Curr Pediatr Res2023; 27 (10): 2058-2063 *ISSN 0971-9032*
www.currentpediatrics.com

Frequency of community-acquired pediatric vasodilatory septic shock: A single-center study.

Radwa Sayed Iraqy[1], Bassem Saad[1], Nabil Mohsen Abdelaziz[1], Yasser Nassef[2], HebatAllah Fadel Algebaly[2], Mostafa Tawfik[2], Ola Youis[2], Elshimaa Salah Ahmed[1]

[1]Department of Pediatric Critical Care, Cairo University School of Medicine, Cairo, Egypt

[2]Department of Medicine, Chung Shan Medical University, Taichung, Taiwan

Received: *22 September 2023, Manuscript No. AAJCP-23-117784;* **Editor assigned:** *26 September, 2023, Pre QC No. AAJCP-23-117784 (PQ);* **Reviewed:** *10 October, 2023, QC No. AAJCP-23-117784;* **Revised:** *17 October, 2023, Manuscript No. AAJCP-23-117784 (R);* **Published:** *24 October, 2023, DOI:10.35841/0971-9032.27.10.2058-2063*

Abstract

Purpose: Various challenges are involved in distinguishing and managing different types of pediatric septic shock, especially when it comes to selecting and titrating inotropes and vasoactive agents. A comprehensive non-invasive hemodynamic study may prove beneficial in improving outcomes, particularly in underserved settings.

We examined the frequency of both vasodilatory and vasoconstricted pediatric fluid-refractory septic shock, as well as the different hemodynamic characteristics associated with each type of shock.

Materials and Methods: This single-center prospective cohort study was conducted on 78 patients with fluid refractory septic shock who were admitted to the Pediatric Intensive Care Unit (PICU) at the children's hospital of Cairo university. Upon admission to the PICU, hemodynamic parameters were acquired using electrical cardiometry. Subsequently, the children were divided into two groups based on their condition: those experiencing vasodilatory shock and receiving norepinephrine, and those with vasoconstrictive shock, who were administered epinephrine and/or milrinone based on their blood pressure and hemodynamic data. The patient's progress was monitored for 24 hours.

Results: Out of these patients, 43.60% (34 children) had vasodilatory septic shock, while the rest experienced vasoconstricted shock. Patients with vasodilatory shock demonstrated significantly higher contractility index, cardiac index, and stroke volume ($p<0.001$). Additionally, their thoracic fluid content and left ventricular ejection time were notably higher ($p<0.001$ and $p=0.002$, respectively) compared to those with vasoconstricted shock. The Pediatric Index of Mortality (PIM) 2 score was found to be a more reliable predictor of survival than the cardiac index and systemic vascular resistance.

Conclusion: In conclusion, this study highlights a significant occurrence of pediatric vasodilatory septic shock. Non-invasive hemodynamic assessment could assist in the effective selection of both inotropes and vasopressors, thus improving resuscitation success rates.

Keywords: Cardiac index, Pediatric, Septic shock.

Accepted on 19th October, 2023

Introduction

Sepsis is defined as a life-threatening organ dysfunction resulting from a dysregulated host response to infection. Septic shock is a consequence of sepsis and is associated with a high mortality rate [1]. According to Rhodes et al., this condition is characterized by fluid-refractory hypotension along with signs of hypoperfusion [2]. The global prevalence of severe sepsis in children is reported to be 8.2% [3] and the mortality rate for patients with septic shock is 17% [4]

Early diagnosis and treatment have significantly impacted the disease outcome [5]. However, diagnosing sepsis in children is challenging due to specific symptoms that require careful interpretation due to the variable range of normality depending on their age [6]. Consequently, differentiating between VC and systemic VD septic shock clinically and selecting the appropriate inotropic medications is fraught with errors. Clinical assessment has been enhanced by the use of non-invasive tools [7].

