are relatively low, more than half of all under-five deaths occur during the neonatal period. The only exception is South Asia, where the proportion of neonatal deaths is among the highest (62 per cent) despite a relatively high under-five mortality rate [3]. According to Bangladesh Demographic and Health Survey, 2022, Infant Mortality Rate (IMR) is 25/1000 live birth and Neonatal Mortality Rate (NMR) in our country is 20/1000 live birth. Cause of Neonatal mortality includes 33% due to preterm related complications, 25% due to intrapartum related events, 10% due to congenital abnormality, 9% due to infection and 8% due to pneumonia and 15% due to other condition⁴. Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life. It has classified as either early onset (within first 72 hours of life) or late onset sepsis (occurring after 72 hours of age) i.e., infections occurring before and after 72 hours of life [4,5]. One study of our country showed 8.9% and 91.1% neonates presented with Early Onset Sepsis (EOS) and Late Onset Sepsis (LOS) respectively⁶. Early diagnosis and treatment of neonatal sepsis may help decreasing neonatal mortality. Cardiovascular complications, myocyte damage and modification of cardiac blood flow induced by inflammatory mediators are the consequences of neonatal sepsis [6,7]. The cardiac symptoms among these infants includes: poor perfusion, cyanosis, desaturation, hypotension and bradycardia [8]. This clinical signs on which physicians traditionally have relied upon, provide limited insight into the adequacy of systemic blood flow and organ perfusion which have been demonstrated to be misleading in their accuracy [9]. New, non-invasive technologies allow to assess the characteristics of hemodynamic and identify its disorders objectively and without any harm to the patient. Echocardiography is the most widely used instrumental examination to assess cardiac function in severely ill patients. Therefore, it has been agreed to consider classical echocardiography as the clinical standard for assessing cardiac function [10]. With the use of bedside echocardiography, it is possible to assess cardiac function, preload, afterload, fluid responsiveness and to estimate and cardiac output. Echocardiography is easily available on bedside, it is non-invasive and portable and it can be used to acquire information of physiological changes in real time. This physiological information, in correlation with clinical assessment, can help in guiding targeted specific therapy [11]. It has been demonstrated in several studies that real time objective physiologic data such as cardiac output and other measurements of central blood flow provide hemodynamic information, which may be different from the assumed underlying physiology [12]. Different terms have been used to describe the use of bedside echocardiography in various settings such as neonatologist-performed echocardiography, targeted neonatal echocardiography, functional echocardiography (FnECHO) or point-of-care-ultrasound [13]. Functional echocardiography is emerging at a rapid pace and currently it is considered as a key tool for hemodynamic assessment in the intensive care settings [14]. The current indications used for FnECHO have been primarily established on the basis of clinical experience in a growing number of neonatal units and recent observational studies and not on the basis of large clinical studies [15]. Early recognition and aggressive supportive therapy of sepsis-associated myocardial dysfunction are important to reduce morbidity and mortality among the neonates [16]. Recent study has shown that the change in the functional Echocardiographic markers (where right ventricular function is represented Tricuspid Annular Plane Systolic Excursion (TAPSE) and left ventricular function is represented by Mitral Annular Plane Systolic Excursion (MAPSE), Ejection Fraction (EF) and Fractional Shortening (FS), right and left ventricular output are significantly different in septic patients [17]. TAPSE, EF and FS have strong predictive value for sepsis [18]. Considering the limited number of studies and the scarcity of data regarding comparison of functional Echocardiographic parameters in both septic and non-septic newborn, this study was conducted with an aim to compare the parameters. Therefore, aim of this study is to assess and compare functional Echocardiographic markers in septic and non-septic neonate.

Materials and Methods

Study Design

This is a cross-sectional comparative study.

Place of Study

Department of Neonatology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh.

Study Period: From March, 2022 to August, 2023.

Study Population

Neonates of term baby and preterm baby ≥ 34 weeks who delivered in this hospital and admitted in NICU, Bangabandhu Sheikh Mujib Medical University during the study period.

Inclusion criteria:

- Neonate with 34 weeks or more having presence of any clinical feature of sepsis with two or more risk factors for sepsis and having suggestive laboratory findings with or without positive blood culture.

