



## ดัชนีภาวะช็อกทำนายการเสียชีวิตในผู้ป่วยเด็กที่ติดเชื้อในเลือดแบบรุนแรงและที่มีภาวะช็อก

ณัฐชยา ไทยานนท์\*

กลุ่มงานกุมารเวชกรรม โรงพยาบาลขอนแก่น จังหวัดขอนแก่น

## Shock Index Predicts Mortality in Children with Severe Sepsis and Septic Shock

Natchaya Thaiyanon\*

Department of Pediatrics, Khon Kaen Hospital, Khon Kaen Province

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### บทคัดย่อ

**หลักการและวัตถุประสงค์:** ค่าดัชนีภาวะช็อก (shock index) เป็นค่าสัดส่วนของชีพจรใน 1 นาทีต่อค่าความดันโลหิตตัวบนในผู้ป่วยเด็กที่มีภาวะติดเชื้อในเลือดแบบรุนแรงและที่มีภาวะช็อกพบว่า ค่าดัชนีภาวะช็อกอาจบ่งชี้อัตราการเสียชีวิต การศึกษานี้มีวัตถุประสงค์เพื่อศึกษาความสัมพันธ์ของค่าดัชนีภาวะช็อกที่ผิดปกติต่อเนื่องภายหลังให้การวินิจฉัยที่ 6 ชั่วโมงกับอัตราการเสียชีวิต

**วิธีการศึกษา:** เป็นการศึกษาย้อนหลังแบบมีกลุ่มเปรียบเทียบ (retrospective cohort study) ในผู้ป่วยเด็กอายุตั้งแต่ 1 เดือน - 15 ปี ที่เข้ารับการรักษานในหอผู้ป่วยกุมารวิกฤตและมีภาวะติดเชื้อในเลือดรุนแรงและที่มีภาวะช็อก โดยผู้ป่วยทุกรายจะได้รับการคำนวณค่าดัชนีภาวะช็อกตั้งแต่ได้รับการวินิจฉัย จากนั้นผู้ป่วยที่มีค่าดัชนีภาวะช็อกที่ผิดปกติจะถูกคัดออก ผู้ป่วยที่เหลือจะได้รับการคำนวณค่าดัชนีภาวะช็อกภายหลังให้การวินิจฉัยที่ 6 ชั่วโมงแล้วแบ่งออกเป็น 2 กลุ่ม คือ กลุ่มที่ค่าดัชนีภาวะช็อกกลับมาปกติ และกลุ่มที่ค่าดัชนีภาวะช็อกผิดปกติต่อเนื่องภายหลังให้การวินิจฉัยที่ 6 ชั่วโมง จากนั้นเปรียบเทียบอัตราการเสียชีวิตที่ 48 ชั่วโมงและอัตราการเสียชีวิตในโรงพยาบาลระหว่างทั้งสองกลุ่ม โดยค่าดัชนีภาวะช็อกที่ผิดปกติตั้งแต่ได้รับการวินิจฉัยในเด็กอายุน้อยกว่า 1, 1-6 และ 6-15 ปี มีค่ามากกว่าหรือเท่ากับ 1.98, 1.50 และ 1.25 ตามลำดับ ในขณะที่ค่าดัชนีภาวะช็อกภายหลังให้การวินิจฉัยที่ 6 ชั่วโมงที่ผิดปกติ คือ ค่าดัชนีภาวะช็อกที่มากกว่าหรือเท่ากับ 1.66, 1.36 และ 1.30 ตามลำดับ

**ผลการศึกษา:** พบผู้ป่วยผู้ป่วย 60 ราย ที่มีภาวะติดเชื้อในเลือดรุนแรงและที่มีภาวะช็อกพบว่า 44 ราย มีค่าดัชนีภาวะช็อกที่ผิดปกติตั้งแต่ได้รับการวินิจฉัย โดยภายหลังให้การรักษาที่ 6 ชั่วโมง พบว่ามีผู้ป่วย 21 ราย ที่ค่าดัชนีภาวะช็อกกลับมาอยู่ในเกณฑ์ปกติ และมีอัตราการเสียชีวิตในโรงพยาบาลต่ำกว่ากลุ่มที่ค่าดัชนีภาวะช็อกที่ผิดปกติต่อเนื่องภายหลังให้การวินิจฉัยที่ 6 ชั่วโมง (AOR 0.07, 95% CI 0.01-0.36,  $p < 0.001$ ) ในขณะที่อัตราการเสียชีวิตที่ 48 ชั่วโมงไม่แตกต่างกัน นอกจากนี้พบว่า ภาวะภูมิคุ้มกันบกพร่อง (AOR 23.88, 95% CI 1.32-431.31,  $p = 0.032$ ) การติดเชื้อในโรงพยาบาล (AOR 45.21, 95% CI 2.28-898.55,  $p = 0.012$ ) รวมถึงค่าดัชนีภาวะช็อกที่ผิดปกติต่อเนื่องภายหลังให้การวินิจฉัยที่ 6 ชั่วโมง (AOR 86.59, 95% CI 3.01-2491.98,  $p = 0.009$ ) สัมพันธ์กับอัตราการเสียชีวิตในโรงพยาบาล

**สรุป:** ค่าดัชนีภาวะช็อกที่ผิดปกติต่อเนื่องภายหลังให้การวินิจฉัยที่ 6 ชั่วโมง สัมพันธ์กับอัตราการเสียชีวิตในโรงพยาบาล ดังนั้นผู้ป่วยที่มีค่าดัชนีภาวะช็อกที่ผิดปกติต่อเนื่องภายหลังให้การวินิจฉัยที่ 6 ชั่วโมง อาจต้องการการประเมินและฟื้นฟูระบบไหลเวียนเพิ่มเติมเพื่อให้ได้ผลการรักษาตามเป้าหมาย

**คำสำคัญ:** เด็ก, ภาวะติดเชื้อในเลือดแบบรุนแรง, ภาวะช็อก, ค่าดัชนีภาวะช็อก

\*Corresponding author: Natchaya Thaiyanon, E-mail: Natchaya\_d@kkumail.com

## Abstract

**Background and Objective:** The shock index (SI) is a ratio of heart rate (HR) to systolic blood pressure (SBP) per minute. It has been found to be correlated with mortality in pediatric severe sepsis and septic shock. This study aimed to investigate whether the persistent abnormal SI at 6 hours after diagnosis (SI6) was associated with mortality.