The Cardiac Index (CI) is one of the most important parameters in hemodynamic monitoring as it provides information about organ perfusion and oxygen delivery in shock [8]. The Systemic Vascular Resistance (SVR) index has also been considered a good predictor of mortality in septic shock patients [9]. Previously, septic shock in children was classified into two types based on CI and SVR index values. That is, vasoconstricted septic shock was defined as CI <3.3 L/min/m^2 and SVR index >1600(dyne s/cm^5/m^2), while vasodilatory

septic shock was defined as CI>5.5 L/min/m^2 and SVR index <800 (dyne s/cm^5/m^2) [10].

In addition, previous guidelines recommended using clinical signs to categorize septic shock in children as either "vasodilatory" (presumably indicating high CO and low SVRI) or "vasoconstricted" (presumably indicating low CO and high SVRI) to guide the management of vasoactive infusions. However, the 2020 guidelines suggest against relying solely on bedside clinical signs and recommend using advanced hemodynamic monitoring when available to guide resuscitation in children with septic shock or organ dysfunction associated with sepsis [11].

Rao et al., recently classified cardiac index (CI) <3.3 L/min/m2 and Systemic Vascular Resistance Index (SVRI) >1600 dyn sec/cm5/m2 as Vasoconstrictive Shock-Electrocardiometry (VCEC) and CI >5.5 L/min/m^2 and SVRI <1000 dyn sec/cm^5/m^2 as Vasodilated Shock-Electrocardiometry (VDEC) [12]. We conducted this study to assess the frequency and characteristics of different hemodynamic patterns of pediatric septic shock and their relationship to survival.

Materials and Methods

Study design and ethical approval

This single-center prospective observational cohort study included patients who were admitted to the PICU of Cairo university children's hospital from 2018 to 2019. The institutional review board at our institution approved our study.

Patient selection

We enrolled patients who presented to the emergency department with community-acquired fluid refractory septic shock. Septic shock was defined as a form of sepsis accompanied by cardiovascular dysfunction including hypotension, need for treatment with vasoactive agents, or impaired perfusion [13]. The definition of septic shock, according to the American college of critical care medicine, involves clinical signs like hypothermia or hyperthermia, altered mental status, and peripheral vasodilatation or vasoconstriction with capillary refill time exceeding 2 seconds before the occurrence of hypotension. We excluded patients with chronic disease, post-cardiac surgery, hospital-acquired infection, congenital abnormalities, or other shock types, as well as those referred from other hospitals or readmitted to the PICU.

Patients' assessments

Non-invasive hemodynamic monitoring was performed by a trained intensivist using the EC device ICON (Osypka Medical (Berlin, Germany)) on the patients during admission to the PICU and 24 hours later. Once the required observations were recorded, the device was disconnected and patients were divided into two groups based on their condition: Those experiencing vasodilatory shock and receiving norepinephrine, and those with vasoconstrictive shock, who were administered epinephrine and/or milrinone based on their blood pressure and hemodynamic data. The patient's progress was monitored for 24 hours.

Electrodes were attached to the skin on the left side of the neck and the lower thorax (approximately at the level of the xiphoid process) if on a child, or to the forehead, lateral neck, and lower thorax if on an infant. An electrical Alternating Current (AC) of constant amplitude was applied *via* the outer pair of electrodes to the thorax and the ascending and descending aorta. The parameters included Heart Rate (HR), Cardiac Output (CO), Cardiac Index (CI), Stroke Volume (SV), Stroke Volume Variation (SVV), Stroke Index (SI), Systemic Vascular Resistance Index (SVRI), Thoracic Fluid Content (TFC), Systolic Time Ratio (STR), and Left Ventricular Ejection Time (LVET). These parameters were recorded during admission and 24 hours later.

Patients were classified (as per Rao and colleagues' protocol) before the initiation of pressors or inotropes and subsequently administered a combination of epinephrine and/or milrinone following their admission to the PICU. Moreover, the Pediatric Index of Mortality (PIM) II score was calculated at the time of admission, and these variables were entered into the system which determined the mortality rate based on standard methods such as logistic regression models [14].

