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Original Article

Role of Inferior Vena Cava Diameters as Predictor of Fluid Responsiveness in Mechanically Ventilated Pediatric Septic Shock

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ABSTRACT

Objective: To evaluate the role of inferior vena cava diameters as predictor of fluid responsiveness in mechanically ventilated pediatric septic shock.

Study Design: Prospective longitudinal study.

Place and Duration of Study: Pediatric Intensive Care unit of The Children's Hospital, Lahore Pakistan, from Nov 2023 to Apr 2024.

Methodology: Utilizing non-probability consecutive sampling, patients with diagnosis of septic shock and on mechanical ventilation were selected from all PICU admissions. Inferior vena cava indices were measured using bedside ultrasound before and after one hour of fluid bolus. IVC diameter/BSA (body surface area) and IVC distensibility index (IVCDI) were calculated.

Results: A total of 97 patients of both genders were included in the study, with a mean age of 9.00 (5.00 –13.00) years. The median of Minimal IVC diameter (cm) at 0-hour and after 1-hour were 0.43(0.31-0.50) and 0.45(0.34-0.56). Maximal IVC diameter (cm) at 0-hour and after 1-hour were 0.56(0.53-0.62) and 0.60(0.54-0.65) respectively. Highest sensitivity was noted for IVC-min/BSA at 1 hour with cut-off of <1.15 cm/m². Highest negative predictive value was demonstrated for IVCDI at 1hr with cut-off value >15.86. 17% was taken as predictor of fluid responsiveness.

Conclusion: Minimal IVC diameter and its distensibility index were found to be practical and noninvasive indicators of fluid responsiveness in pediatric septic shock, demonstrating feasibility at various time points from admission.

Keywords: Cardiac output, Inferior vena cava, Mechanical ventilation, Pulse pressure, Septic shock.

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INTRODUCTION

Septic shock results from an uncontrolled immune response to infection, causing widespread inflammation and impaired blood flow.[1] Sepsis imposes a significant strain on emergency departments worldwide, and individuals presenting with hypoperfusion and shock due to sepsis may experience mortality rates ranging from 22.8% to 48.7%.[2] The first suggested treatment for acute circulatory collapse brought on by sepsis is fluid bolus therapy (FBT) aims to improve cardiac output and stroke distance in order to increase blood flow to organs that are hypoperfused.[3] Correcting fluid overload is essential in the management of critically ill children, as it has been associated with prolonged hospital stays and increased mortality.[4] Patients who may benefit from FBT can be identified using fluid responsiveness, which is defined as an increase in stroke distance of greater than 10%.[5]

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An accurate assessment of intravascular volume status is imperative for the proper care of these patients. Various modalities, including central venous pressure monitoring, hemodynamic variables, and laboratory parameters, have been utilized to measure intravascular fluid status.[6] However, none of these methods has demonstrated accurate correlation or sufficient sensitivity in consistently assessing fluid status septic shock.[7] Point-of-care ultrasound has become increasingly popular in critical care settings, and the measurement of inferior vena cava (IVC) diameters using bedside ultrasonography has proven valuable in assessing fluid responsiveness in septic shock.[8] The inferior vena cava, being a major collapsible vein, serves as a reservoir, exhibiting diameter variations in response to respiration, right heart function, and blood volume. This dynamic response allows for an accurate depiction of the true fluid status of patients.[9] Studies have indicated that healthy children's IVC dimensions rise with height, weight, and BMI, underscoring the necessity of taking individual characteristics into account for a precise fluid status evaluation in clinical practice.[10]

The objective was to evaluate the role of inferior vena cava diameters as predictor of fluid responsiveness in septic shock and hence avoiding fluid overload with unnecessary fluid boluses. This would specify whether this non-invasive approach could serve as a reliable alternative to more invasive monitoring techniques, such as central venous pressure lines.

METHODOLOGY

The prospective longitudinal study was conducted at the Pediatric intensive Care Unit of The Children's Hospital and University of Child Health Sciences, Lahore, from November 2023 to April 2024 after taking a duly signed approval from Institutional Review Board (728/CH-UCHS dated 13th Nov, 2023). The sample size was calculated using the Open Epi software version-3, using the 10% prevalence of pediatric septic shock in developing countries.[11]

Inclusion Criteria: Patients aged 1 month to 15 years regardless of gender diagnosed with septic shock and undergoing mechanical ventilation were included in the study.

