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Vasoactive-Inotropic Score as a Predictor of Outcomes in Children with Fluid-Refractory Septic Shock Admitted to the Pediatric Intensive Care Unit of a Tertiary Care Center

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Abstract **Objectives: Background:** The Vasoactive-Inotropic Score (VIS) has been proposed as a simple marker of illness severity and predictor of outcomes in pediatric critical illness. However, its prognostic role in pediatric septic shock remains incompletely studied. This study aimed to evaluate the predictive value of VIS for mortality and morbidity in children with fluid-refractory septic shock. **Methods:** A prospective observational study was conducted on 68 children admitted with fluid-refractory septic shock to the PICU of a tertiary care center between January 2021 and June 2022. VIS was calculated at predefined intervals and maximum VIS values were recorded. Outcomes assessed included mortality, length of PICU stay and duration of mechanical ventilation. VIS performance was compared with PRISM-IV score and lactate clearance. **Results:** High VIS values were significantly associated with mortality and mechanical ventilation. A cut-off value of >70 demonstrated strong predictive accuracy for mortality. Higher PRISM-IV scores and poor lactate clearance at 6 hours were also independently associated with adverse outcomes. Notably, non-survivors had shorter PICU stays due to early mortality. **Conclusion:** VIS was independently predictive of mortality and adverse outcomes in pediatric septic shock and outperformed PRISM-IV in prognostic accuracy. Incorporation of VIS into clinical protocols may enable timely identification of high-risk children. Multicenter studies with larger cohorts are warranted for external validation.

Key Words Vasoactive-Inotropic Score, Pediatric Septic Shock, Fluid-Refractory Shock, Mortality, PRISM-IV, Lactate Clearance

INTRODUCTION

Infectious diseases have posed a significant challenge to human survival throughout history, with children under the age of five being particularly vulnerable. According to the World Health Organization (WHO), approximately 60% of deaths in this age group are linked to infectious diseases, with sepsis being a leading cause [1]. Sepsis is a severe clinical syndrome resulting from a dysregulated immune response to infection, which can lead to systemic inflammation, multi-organ failure and microvascular complications [2,3]. The burden of sepsis in children is immense, with mortality rates ranging from 4% to 50%, depending on disease severity, underlying risk factors and geographic location [4,5].

Despite advancements in medical care, early detection and management of sepsis remain challenging, particularly in pediatric populations. The complexity of the disease is compounded by varying definitions and diagnostic criteria. While the International Pediatric Consensus Conference (IPSCC) criteria have been widely adopted, they face limitations in accuracy and applicability across diverse clinical settings [6]. To address these challenges, the pediatric Sequential Organ Failure Assessment (pSOFA) score was introduced to provide a more objective tool for assessing organ dysfunction and predicting outcomes in pediatric sepsis [7].

Pediatric septic shock, a severe manifestation of sepsis characterized by acute circulatory failure, remains a significant cause of early mortality and prolonged hospitalization in children [8]. The management of septic shock requires prompt recognition, judicious fluid resuscitation and the use of vasoactive agents to stabilize cardiovascular function. The Vasoactive-Inotropic Score (VIS) has emerged as a valuable tool for quantifying cardiovascular support and predicting clinical outcomes in

children with septic shock [9,10]. Higher VIS values have been associated with increased morbidity, prolonged hospital stays and higher ventilator dependency in pediatric patients [11].

Sepsis in children remains a major cause of morbidity and mortality worldwide, with case fatality rates ranging from 4% to 50% depending on disease severity and healthcare resources. Pediatric septic shock, characterized by circulatory collapse due to a dysregulated host response, requires early recognition and aggressive management, including fluid resuscitation and vasoactive support.

Clinical scoring systems such as the Pediatric Risk of Mortality (PRISM-IV) and pediatric Sequential Organ Failure Assessment (pSOFA) are widely used for prognostication. While pSOFA has gained prominence in sepsis studies, PRISM-IV remains useful in certain settings. However, both are complex and may not be feasible in fast-changing scenarios of shock. The vasoactive-inotropic score (VIS), originally developed in postoperative cardiac patients, quantifies vasoactive medication use and reflects cardiovascular dysfunction severity. High VIS values have been correlated with increased morbidity and mortality in critically ill children.