Statistical analysis

An Excel spreadsheet was established for data entry. We used validation checks on numerical variables and an option-based data entry method for categorical variables to reduce potential errors. The analyses were carried out with SPSS software (Statistical Package for the Social Sciences, version 24, SSPS Inc, and Chicago, IL, USA). Frequency tables with percentages were used for categorical variables and descriptive statistics (median and Interquartile Range (IQR)) were used for numerical variables. Independent Student t-test, paired t-test, or Mann-Whitney tests were used to compare quantitative variables, while Chi-square test or McNemar-Bowker tests were used to analyze categorical variables. A p-value<0.05 was considered statistically significant. The Receiver Operating Characteristic (ROC) curve analysis was performed to determine the optimal value of the PIM5 score, Δ CI, and Δ SVRI for predicting mortality.

Results

This study involved 78 pediatric patients with septic shock; 34 children (43.60%) had VD septic shock, while 44 (56.40%) had VC septic shock. Patients with VD type were older as shown in Table 1. VD shock patients demonstrated higher ICON (cardiac contractility), CI, and SV on admission (p<0.001) compared to VC shock patients as shown in Table 2. Moreover, VD patients also had higher LVET and TFC (p<0.001 and 0.001) respectively. With the use of inotropes 24 hours following admission, both types of shock achieved similar hemodynamic parameters except for the cardiac index and contractility index as they were still higher in those with VD shock (Table 3 and Figure 1). After 24 hours of admission, the PIM II score was a better predictor of mortality than the CI and the SVRI (Table 4).

Types of shock	VD shock	VC shock	P-value
Number of patients (%)	34 (43.6%)	44 (56.4%)	
Age Median (IQR)	11 (6:36)	7 (4:30)	0.009
Weight Median (IQR)	8.8 (6:13)	7 (5:12)	0.006
PIM2 Mean ± SD	76 ± 1.5	77 ± 0.8	0.7
Gastroenteritis	12/34 (35%)	18/44 (41%)	
Pneumonia	10/34 (29%)	17/44 (38%)	0.78
Meningitis	10/34 (29%)	6/44 (14%)	
Bloodstream infection	2 (5%)	3/44 (6%)	
Abbreviation: VD: Vasodilatory Septic Shock; VC: Vasoconstricted Septic Shock; IQR: Interquartile Range; PIM2: (Pediatric Index Of Mortality 2) Score; SD: Standard Deviation.			

Table 1. Demographic characteristics and frequency of vasoconstricted *vs*. vasodilatory shock.

Electrical cardiometry variables	VD shock	VC shock	P-value
CI(l/min/m^2)	6 (5.7:6.4)	2.8 (2.5:3)	<0.001
ICON (n/a)	109 (80:154.5)	68 (47:93)	<0.001
SVV (%)	14 (11:17)	17 (14:23)	0.046
SVRI (dyns/cm5m2)	805 (774:1001)	2047 (1821:2231)	<0.001
TFC	276 (244:305)	240 (199:252)	<0.001
STR(n/a)	0.5 (0.4:0.5)	0.5 (0.4:0.7)	0.015
LVET(sec)	180 (156:205)	149 (126:179)	0.002
HR(bpm)	144 (132:155)	152 (130:161)	0.234
CPI	0.8 (0.6:0.9)	0.5 (0.5:0.6)	<0.001
Abbreviation: CPI: Cardiac Performance Index; SV: Stroke Volume; CI: Cardiac Index; SVRI: Systemic Vascular Resistance Index; FTC: Flow Time Corrected; TFC: Thoracic Fluid Content; STR: Systolic Time Ratio; PEP: Pre-Ejection Period; LVET: Left Ventricular Ejection Time; HRV: Heart Rate Variability; HRC: Heart Rate Complexity; PEP: Pre Ejection Period.			

Table 2. Differences in hemodynamic variables between VC and VD shock during admission.