Exclusion Criteria:

- Major congenital anomalies
- Perinatal Asphyxia
- Antenatally or postnatally diagnosed congenital heart disease
- Parental refusal

Sample Size

50

Study Procedure

All newborn ≥ 34 weeks with clinical features of sepsis were subjected to send septic work up along with blood C/S according to NICU protocol. After getting septic screening positive report, neonates were assessed for eligibility. After meeting the inclusion and exclusion criteria, written informed consent was taken from parents and/ or legal guardians. For every case, same gestational age matched healthy neonates as control were enrolled from post-natal ward. Maternal characteristics such as number of antenatal visits, type of gestation, mode of delivery, prolonged rupture of membrane, oligohydramnios, maternal h/o fever, urinary tract infection and maternal use of antenatal antibiotic and neonatal characteristics such as gestational age, birth weight, sex, birth weight category and fetal growth at birth were collected by interviewing and reviewing medical records. All required information's were recorded in a data collection form during hospital admission. Arrangement of functional echocardiography ensuring proper thermal care and maximum comfortable position was maintained by investigator. The FnECHO was performed by experienced neonatologist with using My Lab Gamma ultrasound machine, with neonatal probe (12 MHz transducer). Neonates with sepsis underwent FnECHO within 12 hours of onset of clinical signs. Echocardiography of healthy neonates matching with same gestational age were performed in ward ensuring proper thermal care within 12 hours of enrollment. Infection control measures were taken in all subject while performing the scan. Echocardiographic markers were calculated and recorded by the investigator during procedure. Functional Echocardiographic markers were measured following standard formula:

- Right Ventricular output (RVO) measurement:

$$\text{Pul CSA} \times \text{VTI} \times \text{Heart Rate}$$

$$\text{RVO} = \frac{\dots\dots\dots}{\text{Weight}}$$

Weight

$$\text{Pulmonary CSA (Pul. Cross-Sectional area)} = \pi \times \text{Pulmonary Diameter}^2/4$$

Normal range of LVO and RVO are defined as 150 to 300 mL/kg/minute each¹⁹.

- Left Ventricular output (LVO) measurement:

$$\text{Ao CSA} \times \text{VTI} \times \text{Heart Rate}$$

$$\text{LVO} = \frac{\dots\dots\dots}{\text{Weight}}$$

Weight

$$\text{Ao CSA (Aortic cross-sectional area)} = \pi \times \text{aortic diameter}^2/4$$

VTI: Velocity Time Integral

- Fractional Shortening was calculated by measuring left ventricular end diastolic diameter (LVEDD) and left ventricular end systolic diameter (LVESD) using M mode echo and applying the following formula:

$$FS (\%) = \frac{LVEDD - LVESD}{LVEDD}$$

Normal neonatal values for FS% are = 25 to 40% [18]

- Ejection Fraction: Normal value of EF in newborn infants is between 56-78% [18]

$$EF (\%) = \frac{LVEDV - LVESV}{LVEDV}$$

LV cavity volume in end diastole (LVEDV) and end systole (LVESV)

- Tricuspid annular plane systolic excursion (TAPSE):

M-Mode was used to measure the distance travelled by annulus towards the apex. Values achieved in neonate range from 0.4 - 1.03 cm is normal [20].

Statistical Analysis

After compilation of data, all the data were entered into a personal computer and edited, analyzed and plotted in tables. Statistical analysis was performed by using the Statistical Package for Social Sciences (SPSS) for windows version 25, (IBM, USA). Comparisons were performed by chi-square test for categorical variables, independent t-test for quantitative variables. P-value less than 0.05 was considered statistically significant.

Results

This cross-sectional comparative study was conducted to compare the Functional Echocardiographic markers in septic and non-septic neonate. During the study period, 76 neonates of suspected sepsis were assessed for eligibility. Among them 51 newborns were excluded as they did not meet inclusion criteria. Finally, 25 newborns were included as case and 25 healthy newborns matching same gestational age from postnatal ward were included as control in this study for analysis (Fig. 1, Table 1).

