

## **Electrical Cardiometry versus Echocardiography in Assessment of Hemodynamic Status in Preterm Neonates with Septic Shock**

### **Abstract:**

**Background:** Severe sepsis combined with hypotension or the requirement for vasopressors in newborns is known as neonatal septic shock and occurs even when the body is receiving enough fluids to revive it.

Hemodynamic monitoring in this condition can be done through clinical assessment or ~~using~~ invasive and non-invasive tools like functional Echocardiography. Electrical Cardiometry (EC) has emerged as a continuous and non-invasive measurement of (CO) cardiac output. It has FDA approval and has been verified for usage in newborns.

**Methods:** All preterm infants admitted to the NICU from where? who have been diagnosed with septic shock and have a gestational age between (34 0/7 and 36 6/7 weeks). in which temporal clipping? 80 healthy neonates (term? Preterm?) ~~who~~ were allocated to for gestational age and sex made up the control group. Prior discharge, electrical cardiometry assessment was carried out throughout the first, second, and third days of sepsis symptoms. Was it also done in the control group?

**Results:** In warm septic shock group; cardiac output (CO), stroke volume (SV), and cardiac index measured by electrical cardiometry (EC) had been substantially greater at the second evaluation contrasted to last evaluations in comparison to control group. Its confuse: was greater on the 2<sup>nd</sup> avaluation compared to first avaluation in intervention group AND control group? There was no significant difference as regard contractility

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index (ICON) between both readings in both groups. Systemic vascular resistance (SVR) was significantly lower at 2nd evaluation in comparison to last evaluation than in control group. In cold septic shock group, SV, CO and cardiac index measured by EC were substantially lower at 2nd evaluation contrasted to last evaluation in comparison to control group. ICON was significantly lower at 2nd readings in comparison to last readings in both groups. SVR was significantly higher at 2nd evaluation in cold septic shock in contrast to control group.

**Conclusion:** Electrical cardiometry is a valuable tool of bedside hemodynamic monitoring and management in cases with neonatal septic shock. [To warm and cold shock?](#)

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**Keywords:** septic shock, electrical cardiometry, inotropes.

### Introduction:

Among the ~~the m~~ most frequently occurring diseases in the newborn intensive care unit (NICU) is neonatal sepsis, which has a high morbidity and fatality rate. (1)

The main newborn risk factors for infection are low birth weight and prematurity. (2)

~~circulatory instability affects many children with sepsis; p~~ Premature infants are more at risk because of the peculiarities of their circulatory function and reserve. (3)

Depends on the core pathophysiology, sepsis could harm the circulatory system and cause many forms of shock states, including septic shock. (4)

~~e~~ Even though cold shock may also happen, septic shock more often manifests in the form of vasodilatory shock ([warm shock](#)) in the newborn period. (3)

Early identification of circulatory impairment in ill neonates helps physicians to make prompt therapeutic choices and objectively track patient response to therapy. (5)

Doppler measurements on an echocardiography are the most popular non-invasive method for estimating [cardiac output \(CO\)](#), although it is technically challenging and relatively intermittently practicable. (6)

A non-invasive, continuous technique for calculating cardiac output (CO) is electrical cardiometry (EC) ([number of reference](#) Xu et al., 2021). EC is frequently suggested as a method for measuring hemodynamics that is reliable, safe, and accurate. [a](#)Also has [Food and Drug Administration?](#) FDA validation and approval for use in newborns (7)

[What is electrical cardiometry? how is it made? How does it relate to the treatment of septic shock? It is necessary to put all of this in context for the reader who is not familiar with using this tool.](#)

**In this research**, we aimed to determine the most effective cardiovascular care [of what?](#)and the responsiveness of such treatment([what treatments?](#)) by evaluating the hemodynamic state and cardiac function in infants with septic shock.

#### **Methods:**

80 healthy controls [newborns \(term or preterm?\)](#)who were allocated for gestational age and sex to the preterm babies ~~and~~(40 cases) who had been confirmed to have septic shock in this prospective cross-sectional research over a period of two years([wich?](#)).

The cases group consisted of all premature newborns admitted to the NICU who had septic shock along with gestational ages between (34 0/7 and 36 6/7) weeks and met Haque's 2005 diagnostic criteria of neonatal sepsis. (Figure 1), (8).

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~~Were all excluded from the research: -F~~full-term newborns, preterm neonates with gestational ages under 34 weeks, IDM, IUGR, what do these acronyms mean? when citing an acronym for the first time always put the meaning in fullmajor congenital malformations, structural cardiac disorders with the exception of hemodynamically insignificant PDAswhat do these acronyms mean? with sizes less than 1.5 mm (9), PFOwhat do these acronyms mean? and tiny ASDswhat do these acronyms mean?~~were all excluded from the research. With~~ an Apgar score of less than 5 at 5 minutes, a failure to tolerate adhesive skin leads, instances requiring high frequency mechanical breathing, Hydrops fetalis, ~~and~~ all surgical cases and patients -there iswith evidence of prenatal asphyxia.

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The Tanta University Pediatrics ethical committee gave the research permission to proceed. Before individuals were enrolled, parental permission was required. The Declaration of Helsinki and the standards of good clinical practice were followed in the conduct of the research.