	VD shock	VC shock	P-value
CI	5.1 (4.7:5.9)	3 (2.5:5)	<0.001
ICON	101 (75:119)	65 (55:92)	0.014
SVV	13 (10:18)	18 (13:23)	0.39
SVRI	1140 (985:1494)	1722 (1001:1971)	0.002
FTC	275 (241:302)	266 (220:300)	0.28
LVET	171 (150:196)	162 (146:200)	0.38
CPI	0.79 (0.65:0.93)	0.62 (0.44:0.87)	0.04
HR	136 (120:154)	140 (125:155)	0.744
Abbreviation: SV: Stroke Volume; CI: Cardiac Index; SVRI: Systemic Vascular Resistance Index; TFC: Thoracic Fluid Content; STR: Systolic Time Ratio; PEP: Pre-Election Period; LVET: Left Ventricular Ejection Time; HRV: Heart Rate Variability; HRC: Heart Rate Complexity; CAO_2: Arterial Oxygen Content.			

Table 3. Difference in hemodynamic variables between VC and VD shock 24 hours after admission.

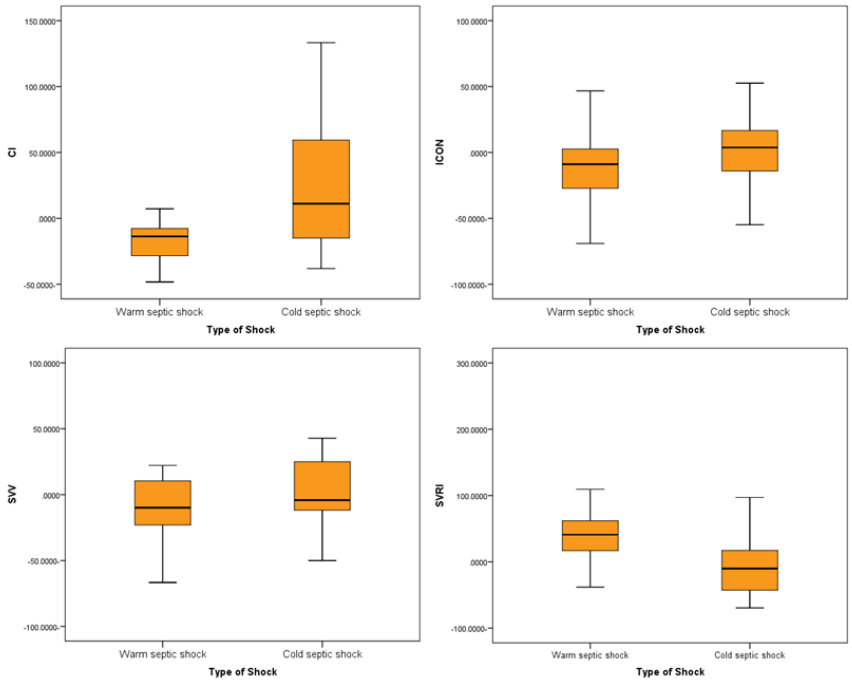

Figure 1. The percentage medium changes in CI, SVRI, SVV, and ICON over 24 hours for cold and warm shock.

	Cut-off	Sen% (95% CI)	Spe% (95% CI)	PPV (95% CI)	NPV (95% CI)	AUC (95% CI)	P-value
PIM	>79	60 (43.3-75.1)	71.79 (55.1-85.0)	68.6 (55.5-79.3)	63.6 (53.3-72.9	0.68 (0.56-0.78)	0.003
CI	≤ 5.5	62.5 (45.8-77.3)	58.97 (42.1-74.4)	61 (50.0-70.9)	60.5 (48.7-71.2)	0.56 (0.44-0.67)	0.405
SVRI	>1400	50 (33.8-66.2)	66.67 (49.8-80.9)	60.6 (47.2-72.6)	56.5 (47.0-65.6)	0.52 (0.40-0.63)	0.805

Abbreviation: CI: 95% Confidence Interval; PPV: Positive Predictive Value; NPV: Negative Predictive Value; AUC=Area Under the Roc Curve; Sen: Sensitivity; Spe: Specificity; PIM: Pediatric Index of Mortality; SVRI: Systemic Vascular Resistance Index; CI: Cardiac Index.

Table 4. CI and SVRI on admission with Area Under the ROC Curve (AUC) for predicting mortality in pediatric septic shock.