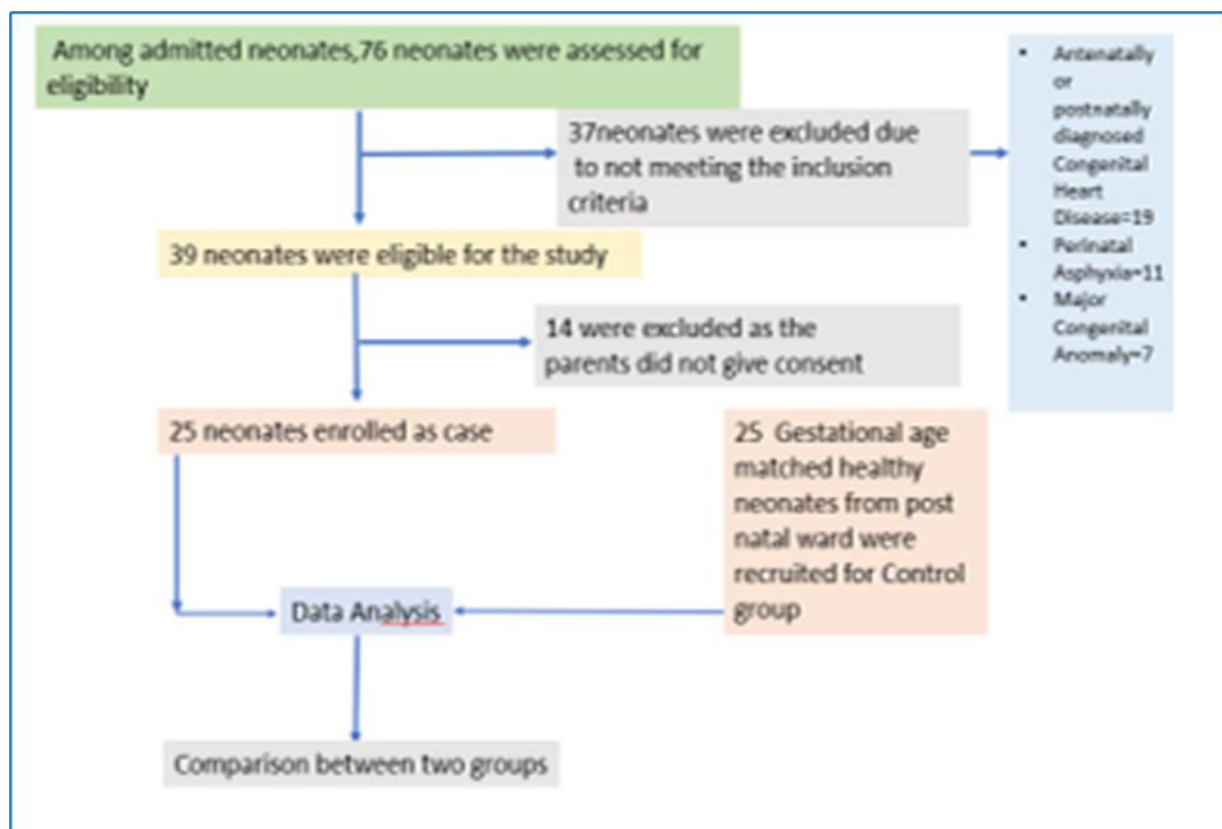


Figure 1: Enrollment of neonate.

Parameter	Septic group	Nos septic group	P- Value
	(n=25)	(n=25)	
Number of Aatrastal visits, n(%)			
<4	9(36)	7(28)	0.54 ^{ns}
>4	16(64)	18(72)	
Type of Gestation, n(%)			
Singleton	25(100)	24(96)	0.312 ^{ns}
Multiple	0(0)	1(4)	
Mode of delivery, n(%)			
NVD	5(20)	7(28)	0.508 ^{ns}
LUCS	20(80)	18(72)	
PROM(>18hours),n(%)	7(28)	5(20)	0.508 ^{ns}
Maternal History of fever, n(%)	4(16)	2(8)	0.380 ^{ns}
Urinary tract infection,n(%)	3(12)	1(4)	0.308 ^{ns}
Oligohydramnios, n (%)	10(40)	6(24)	0.225 ^{ns}
Maternal use of Antibiotica, n (%)			
Yes	8(32)	4(16)	0.85 ^{ns}
No	17(68)	21(84)	

Table 1: Comparison of Baseline maternal characteristics between septic and non-septic neonate (N=50).