A thorough taking of history, and physical assessment were performed on the two research groups.was there a standard document for this? if so, put it as a figure or annex

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Laboratory assessment

Samples of blood were taken for standard laboratory tests from all infants having septic shock (N = 40) as well as the healthy control group (N = 80). what kind of samples and what were they collected for? Only at the beginning of the study or periodically?

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Research Methodology:

Electrical Cardiometry (EC) (6):

The ICON® hemodynamic monitor (ICON Cardiotronics, Inc., La Jolla, CA 92307; Osyka Medical GmbH, Berlin and Germany, version C3, Serial number: 1817406) was used to take the measures.

EC was used to compare the hemodynamic condition of the patient to echocardiogram

on the first, second, and third days after sepsis signs began and before discharge. put that in the summary too  
What data does electrical cardiometry provide that makes it possible to compare the echocardiogram data of the shocked patient? Put this explanation here or in introduction

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Gender, weight, gestational age (GA), body surface area (BSA), and Apgar ratings have been collected along with other demographic data. The experiment's weight was used to calculate the EC. Aesculon (???)calculated the BSA using the Boyd formula. was there a standard document for this? if so, put it as a figure or annex

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The sensor wire was attached to the EC, and the necessary data (age, height, gender, weight, blood pressure, SpO<sub>2</sub>, HR, and Hb) were provided. Iindex of contractility (ICON), Cardiac index (CI), cardiac output (CO), stroke volume (SV), and systemic vascular resistance were all continually presented on the EC.

The research design is not clear. Were EC measurements taken when the patient showed signs of septic shock and after initiation of treatment? I suggest making a flowchart and explaining better.

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what parameter was used to classify the patient as warm or cold shock?

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**Outcomes of the study:** Put before methodology

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Primary outcomes:

1. Use EC to determine the hemodynamic state of healthy preterm newborns.

2- Use e) EC? to evaluate the hemodynamic state in premature newborns having septic shock.

Secondary outcomes:

Determine the response by assessing the value of EC monitoring in deciding about fluid treatment and the administration of vasopressors or inotropes based on the kind of septic shock.

### **Statistical Analysis**

With the aid of the IBM SPSS statistical software program edition 20.0 (IBM Corp, Armonk, NY), information was introduced into the computer and evaluated. The normality of the distribution was examined using the Kolmogorov-Smirnov test. The mean, standard deviation, range (minimum and maximum), median, and interquartile range (IQR) were used to characterize the quantitative information. At the 5% level, significance of the findings was determined. Were only descriptive measures taken?

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Was the EC not compared with the echocardiogram? Was the case group not compared to the control? Was the warm group not compared with cold group? No comparative analysis? No stratification? How was the interference of so many variables measured in the final outcome?

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### **Results:**

(Table 1) provides the demographic information and anthropometric measures, whereby among the case and control groups did not substantially vary (gestational age, sex, post-natal age, length, weight, body surface area, and ponderal index). The Apgar score and delivery method are both the same.

Vital signs are illustrated in (table 2).

Table 3 shows: Warm septic shock group SV, CO, SI, and CI. [This parameters](#) were substantially greater at second measurements contrasted to final measures and in contrast to control group. [\(at second measurements and final measurements?\)](#)

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In the cold septic shock group and in contrast to the control group, SV, CO, SI, and CI were substantially reduced at second readings in contrast to final measurements.

In the combined septic shock group [this classification is not described in the methodology](#), SV, CO, SI, and CI were substantially reduced at second readings compared to the control group, but no discernible change was existed among second and final readings.

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Table 4; In warm septic shock group; no substantial variation was existed as regard Index of Contractility (ICON) between 2nd evaluations in contrast to last readings and in contrast to control group.

In cold septic shock: ICON was significantly lower at second evaluation in contrast to final evaluation and in contrast to control group.

In combined septic shock; ICON was significantly lower at second evaluation in contrast to control group but no substantial variation was existed between 2nd and last evaluations.

Table 5 shows: In warm septic shock: SVR and SVRI were significantly lower at second readings in contrast to last evaluations and in contrast to control group.

In cold septic shock: SVR and SVRI have been substantially greater at second evaluations in comparison to control group while no substantial variation was existed between second evaluation and final evaluations.

In combined septic shock: no substantial variation was existed among second evaluation in contrast to last evaluations or in contrast to control group.

Table 6 shows:

In warm septic shock:

Stroke Volume Variation (SVV): was significantly higher at second evaluation in contrast to last evaluations and in contrast to control group. Corrected flow time (FTC): was significantly lower at second evaluation in contrast to last evaluations and in contrast to control group. Thoracic Fluid Content (TFC): was substantially greater at second evaluation in comparison to last evaluations while no substantial variation was existed in comparison to control group.

In cold septic shock: SVV was significantly higher at second evaluation in contrast to last evaluations and in contrast to control group. FTC was significantly lower at second evaluation in contrast to last evaluations and in contrast to control group. TFC was substantially greater at second evaluation in contrast to last evaluations while no substantial variation was existed in contrast to control group.

In combined septic shock: SVV was significantly higher at second evaluation in contrast to control group while no substantial variation was existed at second evaluation in contrast to last evaluations. FTC was significantly lower at second evaluation in contrast to control group while no substantial variation was existed at second evaluation in contrast to last evaluations. There was no significant difference in TFC in combined septic shock group at second evaluation in contrast to last evaluations and in contrast to control group.