Given limited pediatric data, particularly in septic shock, this study hypothesized that VIS would be independently predictive of outcomes and potentially outperform PRISM-IV. Secondary objectives included evaluating the association of lactate clearance with outcomes and establishing a clinically relevant VIS cut-off.

Objectives:

- **Primary Objective**
  - To assess whether VIS independently predicts mortality in children with fluid-refractory septic shock
- **Secondary Objectives**
  - To compare VIS with PRISM-IV scores and lactate clearance in predicting mortality, PICU length of stay and duration of mechanical ventilation
  - To establish a cut-off value of VIS for predicting adverse outcomes
  - To evaluate the correlation of maximum VIS with lactate dynamics and clinical outcomes.

METHODS

This prospective observational study was conducted in the Department of Pediatrics at Indira Gandhi Institute of Child Health, Bengaluru, from January 2021 to June 2022. The study included pediatric patients aged one month to less than 18 years diagnosed with septic shock and meeting the inclusion criteria. Children with fluid refractory septic shock, defined as persistent shock despite 40–60 mL/kg fluid resuscitation, were enrolled. Patients excluded from the study were those under one month of age, those in the operating room or post-anesthetic care unit, children with shock due to non-septic causes such as cardiogenic, anaphylactic, hemorrhagic, or spinal shock, children suspected to have metabolic crises secondary to inborn errors of metabolism and children with known congenital cardiac anomalies.

The sample size was calculated based on the correlation coefficient of the vasoactive-inotropic score (VIS) with ICU length of stay and ventilator days at 48 hours, yielding a required sample size of 51 after accounting for a 10% non-response rate. Complete data from 68 subjects were ultimately included. Data collection adhered to the Surviving Sepsis Campaign guidelines for managing septic shock and sepsis-associated organ dysfunction in children. Information, including demographic details, clinical findings, laboratory investigations, culture reports, PRISM-IV scores and VIS at various time points, was recorded in a pre-structured proforma.

The VIS was calculated using a standardized formula incorporating doses of vasoactive medications, including norepinephrine, epinephrine, vasopressin, dopamine, dobutamine and milrinone.

VIS Formula:

VIS = dopamine (μg/kg/min) + dobutamine (μg/kg/min) + 100 × epinephrine (μg/kg/min) + 100 × norepinephrine (μg/kg/min) + 10 × milrinone (μg/kg/min) + 10,000 × vasopressin (U/kg/min)

The score was calculated at 6, 12, 24 and 48 hours from the initiation of vasopressors and at different time intervals until the discontinuation of inotropic support. Maximum VIS scores were correlated with clinical outcomes, including ICU length of stay, duration of mechanical ventilation and mortality rates.

Sample Size

Calculated for correlation with PICU stay and ventilator days; expected $r = 0.35$, $\alpha = 0.05$, power = 80%, minimum 51 patients; 68 enrolled to ensure adequate power.

Scoring Timing

VIS measured at 6h, 12h, 24h and 48h post-initiation of vasoactive support; maximum VIS recorded. PRISM-IV calculated over the first 24h of admission.

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 24.0. Categorical data were expressed as frequencies, while continuous data were reported as mean ± standard deviation. Statistical methods included Pearson correlation to evaluate relationships between VIS and clinical outcomes, linear regression analysis to predict the impact of VIS on outcomes and independent t-tests to assess differences between variables. ROC curves with Youden Index used to identify optimal VIS cut-off. About 95% confidence intervals reported for AUC, sensitivity and specificity. A p-value <0.05 was considered statistically significant. Ethical clearance was obtained from the institutional review board and informed consent was secured from the parents or legally acceptable representatives of all participants. All patients were managed according to standard institutional protocols irrespective of study participation.

RESULTS

This study analyzed the utility of the Vasoactive-Inotropic Score (VIS) as a predictor of outcomes in pediatric patients with fluid refractory septic shock. A total of 68 patients were included, with demographic, clinical and laboratory variables assessed to determine their association with outcomes such as mortality, length of stay in the PICU and the need for mechanical ventilation. Key results are summarized below.