Qualitative data were presented as number and percentage (%).

Baseline maternal characteristics of studied neonates were presented in Table 1. The newborns of septic group presented with classic features of neonatal sepsis. Most common clinical presentation was respiratory distress in 24 neonates neonatal sepsis and maternal use of antibiotics. There was no significant difference in both groups regarding type of gestation, mode of delivery, maternal risk factors.

Neonatal baseline characteristics were compared in Table 2. No significant difference was found in respect to birth weight, gestational age, sex and fetal growth at birth between two groups.

Parameter	Septic Group (n=25)	Non-Septic Group (n=25)	p-value
Gestational Age in weeks Mean $\pm$ SD	35.64 $\pm$ 2.018	35.76 $\pm$ 0.970	0.790 ^{ns}
Sex n(%)			
Male	16(64)	14(56)	0.564 ^{ns}
Female	9(36)	11(44)	
Birth weight in grams, Mean $\pm$ SD	2310 $\pm$ 26.5	2399 $\pm$ 113	0.204 ^{ns}
Birth weight in categoring n(%)			
<1500 g	2(8)	0(0)	0.249
1500-2499 g	16(64)	20(80)	

>2500g	7(28)	5(20)	
Fetal growth at birth, n (%)			
AGA	24(96)	25(100)	0.312 ^{ns}
SGA	1(4)	0(0)	

Table 2: Comparison of Baseline neonatal characteristic between septic and non-septic neonate (N=50).

Other encountered clinical features include lethargy in 19 neonates, tachycardia in 13 neonates, hypothermia in 2 neonates and bradycardia in 1 neonate (Table: 3) 0.004 and 0.01) respectively. Other parameters showed no significant difference.

Clinical Characteristics	Septic Group (n=25)
Respiratory distress, n (%)	24(96%)
Lethargy, n (%)	19(76%)
Tachycardia, n (%)	13(52%)
Bradycardia, n (%)	1(4%)
Hypothermia, n (%)	2(8%)
Respiratory distress, n (%)	24(96%)
Seizure, n (%)	9(36%)

Table 3: Clinical characteristics of septic neonates (N=25).

Parameter	Septic Group (n=25)	Non-septic Group (n=25)	p-value	Normal Range
Right Ventricular Output (ml/kg/min) Mean $\pm$ SD	277.4 $\pm$ 74.2	209 $\pm$ 70	0.002	Rigs and left Ventricular Output 150-30ml/kg/min
Left Ventricular Output (ml/kg/min) Mean $\pm$ SD	339.5 $\pm$ 43.2	276 $\pm$ 74.9	0.001	
Ejection Fraction (%) Mean $\pm$ SD	72 $\pm$ 9.4	75.4 $\pm$ 1.47	0.080	56-78%
Fractional Shortening (%) Mean $\pm$ SD	37.1 $\pm$ 3.1	37.5 $\pm$ 1.8	0.900	25-40%
Tricuspid Annular Plane Systolic Excursion(cm) Mean $\pm$ SD	0.49 $\pm$ 0.13	0.74 $\pm$ 0.34	0.001	0.4-1.03cm

Table 4: Comparison of Functional Echocardiographic Parameters between septic and non-septic (N=50).

Functional echocardiographic parameters were compared between the 2 groups in Table: 4 Right Ventricular Output was higher in septic group around 277 ml/kg/min and around 209 ml/kg/min in non-septic group. Left Ventricular Output was also higher in septic group around 339 ml/kg/min compared to 276 ml/kg/min in non-septic group. However, ejection fraction was relatively higher in non-septic group around 76% and in septic group it was 72%. Fractional shortening in both the groups were nearly similar, 37% and 37.5% in septic and non-septic group respectively. Tricuspid Annular Plane Systolic Excursion was comparatively lower in septic neonate around 0.49 cm and then non-septic neonates around 0.74 cm. Comparison between two

groups were statistically significant in respect to right and left ventricular output and tricuspid Annular Plane Systolic Excursion (p- values were 0.002, 0.001 and 0.001) respectively. Other parameters showed no significant difference.