These table (7) and figure (2) show: Types of CVS support medications required in warm septic shock group were (dopamine 94.7 %, noradrenaline 57.9 % and dobutamine 5.3 %) while types of CVS support medications required in cold septic shock group were (dobutamine 100.0%, adrenaline 54.5 %, dopamine 18.2 % and hydrocortisone 18.2 %). As regard types of CVS support medications required in

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combined septic shock group were (dopamine 100.0 %, dobutamine 100.0 %, adrenaline 100.0 %, noradrenaline 20.0 % and hydrocortisone 40.0 %).

it is not necessary to describe the results in such detail, as the tables and graphs have already been presented. The ideal is to call the attention of the data to what is related to the results. I suggest reducing the number of tables, figures and graphs to make reading easier and more interesting.

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Discussion: the discussion is too long. Ideally, the results found should be discussed by comparing them with similar studies and not just describing the findings and the literature.

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**According to bed-side physical assessment findings in both cold and warm shock physiology, sepsis-related impaired cardiovascular function has previously been characterized. (10)**

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**Peripheral vasoconstriction, chilly peripheries, and tachycardia are the typical symptoms of cold shock; hypotension can frequently be a preterminal occurrence.**

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**Hypotension and peripheral vasodilation brought on by endotoxin release are features of warm shock. Various therapy strategies may be helpful for these clinically distinct presentations. (10)**

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**Early identification of cardiovascular impairment in ill newborns helps medical professionals to make prompt therapeutic choices and objectively track patient response to therapy, (11)all this bolded part must be in the introduction**

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AS regard septic shock cases in this current study, they were 40 cases and they were classified into warm shock (19 cases representing 47.5%), cold shock (11 cases representing 27.5%) and combined shock (10 cases representing 25%).

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This classification of septic shock cases in to warm and cold ones came in line with Deep et al. (2013) whom carried out a prospective observational work on 36 cases with septic shock; 21 cases classified as warm septic shock (greater CI and reduced SVRI) and 15 cases classified as cold septic shock (reduced CI and greater SVRI).the entire highlighted part must be in the methodology, as a criterion for classifying the type of shock

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Regarding SV, CO and CI at 2nd readings in septic shock group were different according to the type of septic shock:

In warm septic shock group (19 cases) SV, CO and CI were substantially greater at second readings by EC and significantly higher in comparison with controls.

Deshpande et al.'s 2017 study showed that warm shock physiology, characterized by greater cardiac outputs and reduce estimated SVR relative to controls or reported normative values is the primary trait linked with sepsis in newborns. (12)

This may indicate that vaso-regulatory failure is the primary cause of septic shock in preterm newborns.(13)

In cold septic shock (11 cases); CO,SV, and CI at second by EC were significantly lower contrasted to finalevaluations and in contrast to control group.

Kharrat and Jain (2021) reported that Reduced stroke volume and left ventricular systolic malfunction may occur from sudden elevations in afterload in the neonatal heart, particularly in premature newborns. (3)

In combined septic shock (10 cases); CO,SV, and CI at second evaluation by EC were significantly lower in comparison to control group, these results similar to that of cold septic shock as combined type of shock demonstrate the late stage where there is cardiac depression and falling of both systolic and diastolic blood pressure.

In the present study: Index of contractility (ICON) in group of warm septic shock; When comparing second readings to previous readings and to the control group, there had been no discernible change.

To the best of our knowledge, no prior study has examined this item on newborns or pediatric patients with septic shock or sepsis, and there is a dearth of information on it.

Depending solely on the rate of alteration in thoracic impedance, EC only provides theoretical data about the cardiac contractility, which is displayed by the variable ICON. The capability of the ventricles to contract in order to pump is known as myocardial contractility, and in an echocardiogram, this is often indicated by the ejection fraction. (Gillebert et al., 2004). (14)

While ICON was significantly lower at second evaluation in contrast to last evaluations and in contrast to control group in cold septic shock. As regard combined septic shock; ICON was significantly lower at 2nd reading in comparison to control group but no substantial variation was existed among 2nd and last readings.

This impairment of cardiac contractility had been in line with Habimana et al. (2020) who stated that the primary feature of cardiac problems in sepsis, particularly in the

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hypodynamic phase of shock marked by elevated SVR, inadequate perfusion of tissues, chilly skin, and failure of organs, is contractile dysfunction. (15)

According to de Waal and Evans (2010), neonates may develop cold shock or already have it when they are born. Cold shock is a condition that happens in cases of serious infections when the circulatory system vasoconstricts in an attempt to re-distribute the blood to the vital central circulation in anticipation of impending circulatory failure. These newborns have a low LV myocardial function and a significant SVR. (16)

One element that affects afterload is vascular resistance, and SVR by EC is computed using the formula:  $80 \times (\text{MAP} - \text{CVP})/\text{CO}$ , assuming that CVP (central venous pressure) is 3 mm Hg. (Hsu et al., 2016).(6)

In the current study SVR and SVRI are important items measured by EC and of a great clinical importance; we compared them in different types of septic shock groups with controls. As regard in warm septic shock group; SVR and SVRI were significantly lower at second evaluation in contrast to previous evaluations and in contrast to control group. This low SVR and SVRI with high SV and CO in sepsis group indicating the predominant type of warm sepsis in the studied cases, this was in agreement with Wu and Noori (2021), de Waal and Evans (2010), Deshpande et al. (2017), and Saini et al. (2014) whom stated that warm shock physiology is more common in neonates characterized by reduced estimated SVR, and greater CO contrasted to controls or standards that have been published. (12)(16)(13)(17)

SVR and SVRI in cold septic shock group were substantially greater at the second evaluation in comparison to control group.