Exclusion Criteria: Patients with diagnosis of congenital cardiac diseases, viral myocarditis, abdominopelvic ascites, abdominal mass, undergoing peritoneal dialysis and history of cardiothoracic surgery were excluded from the study.

Non-probability consecutive sampling technique was used for recruitment of samples. Diagnosis of Septic shock was made on presence of at least 2 or more of the later-mentioned criteria as defined by American academy of pediatrics. Criteria includes: (a) Tachycardia, defined as a mean heart rate > 2 standard deviation (SD) above normal for age. (b) Decrease in blood pressure < 5th percentile or systolic BP < 2 SD below normal for age. (c) Urine output < 0.5ml / kg /hr. (d) Prolonged capillary refill > 5 seconds. Inferior vena cava diameters (IVDI) were measured using bedside ultrasound i.e. by performing POCUS (Points of Care Ultrasound) by a trained intensivist before fluid bolus was given. Maximum and minimum inferior vena cava (IVC) diameters (abbreviated as IVC-min and IVC-max) were measured using bedside ultrasonography with patient in supine position at the level it enters the right atrium in subxiphoid view. Since IVC dimensions vary with mass and age thus IVC measurements indexed to body surface area were calculated by dividing IVC (cm) measurement by body surface area (m^2). Inferior vena cava distensibility index is then calculated as follows: ([Maximum IVC diameter – minimum IVC diameter] / minimum IVC diameter) × 100. These values were measured before administration of the bolus and repeated one hour after the bolus infusion. As per the previously published literature ≥17% increase in pulse pressure (PP) is predictor of ≥15 increase in cardiac output. Hence, we used a rise of PP ≥17% as predictor of fluid responsiveness.[12]

Statistical analysis was conducted using Statistical Package for Social Sciences version 23. Normality of numerical variables was assessed with the Shapiro-Wilk test, and due to non-normal distribution, data were presented as median (IQR). Categorical variables were reported as frequencies and percentages. The Wilcoxon Signed-Rank Test was used to compare IVC measurements at 0 and 1 hour. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated to evaluate the predictive ability of IVC parameters for fluid responsiveness. The p-value <0.05 was considered statistically significant.

RESULTS

There were 189 patients admitted. 112 patients were diagnosed as septic shock. However, 15 patients were excluded due to incomplete data and exclusion criteria. Thus, a total of 97 patients of either gender was enrolled with median age of 9.00 (5.00 –13.00). The study cohort comprise 42 males (36.2%) and 55 females (47.4%). The demographic data in the form of median (interquartile range) of all enrolled patients are given in Table-I.Table-II depicts the IVC measurements taken before administration of the bolus and 1 hour after the completion of the bolus administration. Table-III presents the role of IVC dimensions in predicting the fluid responsiveness in septic shock patients. Highest sensitivity was noted for IVC-min/BSA at 1 hour with cut-off of <1.15 cm/m^2. However, IVC min/BSA at 0 hr with cut-off value of <0.93 cm/m was most specific (i-e 100%) at predicting fluid responsiveness and it also demonstrated highest PPV (i-e 100%). Highest negative predictive value was demonstrated for IVCDI 1hr wot cut-off value >15.86.

DISCUSSION

Intravenous (IV) fluid administration plays a crucial role in the management of pediatric septic shock, aiming to reverse organ dysfunction and restore hemodynamic stability.[13] Early and aggressive fluid resuscitation is essential to restore intravascular volume and improve cardiac output.[14] Echocardiography, specifically focused or point-of-care ultrasound (POCUS), can indeed play a crucial role in guiding fluid resuscitation in critically ill patients: especially preventing excessive fluid administration and resultant fluid overload.[15] Boyd and colleagues have reported that approximately two-thirds of patients may not exhibit a favorable response to fluid after an initial volume resuscitation of 30mL/kg. This observation suggests the consideration of alternative hemodynamic interventions, such as the administration of inotropic agents. In the present investigation, inferior vena cava (IVC) parameters were assessed in comparison to the conventional fluid challenge test as indicators of fluid responsiveness. The increasing specificity of IVC-derived parameters over time proved effective in accurately identifying all individuals who did not respond to fluid, implying that hemodynamic instability should be addressed through interventions other than fluid administration.[16]