Parameter	Septic group (n=18)	Non-septic (n=18)	p-value	Normal Range
Right Ventricular Output (ml/kg/min) Mean $\pm$ SD	263.1 $\pm$ 73.2	208.1 $\pm$ 79.8	0.039 _s	Right and left Ventricular Output 150-30ml/kg/min
Left Ventricular Output (ml/kg/min) Mean $\pm$ SD	337.4 $\pm$ 44.1	273.8 $\pm$ 74.3	0.004 _s	
Ejection Fraction (%) Mean $\pm$ SD	74.3 $\pm$ 7.1	75.7 $\pm$ 1.5	0.45 _{ns}	56-78%
Fractional Shortening (%) Mean $\pm$ SD	37.8 $\pm$ 3.0	37.4 $\pm$ 1.7	0.59 _{ns}	25-40%
Tricuspid Annular Plane Systolic Excursion(cm) Mean $\pm$ SD	0.49 $\pm$ 0.136	0.76 $\pm$ 0.39	0.01 _s	0.4-1.03 cm

Table 5: Comparison of Functional Echocardiographic Parameters of preterm (34 to <37 weeks) neonate (N=36).

Functional echocardiographic parameters were compared between the preterm neonates (34 weeks to < 37 weeks) of both groups in Table: 5 Right Ventricular Output was comparatively higher in septic group around 263 ml/kg/min than non-septic group of 208ml/kg/min. Left Ventricular Output was higher in septic group around 337 ml/kg/min and around 273 ml/kg/min in non-septic group. However, ejection fraction was slightly higher in non-septic group around 75% and in septic group it was 74%. Fractional shortening in both the groups were nearly similar, 37.8% and 37.4% in septic and non-septic group respectively. Tricuspid Annular Plane Systolic Excursion was less in septic neonates around 0.45 cm than non-septic neonate of around 0.76 cm. Comparison between two groups were statistically significant in respect to right and left ventricular output and tricuspid Annular Plane Systolic Excursion (p- values were 0.033).

Parameter	Septic group (n=7)	Non-septic (n=7)	p-value	Normal Range
Right Ventricular Output (ml/kg/min) Mean $\pm$ SD	312.8 $\pm$ 68.9	211.4 $\pm$ 41.9	0.006 _s	Right and left Ventricular Output 150-30 ml/kg/min
Left Ventricular Output (ml/kg/min) Mean $\pm$ SD	359.3 $\pm$ 13.36	281.4 $\pm$ 82.4	0.03 _s	

Ejection Fraction (%) Me an $\pm$ SD	66.0 $\pm$ 12.2	74.5 $\pm$ 1.73	0.119 ^{ns}	56-78%
Fractional Shortening (%) Me an $\pm$ SD	34.8 $\pm$ 4.7	36.5 $\pm$ 1.9	0.443 ^{ns}	25-40%
Tricuspid Annular Plane Systolic Excursion(cm) Mean $\pm$ SD	0.51 $\pm$ 0.13	0.71 $\pm$ 0.15	0.025 ^s	0.4-1.03 cm

Table 6: Comparison of Functional Echocardiographic Parameters of term (37 to 40 weeks) neonate between septic and non-septic neonate (N=14).

Functional echocardiographic parameters were also compared between the term neonates (37 weeks to 40 weeks) of both groups in Table 6. Right Ventricular Output was much higher in septic group around 313 ml/kg/min and around 211 ml/kg/min in non-septic group.

There was marked difference in left Ventricular Output too, which was higher in septic group around 359 ml/kg/min and around 281 ml/kg/min in non-septic group. Whereas, Ejection fraction was relatively higher in non-septic group around 75% and in septic group it was 66%. The Fractional shortening in both the groups were nearly similar, around 35% and 37% in septic and non-septic group respectively. Tricuspid annular plane systolic excursion was less in septic neonates around 0.5 cm and higher in non-septic neonates around 0.7 cm. Comparison between two groups were statistically significant in respect to right ventricular output, left ventricular output and tricuspid annular plane systolic excursion (p-values were 0.006, 0.03 and 0.025) respectively. Other parameters showed no significant difference.

