

## Association Between Vasoactive-Inotropic Score and Mortality in Pediatric Septic Shock

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**Objective:** To assess the association between Vasoactive Inotrope Score (VIS) and mortality in children with fluid-refractory septic shock. **Methods:** A retrospective chart review of 71 children (age 1 mo-16y) admitted with fluid-refractory septic shock in pediatric intensive care unit during a two year period was done. We divided our cohort into two groups viz High-vasoactive inotrope score (Group-H) and 'Low-vasoactive inotrope score' (Group-L) based on a cut-off value of 20. **Results:** 73% of the children were in Group-L. The mortality rate was 44% and 100% in Group L and Group H, respectively. **Conclusion:** High inotropic score in children with septic shock is associated with high mortality rate.

**Keywords:** Children, Fluid-refractory, Outcome, Sepsis, Shock.

Pediatric septic shock is associated with a high mortality rate. The mortality in pediatric septic shock is associated with lactic acidosis and presence of multiorgan dysfunction syndrome [1,2]. Inotrope and vasoactive agents are routinely employed in children with septic shock to maintain cardiovascular support for oxygen delivery and tissue perfusion. The Vasoactive-Inotropic Score (VIS) is an objective clinical tool that is used to quantify the need of cardiovascular support in children after cardiac surgery, and used as a predictor of morbidity and mortality [3]. The aim of this study was to assess the correlation between VIS and mortality rate in children with fluid-refractory septic shock.

### METHODS

We conducted a retrospective chart review of all children between the ages of one month and 16 years who were admitted with diagnosis of fluid-refractory septic shock between January 2011 to December 2012. The definition and initial management of all patients with sepsis was according to the current (ACCM/AHA) guidelines [4]. The calculation of Vasoactive Inotropes Score (VIS) was done for first 48 hours in PICU as described by Gaies, *et al.* [3]. The maximum VIS was calculated from hourly recorded inotropes on ICU sheets. We divided our cohort into two group based on the cut-off value of 20. VIS  $\geq$ 21 on two or more readings was considered as 'High VIS' (Group-H), and all others (1-20) were considered as 'Low VIS' (Group-L). Data collected included demographic data (age, gender, Pediatric Risk of

Mortality III [PRISM III] score), as well as clinical data including primary diagnosis, comorbid conditions, VIS and outcome as alive vs. expired.

**Statistical analysis:** All data were entered into SPSS 19 for statistical analysis. Appropriate descriptive and analytical statistical tests were applied for this data and a *P* value less than 0.05 was considered significant. The study was approved by the Institutional ethical review committee.

### RESULTS

6.3% (71) of the 1127 admissions during the study period, were enrolled. The characteristics of patients are summarized in **Table I**. The median age was 25.5 (IQR 2 - 112.5) months. Mean (SD) PRISM III Score was 11 (7.9). More than half of the patients had significant comorbidities, with hematologic-oncological malignancies ( $n=15$ ) and cardiac illnesses ( $n=9$ ) being the most frequent. The presence of co-morbidity significantly increased the risk of mortality in children with fluid-refractory septic shock (62% vs. 31.8%;  $P=0.002$ ). Culture-negative sepsis was present in 53 patients (75%), 18 (25.4%) each had pneumonia and culture-proven bacteremia. Gram-negative organisms were isolated in 12 patients as compared to gram-positive organisms in three subjects. Three patients had positive culture for fungus.

The median VIS was 13 (IQR 10 – 22.8). Group-L had 52 (73.2%) children. The overall mortality rate of PICU admissions was 12% and case-specific mortality

**TABLE I** CHARACTERISTICS OF CHILDREN WITH FLUID-REFRACTORY SEPTIC SHOCK ENROLLED IN THE STUDY

Variables	All (n=71)	VIS ≤ 20 (n=52)	VIS >20 (n=19)	P value
Age (mo)	30 (2-120)	20 (2-105)	72 (2-144)	1.005
*Age <5 y	42	33	9	1.42
*Male sex	47	34	13	-
*Co-morbidity	39	27	12	0.41
*Mechanical ventilation	46	29	17	0.017
Length of stay	6 (3-10)	6 (3-9)	5 (2-14)	0.73
PRISM III score	11 (7.9)	8.5	17	0.002
Total leukocyte count	8.5 (5.1-18.8)	9.1 (5.7-20.2)	7.2 (2.3-14.1)	0.44
C-reactive protein	4.6 (0.4-11.3)	3.8 (0.38-9.3)	8.4 (2.90-15.8)	0.18
*Mortality	42	23	19	

Values in mean (SD) or \* No.

was 59.2%; 23 (38.9%) and 19 (100%) children expired from Group-L and Group-H, respectively (95% CI 1.049 – 1.230;  $P=0.002$ ).

The median PICU stay of our cohort was 6.5 (IQR 3-10.7) days. 64.7% ( $n=46$ ) patients received mechanical ventilation and 7% (5/71) received renal supportive therapy. In a multivariate logistic regression model, the Group-H ( $P=0.01$ ), presence of co-morbidity, and PRISM III score ( $P=0.04$ ) were found to be independent predictors of death in children with septic shock.

## DISCUSSION

We demonstrated that high VIS is associated with poor clinical outcome in children with fluid-refractory septic shock in the PICU of a developing country. Multiple factors have been identified as a predictor for poor outcome of septic shock among children [1,5]. Kutko, *et al.* [5] in their retrospective review of children with septic shock found that the high mortality rate was associated with the presence of multiorgan dysfunction syndrome. Several studies have shown that high serum lactate is another predictor of poor outcome in children with septic shock [1,2]. A recent guideline on pediatric sepsis from American College of Critical Care Medicine (ACCM) has cautioned against monitoring of serum lactate in children with septic shock, as epinephrine infusion is known to increase plasma lactate concentration independent of changes in organ perfusion [6]. Recently, Shock Index (heart rate / systolic blood pressure) was shown to be clinical predictor of mortality in children with septic shock admitted to PICU [7].

The hemodynamic support for children with fluid-refractory shock has been described in recent clinical practice guidelines [4] and advocate the use of epinephrine for 'cold shock' and nor-epinephrine for 'warm shock' [4].

Adult studies have also identified that high doses of vasoactive drugs are associated with poor outcome [8].

In 1995, Wernovsky, *et al.* [9] created an inotrope score for postoperative hemodynamic support following arterial switch operation to quantify amount of inotropic medications. Geiss, *et al.* [10] updated a quantitative index of cardiovascular support as Vasoactive Inotrope Score (VIS) to quantify hemodynamic support in first 48-hour after cardiac surgery in infant in the intensive care unit as a predictor of morbidity and mortality.

Our results demonstrate that there is a strong correlation between high VIS and mortality in children with fluid-refractory septic shock. Jat, *et al.* [1] also reported similar mortality rate (50%) in their cohort of children with septic shock. The vasoactive-inotrope score (VIS) is a simple, clinical tool, easy to use, and based on bedside hemodynamic parameter to monitor cardiovascular support in critically ill child with septic shock. Therefore, it is potentially feasible to use as a predictor of outcome especially in the setting of resource-limited countries. It can be used as one component in the bundle of predictors of poor outcome in children with septic shock. Large scale studies enrolling more patients are required to further justify its value.

There were several limitations to our study, including retrospective data-collection, single center data, and small sample size. The strength of this study is, that it is the first report demonstrating the strong correlation between high inotrope score and mortality in children with fluid-refractory septic shock.

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**WHAT THIS STUDY ADDS?**

- The Vasoactive-Inotropic Score (VIS) is a clinical tool that shows high positive association with mortality in pediatric fluid-refractory septic shock.

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