ORIGINAL ARTICLE

Shock Index and Baseline Lactate Level did not Predict Non survival in Pediatric Patients with Severe Sepsis: A tertiary hospital experience

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Abstract

Background: Limited information exists regarding the shock index (SI) and lactate levels in children with sepsis. Therefore, we performed this study to explore the predictive value of SI (baseline and 6 h later) and baseline lactate levels in pediatric patients with severe sepsis.

Methods: Children with severe sepsis were enrolled in this prospective study. The SI (measured by HR/SBP) and lactate levels were assessed. The study population was categorized into two distinct groups: survivors and nonsurvivors.

Results: The sample size was 46 children, with 21 being survivors and 25 being nonsurvivors. Blood cultures in the survivors revealed Klebsiella pneumoniae and Escherichia coli (E. coli). However, blood cultures in the nonsurvivors revealed Klebsiella pneumonia and Acinetobacter baumannii complex. The SI did not significantly differ between survivors and nonsurvivors. The median (IQR) lactate levels of survivors were 5.2 (2.7 – 14) mmol/L, and those of nonsurvivors were 5.2 (3.1 – 18) mmol/L. The groups' baseline lactate levels did not differ significantly.

Conclusions: We conclude that the shock index and lactate values do not vary notably between survivors and nonsurvivors. Therefore, the shock index (baseline and 6 h later) and baseline lactate levels did not predict nonsurvival in children with severe sepsis. This could be attributed to the limited number of study participants, large variations in normal physiological indicators, and limited pediatric physiological compensatory abilities in response to the shock.

Keywords: children, lactate, nonsurvivors, sepsis, shock index

Introduction

Initial shock management typically involves the restoration of normal hemodynamic and laboratory parameters [1]. Numerous investigations have demonstrated that achieving normal hemodynamic parameter values does not lead to improved morbidity or nonsurvival [2].

The shock index (SI) is estimated with the division of the heart rate (HR) by the systolic blood pressure (SBP). Healthy adults typically exhibit an SI of 0.5 to 0.7 [3]. Studies conducted in adults have indicated that an initial SI and constant elevation of the SI above 0.9 are related to a crucial need for lifesaving measures, hospital admission, and critical care treatment. SI values exceeding 0.9 are

considered significant and correlated with heart failure, reduced oxygen supply to tissues, and a higher death rate in adult patients [4, 5]. Further research is needed to investigate normal SI levels and the impact of SI on pediatric patients' medical care.

Furthermore, determining the SI in pediatric patients is difficult because of the broad diversity of age-specific standard heart rates and blood pressure readings. Consequently, normal SI values differ across age groups [6].

Lactate is vital for energy generation and cellular metabolism. Lactic acidosis may arise due to various conditions, such as hepatic diseases, shock, sepsis, injury, intense exercise, drug poisoning, and malignancy [7, 8]. The 2016 Surviving Sepsis Campaign (SSC) guidelines proposed monitoring lactate levels in septic patients as an indicator of insufficient tissue perfusion [9]. Numerous factors can contribute to increased lactate levels, including mitochondrial abnormalities, impaired pyruvate dehydrogenase function, and an imbalance between oxygen delivery and utilization [10]. Limited investigations have examined the predictive performance of lactate levels and SI in sepsis. Therefore, this study aimed to explore the prognostic value of SI (baseline and 6 h later) and baseline lactate levels in pediatric patients with severe sepsis and septic shock in a pediatric intensive care unit (PICU).

Methods

This study was conducted over six months in the pediatric critical care unit of Zagazig University Hospital (ZUH) in association with the Clinical Pathology Department. It was a prospective observational study. The study population was aged 28 days to 16 years. They were diagnosed with severe sepsis or septic shock upon critical care unit admission. Patient categorization in this study followed the criteria set forth by the International Pediatric Sepsis Consensus Conference (IPSCC) in 2005, along with the international recommendations outlined in the 2020 Surviving Sepsis Campaign [11, 12]. Patients meeting these sepsis criteria during the study period were included, whereas those with conditions known to cause elevated lactate levels, such as inborn metabolic errors, were excluded.