The classification of cases into warm and cold septic shock according to SVRI and CI in our study came in line with Rao et al. (2021) who performed a pilot prospective

observational work of 30 paediatric patients with septic shock revealed that 19 (63.3%) children were having cold shock and 11 (36.7%) had warm shock, this classification was according to CI and SVRI as regards EC, those with reduced CI and greater SVRI had been classified as vasoconstrictive shock, while those with greater CI and reduced SVRI had been classified as vasodilated shock. (18)

One of the important clinical applications of EC is assessment of fluid status in neonates and giving an idea about preload through measurement of corrected flow time (FTC), stroke volume variation (SVV), and thoracic fluid content (TFC).

In this current study; In septic shock groups SVV was substantially greater at second readings in contrast to controls. While FTC was significantly lower at 2nd evaluation in contrast to control group. As regards TFC was substantially greater at second evaluation in contrast to control group. These evaluations mean most septic shock cases had lower blood volume, decreased preload and need for fluid boluses.

This came in agreement with Gupta and Donn (2020) who postulated that, utilizing EC, preload was recently shown to be indirectly assessed. In paediatric groups, rise in thoracic fluid content (TFC) and stroke volume variation (SVV) have been used as a preload marker, although there is a dearth of information in the neonatal population. (19)

In the research done by Rao et al. (2021), it was determined how useful EC was for classifying hemodynamic conditions and determining fluid responsiveness in paediatric septic shock. They discovered that fluid responders had a substantially greater SVV prior to the fluid bolus and a larger decline in SVV following the fluid bolus in contrast to the non-responders. (18)

According to different parameters measured by EC (SV, SI, CO, CI, SVR, SVRI, ICON, FTC and SVV) were useful for assessment of cardiac performance and hemodynamic status of the studied population and were considered as tools for the need of fluid boluses and further cardiac medications and their types.

This present study showed 100% of septic shock group cases required fluid boluses.

As regard types of CVS support medications required in different types of septic shock group. In warm type (low SVR) the medications needed were mainly with vasopressor effect (dopamine 94.7 %, noradrenaline 57.9% and dobutamine 5.3%).

This came in agreement with studies showed that Norepinephrine administration is additionally known to improve blood pressure, CO, and regional blood flow. Dopamine is the most popular vasopressor utilised in the NICU and it's been proven to be effective as well as safe in raising blood pressure throughout transitional hypotension. In a 2010 meta-analysis by Higgins et al.(20)

While CVS support medications required in cold septic shock group (low CO and high SVR) were (dobutamine 100.0%, adrenaline 54.5%, dopamine18.2% and hydrocortisone 18.2%). As regard types of CVS support medications required in combined septic shock group were (dopamine100.0%, dobutamine 100.0%, adrenaline 100.0%, noradrenaline 20.0% and hydrocortisone 40.0%).

Robel-Tillig et al. (2007) stated that, Due to its vasodilator properties, dobutamine was preferred over dopamine. (affecting both beta- and alpha-adrenergic receptors) moreover, the variation in inotropics intensity (Dobutamine is more potent than dopamine).(21)

In the current study; hydrocortisone was found to be useful in some cases with refractory septic shock.

The comparatively small dosage of hydrocortisone would likely prove preferred to the excessive dosage of dexamethasone in the management of refractory hypotension in life-threatening circumstances and emergency, despite the fact that routine and prophylactic usage of systemic corticosteroids shouldn't be advised due to their potential side effects. According to Higgins et al.'s (2010) meta-analysis research, hydrocortisone treatment substantially raises blood pressure in preterm babies who are hypotensive and lowers the need for vasopressors in hypotensive and vasopressor-dependent shock patients.(20)

**Limitations of the study:**

Small sample size, short duration of the study, unblinded design because it was impossible to compare electrical cardiometry and echocardiography in the same NICU, and no invasive hemodynamic methods of measurement were used for some variables, such as blood pressure, in this single-center study. Larger samples are required to confirm our findings. [statistical analysis inappropriate for the purpose of the study](#)

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**Conclusion:**

In late preterm neonates suffering septic shock, electrical cardiometry might be suggested as a helpful method for assessing hemodynamics and can differentiate between different types of septic shock based on the results of cardiac output and systemic vascular resistance.