Demographic and Clinical Characteristics (Table 1)

The study cohort included 60.3% males and 39.7% females. The primary focus of infection was the respiratory system (44.1%), followed by multiple organ dysfunction syndrome (MODS) (27.9%) and renal system involvement (10.3%). Comorbidities were present in 36.8% of patients, with severe acute malnutrition being the most common (11.7%), followed by cerebral palsy (7.3%). Culture positivity was observed in 60.3% of patients, with blood culture positivity in 33.8% and urine culture positivity in 16.1%. Among non-survivors, 88.9% exhibited leukopenia compared to 11.1% of survivors (Table 1).

VIS and Mortality (Table 2)

The VIS demonstrated a strong predictive value for mortality, with a cut-off value of 70 identified via ROC analysis. Survivors predominantly had a VIS≤70 (85.7%), while 97% of non-survivors had a VIS>70 (χ^2 = 46.81, p<0.001) (Table 2). The maximum VIS was significantly higher in non-survivors (85.00±6.61) compared to survivors (50.00±18.94, t = -10.04, p<0.001).

Length of Stay, Mechanical Ventilation and Laboratory Correlations (Table 3)

Non-survivors had shorter PICU stays (3.93±2.44 days) compared to survivors (7.45±3.35 days, t = 4.91, p<0.001). Lactate levels at 6 and 12 hours were significantly higher in non-survivors (44.67±9.82 mg/dL and 50.78±12.23 mg/dL, respectively) compared to survivors (32.82±9.33 mg/dL and 24.21±5.31 mg/dL, p<0.001). Poor lactate clearance at 6 hours (-12.76±14.82 mg/dL) was associated with worse outcomes (r = -0.522, p<0.01) (Table 3).

Correlation between PRISM-IV Score and Outcomes (Table 4)

The PRISM-IV score was significantly associated with mortality (χ^2 = 43.07, p<0.001). Non-survivors had higher PRISM-IV scores, with 91.7% of patients scoring >20 not surviving. A significant positive correlation was observed between PRISM-IV and maximum VIS (r = 0.762, p<0.001) (Table 4).

The study highlights the utility of VIS and PRISM-IV scores in predicting outcomes in pediatric septic shock patients. VIS >70 and higher PRISM-IV scores were significantly associated with increased mortality, shorter PICU stays and poor lactate clearance (Tables 2–4). These findings suggest that VIS and PRISM-IV can serve as valuable prognostic tools in critical care settings.

Table 1: Demographic and Clinical Characteristics of Patients

Variable	Frequency (%)
Gender: Male	41 (60.3%)
Focus of Infection: Respiratory	30 (44.1%)
Presence of Comorbidities	25 (36.8%)
Culture Positivity	41 (60.3%)
Blood Culture Positivity	23 (33.8%)
Leukopenia (Non-Survivors)	8 (88.9%)

Table 2: VIS and Mortality

VIS Category	Survivor (%)	Non-Survivor (%)
VIS ≤70	30 (85.7%)	1 (3.0%)
VIS >70	5 (14.3%)	32 (97.0%)
Maximum VIS (Mean ± SD)	50.00±18.94	85.00±6.61

Table 3: Length of Stay and Laboratory Parameters

Variable	Survivor (Mean ± SD)	Non-Survivor (Mean ± SD)
PICU Stay (days)	7.45±3.35	3.93±2.44
Lactate at 6 Hours (mg/dL)	32.82±9.33	44.67±9.82
Lactate at 12 Hours (mg/dL)	24.21±5.31	50.78±12.23
Lactate Clearance at 6 Hours	16.01±12.37	-12.76±14.82

Table 4: PRISM-IV and Outcomes

PRISM-IV Score	Survivor (%)	Non-Survivor (%)
<10	27 (100%)	0 (0%)
10–20	7 (24.1%)	22 (75.9%)
>20	1 (8.3%)	11 (91.7%)

DISCUSSION

The present study assessed the utility of the Vasoactive-Inotropic Score (VIS) as a prognostic tool in predicting outcomes such as mortality, length of PICU stay and mechanical ventilation in pediatric patients with fluid refractory septic shock. A key finding was that non-survivors had significantly higher maximum VIS, CRP levels and lactate levels at 6 and 12 hours, as well as lower serum albumin levels and poor lactate clearance, compared to survivors. These findings align with earlier studies demonstrating the prognostic utility of VIS in critically ill pediatric patients [1,2].