Data Collection

An initial evaluation was conducted, which involved a thorough assessment of the patient's general and systemic condition as well as a systematic search for the underlying infection. The SI at initial presentation and 6 h later was measured using HR/SBP. Routine hematological and biochemical analyses were performed. A sepsis screen was carried out, comprising a full blood count and C-reactive protein assay and cultures of various specimens. Liver function tests (LFTs), blood gas analysis (BGA), renal function tests (RFTs), and coagulation studies were performed as part of a comprehensive evaluation. Blood samples were collected safely in suitable tubes or containers (Na fluoride/Na heparin plasma or Na fluoride/Koxalate) and centrifuged within 15 minutes. Blood levels of lactate were measured spectrophotometrically using a Roche Cobas 6000 autoanalyzer (c501) in accordance with the producer's guidelines (Roche Diagnostics, Switzerland). The study population was categorized into two distinct groups: survivors and nonsurvivors.

Statistical Analysis

Data management was applied using SPSS software (version 26). Descriptive statistics, such as medians and interquartile ranges, were used for quantitative variables. Categorical variables were reported as absolute frequencies and compared using the chi-square test. For nonnormally distributed data, the Mann-Whitney test was used. We utilized the area under the receiver operating characteristic (AUROC) curves to assess the effectiveness of lactate levels and SI. P-value $\leq$ 0.05 is considered statistically significant.

Results

The sample size was 46 children, with 21 being survivors and 25 being nonsurvivors. The median (IQR) heart rate at baseline was 178.5 (125 – 201) beats/min, the 6-hour heart rate was 175.5 (117 – 197) beats/min, the systolic blood

pressure at baseline was 85 (50 – 105) mmHg, and the 6-hour systolic blood pressure was 89.5 (55 – 110) mmHg(**Table 1).**

In the survivor group, Klebsiella pneumonia was detected in 8 patients (38%), Escherichia coli in 5 patients (24%), and Staphylococcus hominis in 3 patients (15%). In the nonsurvivor group, Klebsiella pneumonia was detected in 6 patients (24%), Escherichia coli in 4 patients (16%), Staphylococcus aureus in 4 patients (16%), and Acinetobacter baumannii complex in 4 patients (16%) (**Table 2).**

The median (IQR) SI at baseline of the survivors was 2.06 (1.49 – 3.67), and that of nonsurvivors was 2.14 (1.49 – 3.67). The median (IQR) SI at 6 hours of survivors was

1.86 (1.18 – 3.58), and that of nonsurvivors was 2.03 (1.2 – 3.7). The SI did not vary significantly between survivors and nonsurvivors upon admission or 6 h later. The median (IQR) lactate levels of the survivors were 5.2 (2.7 – 14) mmol/L, and those of nonsurvivors were 5.2 (3.1 – 18) mmol/L. The groups' baseline lactate levels did not differ significantly (**Table 3).**

Area under the curve (AUC) of the SI at baseline was 0.418, 95% CI [0.250, 0.587], p= 0.343), SI after 6 hours was 0.386, 95% CI [0.218, 0.55], p= 0.186), and lactate levels at baseline was 0.453, 95% CI [0.283, 0.624], p= 0.589), suggesting that SI and lactate levels did not predict mortality (**Table 4)** and (**figure 1).**