## References attention: the references are not cited correctly

1. **Fleischmann, C., Reichert, F., Cassini, A., et al. (2021). Global incidence and mortality of neonatal sepsis: a systematic review and meta-analysis. Arch Dis Child: 100-39.**
2. **Adam, Z., Ameme, D. K., Nortey, P., et al. (2019). Determinants of low birth weight in neonates born in three hospitals in Brong Ahafo region, Ghana, 2016- an unmatched case-control study. BMC Pregnancy Childbirth and 174-81., 19:.**
3. **Kharrat, A. & Jain, A. (2021). Hemodynamic dysfunction in neonatal sepsis. Pediatr Res: 13-33.**
4. **Fathi, E. M., Narchi, H. & Chedid, F. (2018). Noninvasive hemodynamic monitoring of septic shock in children. World J Methodol and 1-8., 8:.**
5. **Pinsky, M. R. & Payen, D. (2005). Functional hemodynamic monitoring. Crit Care and 566-72., 9:.**
6. **Hemodynamic reference for neonates of different age and weight: a pilot study with electrical cardiometry. Hsu, K. H., Wu, T. W., Wang, Y. C., et al. 2016, J Perinatol, pp. 36: 481-5.**
7. **Continuous non-invasive cardiac output measurements in the neonate by electrical velocimetry: a comparison with echocardiography. Noori, S., Drabu, B., Soleymani, S., et al. 2012, Arch Dis Child Fetal Neonatal Ed, pp. 97: 340-3.**
8. **Definitions of bloodstream infection in the newborn. Haque, K. N. 2005, Pediatr Crit Care Med, pp. 6: 45-9.**
9. **Changes in hemodynamics after rescue surfactant administration. Katheria, A. C. & Leone, T. A. 2013, J Perinatol, pp. 33: 525-8.**
10. **Weiss, S. L., Peters, M. J., Alhazzani, W., et al. (2020). Surviving sepsis campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. Intensive Care Med and 10-67., 46:.**
11. **Neonatologist-performed functional echocardiography in the neonatal intensive care unit. El-Khuffash, A. F. & McNamara, P. J. 2011, Semin Fetal Neonatal Med, pp. 16: 50-60.**
12. **Cardiac output in late onset neonatal sepsis. Deshpande, S., Suryawanshi, P., Chaudhary, N., et al. 2017, J Clin Diagn Res , pp. 11: 25-8.**
13. **Saini, S. S., Kumar, P. & Kumar, R. M. (2014). Hemodynamic changes in preterm neonates with septic shock: a prospective observational study. Pediatr Crit Care Med and 443-50., 15:.**
14. **Gillebert, T. C., Van de Veire, N., De Buyzere, M. L., et al. (2004). Time intervals and global cardiac function. Use and limitations. Eur Heart J and 2185-6., 25:.**
15. **Habimana, R., Choi, I., Cho, H. J., et al. (2020). Sepsis-induced cardiac dysfunction: A review of pathophysiology. Acute Crit Care and 57-66., 35:.**
16. **Hemodynamics in preterm infants with late-onset sepsis. de Waal, K. & Evans, N. 2010, J Pediatr, pp. 156: 918-22.**

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17. **Wu, T.-W. & Noori, S. (2020).** Recognition and management of neonatal hemodynamic compromise. *Pediatr Neonatol* and 12-30., 62:.
18. **Rao, S. S., Lalitha, A. V., Reddy, M., et al. (2021).** Electrocardiometry for hemodynamic categorization and assessment of fluid responsiveness in pediatric septic shock: A pilot observational study. *Indian J Crit Care Med* and 185-92., 25:.
19. **Gupta, S. & Donn, S. M. (2020).** Assessment of neonatal perfusion. *Semin Fetal Neonatal Med* and 10-44., 25:.
20. **Higgins, S., Friedlich, P. & Seri, I. (2010).** Hydrocortisone for hypotension and vasopressor dependence in preterm neonates :a meta-analysis. *J Perinatol* and 373-8., 30:.
21. **Robel-Tillig, E., Knüpfer, M., Pulzer, F., et al. (2007).** Cardiovascular impact of dobutamine in neonates with myocardial dysfunction. *Early Hum Dev* and 307-12., 83:.
22. Early-onset neonatal sepsis. **Simonsen, K. A., Anderson-Berry, A. L., Delair, S. F., et al.** 2014, *Clin Microbiol Rev*, pp. 27: 21-47.
23. Neonatal sepsis. **Voller, S. M., & Myers, P. J.** 2016, *Clinical Pediatric Emergency Medicine*, pp. 17: 129-13.
24. Clinical presentations of neonatal shock: the VLBW infant during the first postnatal day. **Kluckow, M. & Seri, I.** 2008, *Hemodynamics and cardiology. Neonatology questions and controversies. Philadelphia, saunders*, pp. 147-77.
25. Cardiac output assessed by non-invasive monitoring is associated with ECG changes in children with critical asthma. **Wong, J., Dorney, K., Hannon, M., & Steil, G. M.** 2014, *J Clin Monit Comput*, pp. 28: 75-82.
26. The pilot study of role of electrical cardiometry in non-invasive assessment of hemodynamic parameters in patients with pulmonary arterial hypertension (RCD code: II-1A. 1). **Kazimierczyk, R., Marcinkiewicz-Siemion, M., Lisowska, A., et al.** 2017, *J Rare Cardiovas Dis*, pp. 3: 44-49.
27. Guidelines and standards for performance of a pediatric echocardiogram: A report from the task force of the pediatric council of the american society of echocardiography. **Lai, W. W., Geva, T., Shirali, G. S., et al.** 2006, *J Am Soc Echocardiogr*, pp. 19: 1413-30.
28. Targeted Neonatal Echocardiography in the Neonatal Intensive Care Unit: practice guidelines and recommendations for training. **Mertens, L., Seri, I., Marek, J., et al.** 2011, *Am Soc Echocardiogr*, pp. 24: 1057-78.
29. Estimates of possible severe bacterial infection in neonates in sub-Saharan Africa, south Asia, and Latin America for 2012: a systematic review and meta-analysis. **Seale, A. C., Blencowe, H., Manu, A. A., et al.** 2014, *Lancet Infect Dis*, pp. 14: 731-41.
30. Neonatal Sepsis. **Odabasi, I. O. & Bulbul, A.** 2020, *Sisli Etfal Hastan Tip Bul;* pp. 54: 142-58.
31. Clinical monitoring of systemic hemodynamics in critically ill newborns. **de Boode, W. P.** 2010, *Early Hum Dev*, pp. 86: 137-41.
32. Advances in diagnosis and management of hemodynamic instability in neonatal shock. **Singh, Y., Katheria, A. C. & Vora, F.** 2018, *Front Pediatr*, pp. 6: 2-9.