Discussion

The prevalence of severe sepsis and septic shock among hospitalized

Children range from 1% to 26%. Globally, mortality rates are high, ranging from 5% in developed countries to 35% in developing countries [7]. The American college of critical care medicine clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock recommended the following endpoints: Capillary refill less than or equal to 2 seconds, threshold HRs, normal pulses with no differential between the quality of the peripheral and central pulses, warm extremities, urine output greater than 1 mL/kg/hr, normal mental status, CI greater than 3.3 and less than 6.0 L/min/m^2 with normal perfusion pressure (MAP-CVP or MAP-IAP) for agem [15]. Furthermore, measurements of BP, CI, and SVRI allow the selection of the most appropriate pressors and inotropes based on the different combinations of these parameters [11].

In our group of patients with community-acquired septic shock, 43% had VD shock and 58% had VC shock. Most of the patients were infants below 2 years of age. However, patients with VC shock were younger. There was no significant difference in the septic focus between patients with both types of shock. Limited data are available in the literature regarding pediatric pediatric VD septic shock. Previous literature described septic shock in infants and children as VC shock, whereas in adults, "warm shock" predominates [16].

In clinical assessment, categorizing shock as vasoconstricted or vasodilatory likely overestimated the prevalence of vasoconstricted shock in pediatric patients. Davis et al., reported that 66% of children judged by experienced clinicians to be in "cold shock" were noted to be vasodilated when monitored invasively [16]. Furthermore, a poor agreement was reported between physician-assessed CI and SVRI and advanced cardiac non-invasive CO monitoring [17]. Few researchers have described the frequency of different types of shock in children, with some reporting 50% and 58% for VC shock but no specific reference was available regarding the frequency of VD shock [11,18,19].

According to USCOM, the frequency of warm shock was 49% among pediatric patients in PICUs in India [20]. According to

an etiological study conducted in the United Kingdom, cold shock was associated with community-acquired sepsis, whereas warm septic shock was linked to catheter-associated bloodstream infections [13]. In the current study, children with VD shock had a higher SV, CPI, and LVET compared to those with VC shock denoting an increase in stress and attempts by the heart to compensate for the shock.

Additionally, TFC was higher in patients with VD shock probably due to capillary leak; larger TFC was previously suggested to be indicative of a higher total thoracic liquid volume [21] LVET represents the interval from the beginning to the termination of aortic flow [22] and is known to increase CO as seen in systemic vasodilation. In addition, STR was previously described as a measure of left ventricular performance with a mean value of 0.3+0.04 in normal children [23]. Compared to the values described by these authors, our values are larger for both types of shock. The above variables suggest higher cardiac performance in VD shock 24 hours after admission to the PICU. Additionally, hemodynamic parameters improved more in VC than in VD shock.

Conclusion

Based on this study, VD warm shock was more frequent than previously described in the literature. Non-invasive hemodynamic assessment would assist in the selection of both inotropes and vasopressors, as well as may improve the chance of successful resuscitation. The limitation of this study is the inability to perform simultaneous bedside echocardiography since the procedure was performed by an intensivist who was trained exclusively in noninvasive procedures. Future studies involving larger sample sizes and focusing on different aspects of infections (or a wider range of variables) may be beneficial.

Statement and Declaration

Data availability statement

The data used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Acknowledgement

We acknowledge all nurses and parents accepting to share in this work.

Conflict of interest

No conflict of interest.

Funding

No funding.

Institutional review board statement

The institutional review board at Cairo university children's hospital approved our study (N-98-2022).

Informed consent statement

Informed consent was obtained from subjects involved in this study.