Table 1: Our patients' clinical data

	Both groups (N= 46)	Survivors (N=21)	Nonsurvivors (N=25)	Test	P value
Age (months) median (IQR)	11 (2 –165)	12 (2 – 165)	8 (2 – 144)	U= 213	0.27
Sex Male Female	26 (57%) 20 (43%)	14 (66.7%) 7 (33.3%)	12 (48%) 13 (52%)	$X^2 = 1.62$	0.20
No malnutrition	18 (39%)	11 (23.91%)	7 (15.22%	$\chi^2= 3.37$	0.2
Severe acute malnutrition	8 (17.5%)	2 (4.35%)	6 (13.04%)		
Moderate acute malnutrition	20 (43.5%)	8 (17.39%)	12 (26.09)		
Baseline heart rate (HR) (beat/min), median (IQR)	178.5 (125 – 201)	176 (130 – 201)	185 (125 – 200)	U= 221.5	0.37
Heart rate (HR) after 6 hours (beat/min), median (IQR)	175.5 (117 – 197)	165 (117 – 197)	180 (120 – 196)	U= 204	0.2
Baseline respiratory rate (breath/min), median (IQR)	47 (28 – 56)	46 (28 – 55)	48 (29 – 56)	U= 214.5	0.29
Baseline Temperature (cᵒ) median (IQR)	38.5 (37 – 39)	39 (37 – 39)	38 (37 – 39)	U= 171	0.06
Baseline systolic blood pressure (mmHg), median (IQR)	85 (50 – 105)	86 (54 – 105)	82 (50 – 100)	U= 226	0.42
Systolic blood pressure after 6	89.5 (55 – 110)	91 (55 – 110)	87 (53 – 105)	U= 202.5	0.19

hours (mmHg), median (IQR)					
Baseline diastolic blood pressure (mmHg), median (IQR)	49 (30 – 77)	48 (32 – 66)	50 (30 – 77)	U= 262	0.99
Diastolic blood pressure after 6 hours (mmHg), median (IQR)	52.5 (34 – 80)	54 (35 – 70)	52 (34 – 80)	U= 249	0.77

U; Mann–Whitney, X^2; Chi-square, IQR; interquartile range

Table 2: Microorganisms detected in the blood culture

Survivors, n=21			Nonsurvivors, n=25		
Blood culture	**N**	**%**	**Blood culture**	**N**	**%**
Klebsiella pneumonia	8	38%	Klebsiella pneumonia	6	24%
Acinetobacter baumannii complex	1	5%	Escherichia coli	4	16%
Escherichia coli	5	24%	Enterococcus faecalis	1	4%
Staphylococcus hemolyticus	2	10%	Staphylococcus hominis	2	8%
Staphylococcus hominis	3	15%	Coagulase negative staphylococcus	3	12%
Enterococcus faecalis	2	10%	Staphylococcus aureus	4	16%
Staphylococcus aureus	2	10%	Acinetobacter baumannii complex	4	16%
Pseudomonas aeruginosa	1	5%	Pseudomonas aeruginosa	1	4%

Table 3: Shock index and baseline lactate level

	Overall (N= 46) median (IQR)	Survivors (N=21)	Nonsurvivors (N=25)	Test	P value
Baseline shock index	2.12 (1.49 -3.67)	2.06 (1.49 -3.67)	2.14 (1.49-3.67)	U= 219.5	0.34
Shock index after 6 hours	1.97 (1.18-3.7)	1.86 (1.18 -3.58)	2.03 (1.2-3.7)	U= 202.5	0.18
Baseline Lactate (mmol/L)	5.2 (2.7-18)	5.2 (2.7-14)	5.2 (3.1-18)	U= 238	0.59

U; Mann–Whitney, IQR; interquartile range

Table (4): The prognostic performance of shock index and lactate levels for predicting nonsurvival in the studied group.