Parameter	EONS Group (n=8)	LONS Group (n=17)	p-value	Normal Range
Right Ventricular Output (ml/kg/min) Mean $\pm$ SD	301.3 $\pm$ 92.1	265.6 $\pm$ 64.1	0.27 ^s	Right and left Ventricular Output 150-30ml/kg/min
Left Ventricular Output (ml/kg/min) Mean $\pm$ SD	313.2 $\pm$ 55.6	351.9 $\pm$ 30.7	0.09 ^s	
Ejection Fraction (%) Mean $\pm$ SD	74.3 $\pm$ 9.8	70.9 $\pm$ 9.3	0.42 ^{ns}	56-78%
Fractional Shortening (%) Mean $\pm$ SD	37.4 $\pm$ 6.35	36.8 $\pm$ 1.9	0.77 ^{ns}	25-40%
Tricuspid Annular Plane Systolic Excursion(cm) Mean $\pm$ SD	0.51 $\pm$ 0.12	0.5 $\pm$ 0.15	0.68 ^s	0.4-1.03 cm

Table 7: Comparison of Functional Echocardiographic Parameters between EONS and LONS group (N=25).

Functional echocardiographic parameters were also compared between EONS and LONS in Table: 7. EONS neonates were 8 (32%) and LONS neonates were 17(68%). Comparison between two groups were not statistically significant. Among this septic group, culture positive neonates were 17(68%), in EONS group 3(12%) and in LONS group 14(56%) neonates were culture positive. Among these culture positive neonates, *Klebsiella pneumoniae* was more predominant.

Parameter	Preterm (n=18)	Term (n=07)	p-value	Normal Range
Right Ventricular Output (ml/kg/min) Mean $\pm$ SD	263.1 $\pm$ 73.2	312.8 $\pm$ 68.9	0.27 ^s	Right and left Ventricular Output 150-30 ml/kg/min
Left Ventricular Output (ml/kg/min) Mean $\pm$ SD	337.4 $\pm$ 44.1	345 $\pm$ 43.7	0.7 ^s	
Ejection Fraction (%) Mean $\pm$ SD	74.3 $\pm$ 7.17	66 $\pm$ 12.3	0.13 ^{ns}	56-78%
Fractional Shortening (%) Mean $\pm$ SD	37.8 $\pm$ 3.1	34.8 $\pm$ 4.7	0.16 ^{ns}	25-40%
Tricuspid Annular Plane Systolic Excursion(cm) Mean $\pm$ SD	0.48 $\pm$ 0.14	0.51 $\pm$ 0.13	0.67 ^s	0.4-1.03 cm

Table 8: Comparison of Functional Echocardiographic Parameters between Term and preterm septic group (N=25).

Functional echocardiographic parameters were compared between Term and preterm septic group in Table: 8. Comparison between two groups were not statistically significant.

Discussion

This cross-sectional comparative study was conducted to compare the functional Echocardiographic markers in septic and non-septic neonate. In this study, a total of 25 (septic) neonates diagnosed were enrolled as case and compared with 25 same gestational age matched healthy neonate from post-natal ward. In this study, there were a non-significant difference between both groups regarding baseline maternal characteristics (Maternal number of antenatal visits, type of gestation, mode of delivery, prolonged rupture of membrane, maternal h/o fever, urinary tract infection, oligohydramnios, maternal use of antibiotic) and baseline neonatal characteristics (the gestational age, sex, birth weight, birth weight category). This non-significant difference supported that all these factors had no impact on the results of this study.

This study found comparison of functional Echocardiographic markers between septic and non-septic groups were statistically significant in respect to right and left ventricular output and tricuspid Annular Plane Systolic Excursion (p- values were 0.002, 0.001 and 0.001) respectively. Other parameters (ejection fraction and fractional shortening) showed no significant difference. The findings of high cardiac output compared to non-septic group in a similar study conducted by Deshpande et al., which is consistent to our study findings. The study compared both Right and Left Ventricular Output (RVO and LVO) only in late onset neonatal sepsis, enrolled all infants admitted in the NICU with suspected late onset sepsis based on clinical and laboratory findings. The study compared the cardiac outputs of infants with gram-negative sepsis and those with gram-positive sepsis. Neonates with late onset sepsis showed high RVO and LVO as demonstrated by FnECHO. The study explained this pattern of low systemic vascular resistance with increased cardiac output is a predominant feature of gram-negative sepsis. These findings