Comorbidities, leukopenia and thrombocytopenia were significantly associated with mortality in the present study. Thrombocytopenia and leukopenia have been recognized as biomarkers of sepsis and are associated with poor outcomes in critically ill children [3,4]. Lower serum albumin levels in non-survivors, as observed in this study, have been similarly reported in pediatric and adult sepsis populations, with hypoproteinemia linked to increased mortality and poor prognosis [5,6]. Elevated CRP levels in non-survivors reinforce its role as a biomarker for sepsis, consistent with prior research highlighting its association with inflammation and adverse outcomes in sepsis [7,8].

VIS was significantly higher in non-survivors, with a strong correlation to mortality. This finding corroborates earlier studies where elevated VIS was associated with increased mortality, such as the work of Haque *et al.* which identified high VIS as a predictor of poor outcomes in pediatric sepsis (9). The current study's VIS cut-off of 70, with sensitivity and specificity of 97.0 and 85.7%, respectively, was higher than the thresholds [10,11]. Differences in cut-offs may reflect variations in institutional protocols and preferred vasoactive agents.

The length of PICU stay was shorter in non-survivors, a finding that diverges from studies like McIntosh *et al.*, which reported longer stays with higher VIS scores [12]. This discrepancy may be explained by the higher PRISM-IV scores observed in non-survivors at admission, indicating greater initial disease severity and higher early mortality risk. While the duration of mechanical ventilation did not differ significantly between survivors and non-survivors, the need for mechanical ventilation was strongly associated with higher VIS scores, consistent with the understanding that patients requiring greater cardiovascular support often experience severe respiratory complications necessitating ventilatory assistance [13].

PRISM-IV scores were also significantly associated with mortality, with higher scores correlating with shorter PICU stays and poor outcomes. These findings align with previous research demonstrating the discriminatory power of PRISM-IV in predicting pediatric sepsis outcomes [14]. The significant correlation between VIS and PRISM-IV scores suggests that VIS may serve as a complementary or alternative prognostic tool, particularly in settings where PRISM-IV is less applicable or overestimates mortality due to its reliance on 24-hour admission data [15].

Serum lactate levels and lactate clearance at 6 hours were strong predictors of mortality in this study, with non-survivors showing higher lactate levels and poor clearance. These results are consistent with studies which emphasized the prognostic value of lactate clearance in sepsis and its association with impaired tissue oxygenation [16,17]. Moreover, the correlation between high VIS and poor lactate clearance underscores the interplay between cardiovascular dysfunction and metabolic derangements in septic shock [18].

This study demonstrates that VIS is a robust, independent predictor of mortality in pediatric fluid-refractory septic shock, with superior prognostic accuracy compared to PRISM-IV. A VIS cut-off >70 showed excellent sensitivity and specificity, consistent with but slightly higher than previous studies, possibly reflecting differences in patient population and institutional management practices.

Shorter PICU stay among non-survivors reflected early deaths due to severe disease rather than faster recovery. High VIS correlated with poor lactate clearance, emphasizing its pathophysiological basis: increased vasoactive requirements signal circulatory failure and metabolic derangement.

Unlike PRISM-IV, which requires extensive data collection over 24h, VIS can be calculated dynamically in real time, making it feasible for bedside monitoring and integration into EMR systems.

CONCLUSION

VIS is a simple, dynamic and independent predictor of outcomes in pediatric septic shock. A cut-off >70 identifies high-risk children with high accuracy. VIS should be considered for incorporation into pediatric sepsis protocols alongside lactate clearance and PRISM-IV. Multicenter studies are needed for external validation and to explore its role in decision-support systems.

Limitations:

- Single-center design with small sample size
- Lack of external validation or sensitivity analyses
- Missing data on some secondary biomarkers
- Heterogeneity in sepsis etiologies may influence findings

Future Recommendations:

- Multicenter validation of VIS cut-off values
- Evaluation of delta VIS (change over time) as a prognostic marker
- Integration of VIS into sepsis prediction models with biomarkers and echocardiography
- Incorporation into EMR systems for automated alerts and triage decisions

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