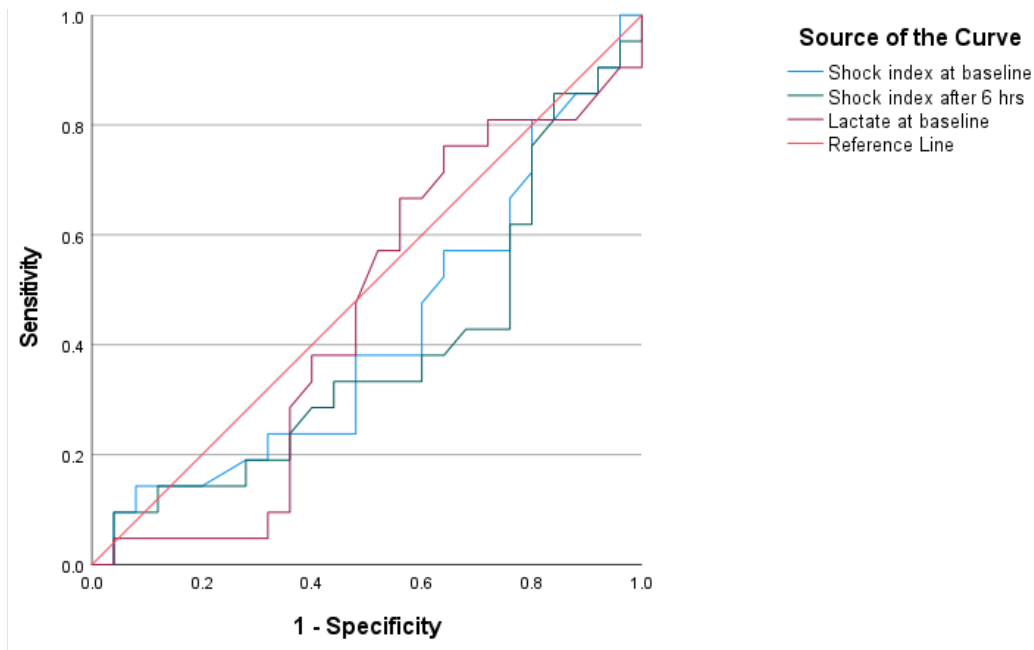| Variables	Area under the curve	95% Confidence Interval		p-value
Shock index at baseline	0.418	0.250	0.587	0.343
Shock index after 6 hrs.	0.386	0.218	0.553	0.186
Lactate at baseline	0.453	0.283	0.624	0.589

Figure (1): Receiver operating characteristic curve of shock index and lactate levels for predicting nonsurvival in the studied group.

Discussion

In the present research, we aimed to explore the SI in the PICU for children with sepsis and examine the relationship between SI (baseline and 6 h later), baseline lactate level, and in-hospital nonsurvival. Additionally, we analyzed how variations in SI during the initial phase of hospital admission were linked to patient outcomes. Studies in adults have identified specific SI cutoff values associated with unfavorable effects and have shown that persistent elevations in the shock index are correlated with poor prognosis [5, 6].

This was a prospective study that included a total of 46 patients. The study included 20 (43%) females and 26 (57%) males. Gender differences between survivors and nonsurvivors were not significant (p > 0.05), as reported by **Nazir et al.,** who found that sex does not appear to significantly predict nonsurvival in septic children [13].

In the present study, blood cultures in the survivors revealed Klebsiella pneumoniae and Escherichia coli (E. coli). However, blood cultures in the nonsurvivors revealed Klebsiella pneumonia and Acinetobacter baumannii complex. These results were in accordance with those of **Wu et al.** and **Saleem et al** [14, 15].

In the current study, the initial median (IQR) lactate levels of survivors were 5.2 (2.7 – 14) mmol/L, and the initial median (IQR) lactate levels of nonsurvivors were 5.2 (3.1 – 18) mmol/L. The groups' baseline lactate levels did not differ significantly. **Loomba et al.** found comparable results in that baseline lactate levels did not predict mortality in children, as manifested by the clinical picture of severe sepsis [16].

The median SI at baseline of survivors was 2.06, and that of nonsurvivors was 2.14. The median SI at 6 h of survivors was 1.86, and that of nonsurvivors was 2.03. There were no statistically significant differences in SI between survivors and nonsurvivors at baseline or 6 hours later.

In febrile children, Hagedoorn and his colleagues showed that elevated SI was associated with severe disease [17]. However, it is useless as a tool for the categorization of all febrile children. **Rappaport et al**. revealed that SI reference values for people aged >8 years depend on blood pressure readings [18]. In research on children with sepsis, Gupta and Alam proposed SI values for mortality [19].