Table-I: Demographic Characteristics of Enrolled Patients (n=97)

Variables	Median (IQR)
Age	9.00 (5.00 –13.00)
Weight (kg)	7.00 (6.00 –8.95)
Height (cm)	65.00 (56.50-75.15)
Disseminated Intravascular Coagulation (DIC) Score	6.00 (4.50-8.00)
Systolic blood pressure (mm Hg)	107.00 (97.00-111.00)
Mean arterial pressure (MAP; mm Hg)	85.00 (78.00-90.00)
Heart rate (beats/min)	189.00 (178.00-194.00)
Oxygen saturation (%)	80.00 (75.00-93.50)
Capillary refill time (sec)	5.00 (4.00-5.00)
Urine output (mL/kg/h)	0.96 (0.89-1.30)
Cumulative fluid (mL/kg)	47.00 (43.00-53.00)
Source of Infection	n (%)
Blood stream infection	64 (66.0%)
Pneumonia	46 (47.4%)
Abdominal infection	43 (44.3%)
Meningitis	23 (23.7%)

Table-II: Inferior Vena Cava Measurements (n=97)

	At 0 hour Median (IQR)	After1 hour Median (IQR)	*p*-value
Minimal Inferior Vena Cava Diameter (cm)	0.43 (0.31-0.50)	0.45 (0.34-0.56)	0.007
Maximal Inferior Vena Cava Diameter (cm)	0.56 (0.53-0.63)	0.60 (0.54-0.65)	<0.001
Inferior Vena Cava Diameters (IVC-DI) (%)	13.00 (5.00-23.00)	15.00 (6.00-23.00)	0.372

The IVC-DI measures how much the IVC changes in size with respiration. Yıldızdaş *et al.*, Found that an IVC-DI greater than 22.73% indicates a strong response to intravenous fluids, with 100% sensitivity and specificity.[17] Additionally, Achar *et al.*, discovered that an IVC-DI threshold of 23.5% effectively differentiated between individuals who responded to treatment and those who did not.[18]

Table-III: Sensitivity and Specificity of the Inferior Vena Cava Parameters as Predictors of fluid Responsiveness (n=97)

Inferior Vena Cava min/BSA 0hr	Fluid Responsiveness		*p*-value
	Positive	Negative	
<0.93	35 (TP)	0 (FP)	<0.0001
>0.93	15 (FN)	47 (TN)	

Sensitivity= TP/(TP+FN)= 35/(35+15)*100=70.00 %
Specificity= TN/(TN+FP)= 47/(47+0)*100=100.00%
Positive Predictive Value= TP/(TP+FP)*100= 35/(35+0)= 100.00%
Negative Predictive Value= TN/(TN+FN)*100=47/(47+15)= 75.80%

Inferior Vena Cava min/BSA 1hr	Fluid Responsiveness		*p*-value
	Positive	Negative	
≤1.15	46 (TP)	14 (FP)	<0.001
>1.15	4 (FN)	33 (TN)	

Sensitivity= TP/(TP+FN)= 46/(46+4)*100=92.00 %
Specificity= TN/(TN+FP)= 33/(33+14)*100=70.21%
Positive Predictive Value= TP/(TP+FP)*100= 46/(46+14)= 76.66%
Negative Predictive Value= TN/(TN+FN)*100=33/(33+4)= 89.18%

Inferior Vena Cava Diameters (IVC-DI) 0hr	Fluid Responsiveness		*p*-value
	Positive	Negative	
>12.32	42 (TP)	12 (FP)	<0.0001
<12.32	8 (FN)	35 (TN)	

Sensitivity= TP/(TP+FN)= 42/(42+8)*100=84.00 %
Specificity= TN/(TN+FP)= 35/(35+12)*100=74.47%
Positive Predictive Value= TP/(TP+FP)*100= 42/(42+12)= 77.78%
Negative Predictive Value= TN/(TN+FN)*100= 35/(35+8)= 81.40%