33. Excitation-contraction coupling of human induced pluripotent stem cell-derived cardiomyocytes. **Kane, C., Couch, L. & Terracciano, C. M.** 2015, *Front Cell Dev Biol*, pp. 3: 59-62.
34. Impact of preterm birth on the developing myocardium of the neonate. **Bensley, J. G., Moore, L., De Matteo, R., et al.** 2018, *Pediatr Res*; , pp. 83: 880-8.
35. Point of care neonatal ultrasound in late-onset neonatal sepsis. **Yengkhom, R., Suryawanshi, P., Murugkar, R., et al.** 2021, *J Neonatol*, pp. 35: 59-63.
36. Cardiac functions by tissue doppler and speckle tracking echocardiography in neonatal sepsis and its correlation with sepsis markers and cardiac troponin-T. **Awany, M., Tolba, O., Al-Biltagi, M., et al.** 2016, *J Ped Neonatal Care*, pp. 5: 184-1.
37. Myocardial dysfunction in neonatal sepsis: a tissue Doppler imaging study. . **Abdel-Hady, H. E., Matter, M. K. & El-Arman, M. M.** 2012, *Pediatr Crit Care Med*, pp. 13: 318-23.
38. The use of electrical cardiometry for continuous cardiac output monitoring in preterm neonates: A validation study. **Song, R., Rich, W., Kim, J. H., et al.** 2014, *Am J Perinatol*, pp. 31: 1105-10.
39. Hemodynamic dysfunction in neonatal sepsis. **Kharrat, A. & Jain, A.** 2021, *Pediatr Res*; , pp. 13-33.
41. **de Waal, K. & Evans, N. (2010). Hemodynamics in preterm infants with late-onset sepsis. J Pediatr and 918-22., 156:.**

Tables:

(Table 1) Demographic data:

	Septic shock cases (n = 40)	Control (n = 80)	P
Sex			
Male	20 (50.0%)	33 (41.3%)	0.363
Female	20 (50.0%)	47 (58.8%)	
Weight (kg)	2.48 ± 0.23	2.58 ± 0.32	0.063
Length (cm)	46.5 ± 1.47	47.0 ± 2.14	0.087
GA (weeks)	35.2 ± 0.83	35.3 ± 0.87	0.821
BSA (kg/M <sup>2</sup> )	0.18 ± 0.01	0.18 ± 0.02	0.062
Ponderal index	2.45 ± 0.12	2.46 ± 0.15	0.804
Postnatal age days	6.45 ± 4.04	6.54 ± 4.30	0.895
Delivery			
C.S	26 (65.0%)	49 (61.3%)	0.689
NVD	14 (35.0%)	31 (38.8%)	
Apgar score 5 min	9.53 ± 0.51	9.58 ± 0.50	0.607

GA: gestational age, BSA: body surface area, CS: cesarian section, NVD: normal vaginal delivery. Data presented as mean + SD (Standard deviation)

(Table 2) vital signs:

Vital signs	Septic shock (n = 40)	Control (n = 80)	F	P
Temperature °C				
Min. – Max.	35.0 – 37.0	36.60 – 37.20		
Mean ± SD.	36.31 ± 0.71	36.94 ± 0.13	34.051*	<0.001*
Respiratory rate (C/min)				
Min. – Max.	55.0 – 70.0	34.0 – 54.0		
Mean ± SD.	59.38 ± 3.24	42.96 ± 4.83	226.726*	<0.001*
Heart Rate (B/min)				
Min. – Max.	100.0 – 190.0	132.0 – 158.0		
Mean ± SD.	156.2 ± 21.97	144.6 ± 7.04	13.588*	<0.001*
Systolic BP(mmHg)				
Min. – Max.	43.0 – 70.0	55.0 – 80.0		
Mean ± SD.	56.95 ± 9.23	65.79 ± 5.74	22.453*	<0.001*
Diastolic BP (mmHg)				
Min. – Max.	16.0 – 46.0	34.0 – 53.0		
Mean ± SD.	28.72 ± 8.66	42.35 ± 4.41	77.906*	<0.001*
MBP(mmHg)				
Min. – Max.	27.60 – 51.0	41.0 – 60.0		
Mean ± SD.	38.19 ± 5.25	50.04 ± 4.50	86.864*	<0.001*

Data presented as mean + SD (Standard deviation).