References

1. Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of clinical criteria for sepsis: For the third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016; 315(8): 762-774.
2. Rhodes A, Evans LE, Alhazzani W, et al. Surviving sepsis campaign: International guidelines for management of sepsis and septic shock: 2016. Intensive Care Med 2017; 43: 304-377.
3. Weiss S, Fitzgerald J, Pappachan J, et al. Global epidemiology of pediatric severe sepsis: The sepsis prevalence, outcomes, and therapies study. Am J Respir Crit Care Med 2015; 191(10): 1147-1157.
4. Schlapbach LJ, Straney L, Alexander J, et al. Mortality related to invasive infections, sepsis, and septic shock in critically ill children in Australia and New Zealand, 2002–13: A multicentre retrospective cohort study. Lancet Infect Dis 2015; 15(1): 46-54.
5. Pruinelli L, Westra BL, Yadav P, et al. Delay within the 3-hour surviving sepsis campaign guideline on mortality for patients with severe sepsis and septic shock. Crit Care Med 2018; 46(4): 500.
6. Brierley J, Carcillo JA, Choong K, et al. Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American college of critical care medicine. Critical Care Med 2009; 37(2): 666.
7. Fathi EM, Narchi H, Chedid F. Noninvasive hemodynamic monitoring of septic shock in children. World J Methodol 2018; 8(1): 1.
8. Reddy YN, Melenovsky V, Redfield MM, et al. High-output heart failure: A 15-year experience. J Am Coll Cardiol 2016; 68(5): 473-482.
9. Lee E-P, Hsia S-H, Lin JJ, et al. Hemodynamic analysis of pediatric septic shock and cardiogenic shock using transpulmonary thermodilution. BioMed Res Int 2017; 2017: 3613475.
10. Brierley J, Peters MJ. Distinct hemodynamic patterns of septic shock at presentation to pediatric intensive care. Pediatrics 2008; 122(4): 752-759.
11. Weiss SL, Peters MJ, Alhazzani W, et al. Surviving sepsis campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. Intensive Care Med 2020; 46: 10-67.
12. Rao SS, Lalitha A, Reddy M, et al. Electrocardiometry for hemodynamic categorization and assessment of fluid responsiveness in pediatric septic shock: A pilot observational study. Indian J Crit Care Med 2021; 25(2): 185.
13. Scott L Weiss, Mark J Peters, Waleed Alhazzani, et al. Surviving sepsis campaign international guidelines for the

management of septic shock and sepsis-associated organ dysfunction in children. Pediatr Crit Care Med 2020; 21(10): 924-925.

14. Slater A, Shann F, Pearson G, et al. PIM2: A revised version of the Paediatric Index of Mortality. Intensive Care Med 2003; 29: 278-285.
15. Davis AL, Carcillo JA, Aneja RK, et al. The American College of critical care medicine clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock. Crit Care Med 2017; 18(9): 884.
16. Tibby SM, Hatherill M, Marsh MJ, et al. Clinicians' abilities to estimate cardiac index in ventilated children and infants. Arch Dis Child 1997; 77(6): 516-518.
17. Razavi A, Newth CJ, Khemani RG, et al. Cardiac output and systemic vascular resistance: clinical assessment compared with a noninvasive objective measurement in children with shock. J Critical Care 2017; 39: 6-10.
18. Aneja R, Carcillo J. Differences between adult and pediatric septic shock. Minerva Anestesiol 2011; 77(10): 986-992.
19. Ceneviva G, Paschall JA, Maffei F, et al. Hemodynamic support in fluid-refractory pediatric septic shock. Pediatrics 1998; 102(2): e19-e19.
20. Ranjit S, Natraj R, Kandath SK, et al. Early norepinephrine decreases fluid and ventilatory requirements in pediatric vasodilatory septic shock. Indian J Crit Care Med 2016; 20(10): 561.
21. Van De Water JM, Mount BE, Chandra KD, et al. TFC (thoracic fluid content): A new parameter for assessment of changes in chest fluid volume. Am Surg 2005; 71(1): 81-86.
22. Reant P, Dijos M, Donal E, et al. Systolic time intervals as simple echocardiographic parameters of left ventricular systolic performance: Correlation with ejection fraction and longitudinal two-dimensional strain. Eur J Echocardiogr 2010; 11(10): 834-844.
23. Cantor A, Wanderman KL, Karolevitch T, et al. Systolic time intervals in children: Normal standards for clinical use. Circulation 1978; 58(6): 1123-1129.

*Correspondence to:

Radwa Sayed Iraqy

Department of Pediatric Critical Care,

Cairo University School of Medicine,

Cairo, Egypt

E-mail: Hebatallah.gebaly@kasralainy.edu.eg