Inferior Vena Cava Diameters (IVC-DI) 0hr	Fluid Responsiveness		*p*-value
	Positive	Negative	
>15.86	39 (TP)	3 (FP)	<0.001
<15.86	11 (FN)	44 (TN)	

Sensitivity= TP/(TP+FN)= 39/(39+11)*100=78.00 %
Specificity= TN/(TN+FP)= 44/(44+3)*100=93.61%
Positive Predictive Value= TP/(TP+FP)*100= 39/(39+3)= 92.85%
Negative Predictive Value= TN/(TN+FN)*100= 44/(44+11)= 80.00%

In our study, the minimal IVC diameter increased from 0.43 cm to 0.45 cm, while the maximal IVC diameter increased from 0.56 cm to 0.60 cm. These changes suggest dilation of the IVC in response to fluid administration, which aligns with the concept of fluid responsiveness. However, it's crucial to interpret these findings in the context of the established thresholds for IVC-DI response. While this data on changes in IVC diameter, it's essential to calculate the corresponding IVC-DI values and compare them against the thresholds established by Yıldızdaş *et al.*, and Achar *et al.*, This comparison will help determine whether the observed changes in IVC diameter indicate a strong response to fluid therapy, as defined by the established thresholds.

In patients who are intubated and receiving positive-pressure mechanical ventilation, the diameter of the inferior vena cava (IVC) expands during inspiration and contracts during expiration. This is different from spontaneously breathing patients. Because of this difference, it is suggested to use the Inferior Vena Cava Distensibility Index (IVCDI) rather than the IVC collapsibility index to assess fluid responsiveness in individuals undergoing positive-pressure mechanical ventilation. The IVCDI takes into account the changes in IVC diameter during the breathing cycle and is considered a more suitable measure.[19] Very little data is available in the literature because Inferior Vena Cava Distensibility Index (IVCDI) is not a widely recognized or established term in pediatric practice. Our study was supported by another study in which they stated that the minimal diameter of the inferior vena cava (IVC) and its distensibility index were found to be practical and noninvasive indicators of fluid responsiveness in pediatric septic shock. The maximum diameter of the inferior vena cava (IVC) was unable to predict fluid responsiveness at any point from admission.[20]

This observation aligns with the findings of Ilyas *et al.,* who similarly reported no significant difference in maximal IVC diameter between the euvolemic and hypovolemic groups. Indeed, the evaluation of the inferior vena cava (IVC) diameters and its respiro-phasic variation is a well-studied method, particularly in the field of critical care and cardiology. IVC assessment remains a valuable tool in the clinical setting, especially when combined with other hemodynamic parameters. It is often used as part of a comprehensive approach to assess a patient's volume status and guide fluid management in conditions such as sepsis, heart failure, or other critical illnesses.[21] Furthermore, a meta-analysis conducted by Orso *et al.,* found that, with a pooled AUC of 0.71, sensitivity and specificity of 0.74 and 0.68, respectively, ultrasonography measurement of the IVC width and its respiratory changes did not appear to be a valid way to predict the fluid responsiveness.[13] A pooled AUROC of 0.79 indicates that fluid responsiveness is somewhat predicted by respiratory change in IVC diameter. While a negative result has poor sensitivity (63%) and is unable to rule out fluid responsiveness, a positive result has intermediate specificity (73%). In this situation, the test is more reliable since it performs better in patients on mechanical ventilation than in those who are ventilating themselves. A study conducted by Long *et al.,* indicated that the large range of outcomes among studies can be attributed to variations in patient populations, fluid responsiveness definition and measurement techniques, fluid challenge volume, and threshold change in IVC diameter.[22]

Additionally, considering the variability in individual patient responses and the limitations of ultrasound measurements, it's advisable to validate these findings in a larger cohort or through further studies. Nonetheless, our study contributes valuable insights into the assessment of fluid responsiveness using IVC diameter changes and warrants further investigation in clinical practice.

CONCLUSION

The study found that both the inferior vena cava (IVC) minimal diameters and distensibility index (IVCDI) are reliable in predicting fluid responsiveness in pediatric septic shock patients undergoing mechanical ventilation: making these parameters practical, non-invasive tools for assessing fluid responsiveness in this patient population and thus guiding fluid resuscitation more accurately.

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Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

MK & NS: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

MP & AA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SM & MS: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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