(Table 3)EC data at 2<sup>nd</sup> and last readings in different types of septic shock group and in comparison to control group:

EC	Septic shock (n = 40)						Control (n = 80)
	Warm (n = 19)		Cold (n = 11)		Combined (n = 10)		
	2 <sup>nd</sup> reading	last reading	2 <sup>nd</sup> reading	last reading	2 <sup>nd</sup> reading	last reading	
SV (ml)							
Min. – Max.	1.67 – 4.33	2.51 – 3.65	1.56 – 2.31	1.32 – 3.41	1.53 – 2.43	1.97 – 3.52	2.15 – 3.82
Mean ± SD.	3.85 ± 0.62	3.21 ± 0.44	1.84 ± 0.31	2.67 ± 0.74	2.04 ± 0.40	2.51 ± 0.58	3.15 ± 0.44
p <sub>1</sub>	<0.001*		0.001*		0.125		
p <sub>2</sub>	<0.001*		<0.001*		<0.001*		
CO (L/min)							
Min. – Max.	0.24 – 0.72	0.35 – 0.50	0.21 – 0.36	0.14 – 0.45	0.22 – 0.37	0.19 – 0.52	0.31 – 0.54
Mean ± SD.	0.63 ± 0.11	0.44 ± 0.06	0.26 ± 0.07	0.36 ± 0.12	0.29 ± 0.05	0.32 ± 0.12	0.45 ± 0.05
p <sub>1</sub>	<0.001*		0.005*		0.542		
p <sub>2</sub>	<0.001*		<0.001*		<0.001*		
CI (L/min/m <sup>2</sup> )							
Min. – Max.	1.60 – 4.40	2.31 – 3.33	1.37 – 2.0	0.93 – 2.66	1.46 – 2.05	1.11 – 2.73	2.05 – 3.37
Mean ± SD.	3.75 ± 0.61	2.64 ± 0.31	1.57 ± 0.24	2.15 ± 0.62	1.71 ± 0.21	1.92 ± 0.75	2.51 ± 0.25
p <sub>1</sub>	<0.001*		0.008*		0.485		
p <sub>2</sub>	<0.001*		<0.001*		<0.001*		

Table (4): ICON (index of contractility) by EC at 2<sup>nd</sup> and last readings in different types of septic shock group and in comparison to control group:

ICON	Septic shock (n = 40)						Control (n = 80)
	Warm (n = 19)		Cold (n = 11)		Combined (n = 10)		
	2 <sup>nd</sup> day	last reading	2 <sup>nd</sup> day	last reading	2 <sup>nd</sup> day	last reading	
Min. – Max.	62.30 – 90.30	65.0 – 93.3	56.70 – 63.80	65.90 – 91.20	55.30 – 65.0	53.80 – 63.0	64.20 – 93.0
Mean ± SD.	81.77 ± 8.63	78.92 ± 8.25	60.04 ± 2.64	79.64 ± 10.34	60.69 ± 3.93	60.11 ± 2.91	79.80 ± 6.84
p <sub>1</sub>	0.364		<0.001*		0.589		
p <sub>2</sub>	0.287		<0.001*		<0.001*		

SD: Standard deviation

p<sub>1</sub>: p value for Paired t-test for comparing between 2<sup>nd</sup> day and Last reading in each Septic shock

p<sub>2</sub>: p value for Student t-test for comparing between 2<sup>nd</sup> day in each septic shock and control

\*: Statistically significant at p ≤ 0.05

Table (5): SVR and SVRI by EC at 2<sup>nd</sup> and last readings in different types of septic shock and in comparison to control group:

	Septic shock (n = 40)						Control (n = 80)
	Warm (n = 19)		Cold (n = 11)		Combined (n = 10)		
	2 <sup>nd</sup> reading	last reading	2 <sup>nd</sup> reading	last reading	2 <sup>nd</sup> reading	last reading	
SVR (dyn-s/cm <sup>5</sup> )							
Min. – Max.	3255 – 12200	7136 – 11428	10577 – 15018	9120 – 16533	6560 – 11636	7136 – 11043	6074 – 10871
Mean ± SD.	4678.7±1898.5	9164.6±1340.3	12764 ± 1824	10908.8 ± 2810	8799.1±2019.5	9157.8±1578.1	8487.1±990.0
p <sub>1</sub>	<0.001*		0.056		0.273		
p <sub>2</sub>	<0.001*		<0.001*		0.641		

SD: Standard deviation

p<sub>1</sub>: p value for Paired t-test for comparing between 2<sup>nd</sup> day and Last reading in each Septic shock

p<sub>2</sub>: p value for Student t-test for comparing between 2<sup>nd</sup> day in each septic shock and control

\*: Statistically significant at p ≤ 0.05

Table (6): Fluid status at 2<sup>nd</sup> and last readings in different types of septic shock group and in comparison to control group:

Fluid Status	Septic shock (n = 40)						Control (n = 80)
	Warm (n = 19)		Cold (n = 11)		Combined (n = 10)		
	2 <sup>nd</sup> day	last reading	2 <sup>nd</sup> day	last reading	2 <sup>nd</sup> day	last reading	
SVV%							
Min. – Max.	15.0 – 39.0	7.0 – 13.0	16.0 – 39.0	8.0 – 29.0	13.0 – 26.0	10.0 – 33.0	5.0 – 15.0
Mean ± SD.	21.37 ± 5.79	9.84 ± 1.71	22.09 ± 6.82	13.36 ± 7.86	20.50 ± 5.23	20.10 ± 9.43	11.19 ± 2.80
p <sub>1</sub>	<0.001*		0.023*		0.919		
p <sub>2</sub>	<0.001*		<0.001*		<0.001*		
FTC (ms)							
Min. – Max.	165.0 – 212.0	230.0 – 334.0	167.0 – 200.0	110.0 – 267.0	175.0 – 218.0	132.0 – 282.0	160.0 – 300.0
Mean ± SD.	187.4 ± 14.35	256.4 ± 30.24	182.1 ± 10.20	230.1 ± 60.65	189.6 ± 16.85	194.2 ± 67.01	250.4 ± 27.32
p <sub>1</sub>	<0.001*		0.023*		0.858		
p <sub>2</sub>	<0.001*		<0.001*		<0.001*		