Huang et al. observed that abnormal shock index, pediatric age-adjusted values correctly recognized pediatric patients with an elevated death rate, mechanical ventilation assistance, vasopressor treatment and prolonged hospital stay. Previous findings suggest that the shock index, pediatric age-adjusted, is better than the adult-based SI. Remarkably, higher values of SI did not correlate with any of the assessed outcomes. This disparity may be due to early intervention and care, which may have affected patient outcomes. Patients who present with initially unstable circumstances receive intensive care management; consequently, those with an aberrant shock index, pediatric age-adjusted levels can be protected from negative consequences. Additionally, younger children have an inadequate physiological ability to compensate in response to illness progression [5].

Nordin et al. found that changes in shock index, pediatric age-adjusted levels predicted the requirement for blood transfusions and death in trauma patients. Admission with a normal shock index, pediatric age-adjusted value that increased during the first 48 hours were associated with unfavorable results in pediatric blunt trauma patients. Changes in shock index, pediatric age-adjusted levels within the first 24 hours were linked to an increased mortality risk in children with consistently elevated shock index, pediatric age-adjusted levels at admission or 24 hours later [19].

Among children over one year, those with an SI exceeding 2.3 exhibited a nearly fourfold higher likelihood of mortality than those with an SI below 2.3. Although a specific cutoff value for PICU mortality could not be established, SI can be easily obtained from routine bedside vital signs based on the specific clinical scenario, which has the potential to function as a suitable indicator for identifying pediatric patients necessitating intensified resuscitation efforts and an elevated level of medical attention [20-22].

The disparities in SI between adults and children and its association with outcomes can be attributed to various factors. The broad spectrum of typical physiological indicators based on age contributed to a comprehensive standard range of SI values. Upon categorizing the analysis based on age, the correlation between the shock index and death rates from intensive care was maintained solely for particular ages [20]. The reason for this could be attributed to the limited number of study participants underneath these subcategories, large variations in typical physiological indicators, particularly in pediatric populations younger than one year, limited physiological compensatory abilities in response to shock, particularly in the youngest individuals, and varying initial mortality rates across age cohorts. These elements additionally contribute to the difficulty in establishing a definitive threshold for fatality in each pediatric age range.

Nevertheless, the progressive relationship observed with elevated positive likelihood ratios at higher SI thresholds strengthens the probable effectiveness of the SI as a prognostic indicator in at-risk pediatric patients. For example, children over one year with an SI exceeding 2.3 exhibited a nearly fourfold higher likelihood of mortality than those with an SI below 2.3. Although there is no precise threshold for mortality in pediatric patients, greater shock indices correlate with a higher probability of undesirable consequences. Given that the shock index can be easily obtained from routine bedside vital signs, depending on the clinical condition, it has the potential to function as an appropriate indicator for identifying pediatric patients who require increased resuscitation efforts and a higher level of medical attention [21]. The change in shock index within the 6-hour time window studied may need to be more sensitive or brief to assess disease resolution or the adequacy of resuscitation [22].

A reduction in SI within six hours was associated with better outcomes in pediatric patients who initially presented with a high SI.

This pattern, applicable only to specific age groups owing to the extensive divergence in SI according to age, implies that tracking changes in SI, especially a reduction after the first six hours of hospitalization approaching a preset goal, might serve as an additional way of assessing responsiveness to resuscitation therapy and its association with ICU mortality [23, 24].

Conclusion

We conclude that the shock index and lactate levels do not differ significantly between survivors and nonsurvivors. Therefore, the shock index (baseline and 6 h later) and baseline lactate levels did not predict nonsurvival in children with severe sepsis. This could be attributed to the limited number of study participants, large variations in normal physiological indicators, and limited pediatric physiological compensatory abilities in response to the shock. Further investigation is needed to explore the change in the shock index over an extended period and the relationship between the shock index and organ dysfunction.

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