of higher cardiac outputs in patients with gram-negative sepsis were seen in term as well as preterm infants in their study. Majority of infants in their study had gram-negative infection, with *Klebsiella pneumoniae* being the most common organism isolated. The difference in pathophysiology and host response in gram-negative and gram-positive bacteremia could explain the differences in hemodynamics. The nature of endotoxins produced by gram-negative bacteria (for e.g., the lipid A moiety of lipopolysaccharide complex present on bacterial cell wall) is responsible for the hemodynamic alterations [17]. This study also found increased cardiac output and possible explanation may be that LONS is more in this study.

This study also found most prevalent organism *Klebsiella pneumoniae* which is also consistent with the study. In preterm and term group, our study also found statistically significant result in respect to right and left ventricular output and tricuspid Annular Plane Systolic Excursion (p- values were 0.039, 0.004 and <0.001 in preterm and 0.006, 0.030 and 0.025 in term respectively) Other parameters showed no significant difference. The findings is also consistent with these two previous study, Murasi, et al., and de Waal K and Evans where ventricular output was significantly higher in septic group [12,21]. These two studies only included preterm babies. But this study included both preterm and term. Regarding Tricuspid Annular Plane Systolic Excursion (TAPSE), this study shows statistically significant result. TAPSE was lower in septic group compared to non-septic groups on all aspect. Previous study done by Alzahrani, et al. and Abdel, et al., showed that TAPSE was significantly lower in both preterm and full-term septic patients group compared to control group [15,22]. This indicated impaired longitudinal myocardial functions of right ventricle. This study findings' result was in also agreement with study of Alzahrani, et al., as they also reported that TAPSE is considerably affected among septic patients.

Regarding other two functional echocardiographic marker, Ejection Fraction (EF) and Fractional Shortening (FS), this study found no statistically significant result which are similar to Abdel, et al., and Tomerak et al., as these two studies also noticed no significant difference in EF and FS [22,23]. Another study, Alzahrani, et al., found ejection fraction significantly affected in their study which is not consistent with this study¹⁵. This study also compared functional echocardiographic markers between Early Onset Neonatal Sepsis (EONS) and Late Onset Neonatal Sepsis (LONS) group; between preterm and term septic, but found no statistically significant difference, that indicates changes in these markers not depends on timing of postnatal age of onset of sepsis or gestational age. This study findings suggest that echocardiography can provide real-time information on cardiovascular performance, complementing clinical signs and aiding in accurate diagnosis and management of septic neonates.

Conclusion

Significant cardiovascular changes take place in the septic neonate evidenced by functional echocardiographic marker's changes like left and right ventricular output increases and tricuspid annular plane systolic excursion decreases significantly in compared to non-septic neonate.

Limitation

As it is a cross sectional comparative study, data were taken at a point of time. Hemodynamic in sepsis changes with time, serial measurements of Functional echocardiographic markers could have provided more accurate information on clinical progress and response to therapy, as well as predictors of mortality if any. Performing Functional Echocardiography by a single neonatologist could not be possible.

Recommendations

The increased use of Functional Echocardiography may help corroborate clinical hemodynamic variables, add to our existing knowledge regarding mechanisms of action of common therapies used for hemodynamic instability and support our understanding of short- and long-term outcomes in infants with abnormal cardiovascular health states. Large-scale, multicentered, Prospective studies are still needed to establish the relevance of both static and dynamic hemodynamic variables, as well as to compare commonly used therapeutic options.

Conflict of Interest

The authors declare that they have no conflict of interest.

Author Contribution

All authors contributed to the study conception and design. Material preparation, data collection and statistical analysis was performed by first author. The first draft of the manuscript was written by first author and respected other authors further reviewed and commented on the first and the following drafts, until the final version of the article. All authors commented on previous versions of the manuscript. All authors read the final manuscript.

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Ethical Approval

The study was approved by the Institutional Review Board of BSMMU. Informed consent from parents and caregivers was taken.

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