SD: Standard deviation

p<sub>1</sub>: p value for Paired t-test for comparing between 2<sup>nd</sup> day and Last reading in each Septic shock

p<sub>2</sub>: p value for Student t-test for comparing between 2<sup>nd</sup> day in each septic shock and control

\*: Statistically significant at p ≤ 0.05

SVV: Stroke Volume Variation, FTC: Corrected Flow Time, TFC: Thoracic Fluid Content

Table (7): CVS support (fluid boluses and medications) in different types of septic shock group (n = 40):

CVS medication	Septic shock (n = 40)					
	Warm (n = 19)		Cold (n = 11)		Combined (n = 10)	
	No.	%	No.	%	No.	%
Bolus fluids	19	100.0	11	100.0	10	100.0
Dopamine	18	94.7	2	18.2	10	100.0
Noradrenaline	11	57.9	0	0.0	2	20.0
Dobutamine	1	5.3	11	100.0	10	100.0

Adrenaline	0	0.0	6	54.5	10	100.0
Hydrocortisone	0	0.0	2	18.2	4	40.0

Figures:

UNDER PEER REVIEW

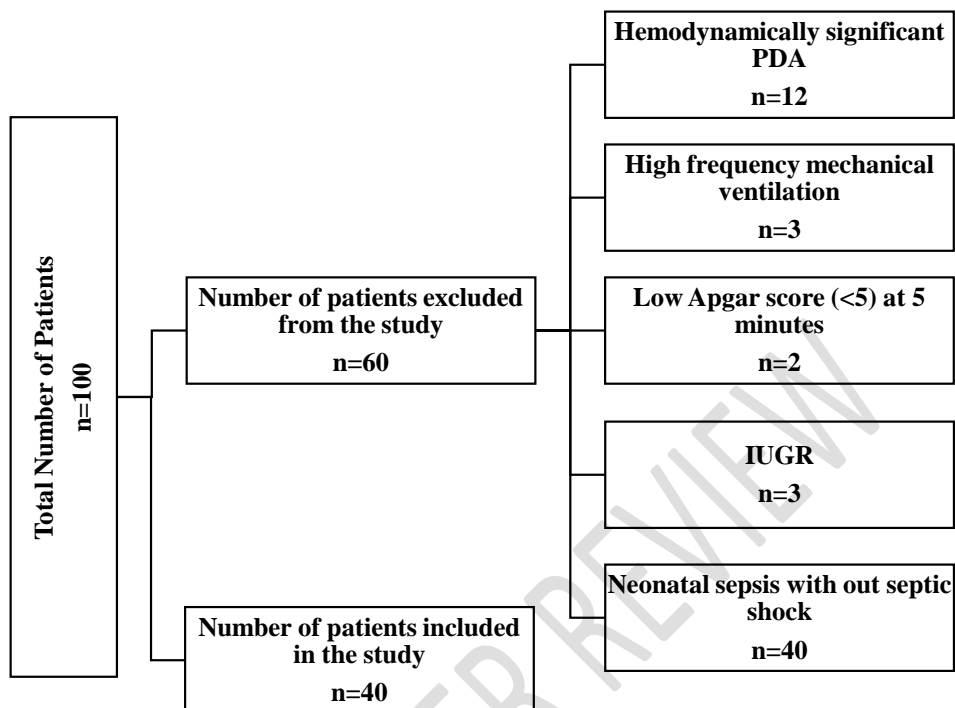


Figure 1: Illustration of the study design

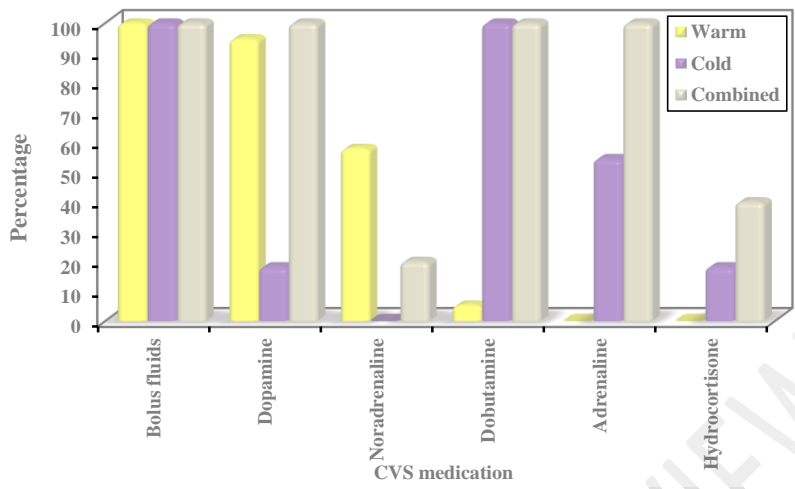


Figure (2): CVS support (fluid boluses and medications) in different types of septic shock group (n = 40)