**Methods:** This retrospective cohort study involved pediatric patients aged 1 month to 15 years admitted to the Pediatric Intensive Care Unit (PICU) with severe sepsis and septic shock. The SI was assessed at the time of diagnosis (SI0). Patients with normal SI0 were excluded, while those with abnormal SI0 were included and assessed for the SI at 6 hours after diagnosis (SI6). Subsequently, they were classified into the group with resolution of abnormal SI (normal SI6) and the group with persistent abnormal SI (abnormal SI6) at 6 hours, based on age-specific shock index cut-offs. Mortality at 48 hours was the primary outcome, while in-hospital mortality was the secondary outcome. The age-specific shock index cut-offs at the time of diagnosis indicate a SI greater than or equal to 1.98, 1.50, and 1.25 in children aged under 1, 1-6, and 6-15 years, respectively. Similarly, age-specific shock index cut-offs at 6 hours after diagnosis represent a SI greater than or equal to 1.66, 1.36, and 1.30 in children aged under 1, 1-6, and 6-15 years, respectively.

**Results:** All 60 patients with severe sepsis and septic shock were enrolled and assessed for the SI at the time of diagnosis (SI0). Subsequently, 44 patients with abnormal SI0 were assessed for the SI at 6 hours after diagnosis (SI6). There were 21 patients in the group with resolution of abnormal SI (normal SI6) and demonstrated a significantly decreased risk of in-hospital mortality compared to the group with persistent abnormal SI (abnormal SI6) at 6 hours (OR 0.07, 95% CI 0.01-0.36,  $p < 0.001$ ). However, there was no significant difference in mortality at 48 hours between the two groups. Furthermore, factors such as immunocompromise (AOR 23.88, 95% CI 1.32-431.31,  $p = 0.032$ ), nosocomial infection (AOR 45.21, 95% CI 2.28-898.55,  $p = 0.012$ ), and persistent abnormal SI at 6 hours after diagnosis (SI6) (AOR 86.59, 95% CI 3.01-2491.98,  $p = 0.009$ ) were found to be associated with an increased risk of in-hospital mortality.

**Conclusion:** A persistent abnormal SI at 6 hours after diagnosis (SI6) was significantly associated with increased in-hospital mortality, indicating potential inadequate hemodynamic resuscitation and the need for additional stabilization.

**Keywords:** children, severe sepsis, septic shock, shock index.

## Introduction

Severe sepsis and septic shock significantly contribute to the mortality and morbidity of critically ill patients, affecting both pediatric and adult populations. Globally, sepsis affects 22 out of every 100,000 children annually, with a mortality rate ranging from 4% to 50%<sup>1</sup>. A study conducted by the National Children's Health Institute in Thailand found that severe sepsis and septic shock in pediatric patients led to a 20% mortality rate, and 7% of survivors experiencing disabilities<sup>2</sup>.

The assessment of severe sepsis and septic shock requires imperative hemodynamic monitoring. However, obtaining advanced hemodynamic monitoring in pediatric patients is often challenging, and this modality may come with limitations. Therefore, it would be more available, safe, and effective to have bedside hemodynamic monitoring to assess therapeutic measures in real-time.

The shock index (SI) is a ratio of heart rate (HR) to systolic blood pressure (SBP) per minute ( $SI = HR/SBP$ ). It reflects the relationship between HR and SBP, providing insights into the cardiovascular status of an individual. In situations of hemodynamic instability, the heart rate tends to increase. An elevated heart rate may serve as a compensatory mechanism to maintain cardiac output and perfusion to vital organs, especially when blood pressure is compromised. An increase in the shock index suggests that the heart rate is rising relative to blood pressure, indicating increased cardiovascular stress.<sup>3</sup>

Gupta and Alam<sup>4</sup> found that higher shock index values were associated with increased mortality at 48 hours in pediatric severe sepsis and septic shock and established age-specific shock index cut-offs. The age-specific shock index cut-offs at the time of diagnosis indicate a shock index greater than or equal to 1.98, 1.50, and 1.25 in children aged under 1, 1-6, and 6-15 years, respectively. Similarly, age-specific shock index cut-offs at 6 hours after diagnosis represent a shock index greater than or equal to 1.66, 1.36, and 1.30 in children aged under 1, 1-6, and 6-15 years, respectively.

The abnormal shock index, defined as a shock index higher than age-specific shock index cut-offs, was the focus of this study. Our aim was to investigate whether the persistent abnormal shock index at

6 hours after diagnosis (SI<sub>6</sub>) was associated with mortality. Additionally, we examined whether the resolution of the abnormal shock index at 6 hours following hemodynamic resuscitation was associated with favorable outcome.

## Methods

This retrospective cohort study was approved by Khon Kaen Hospital Institute Review Board in Human Research (KEXP66050). Pediatric patients aged 1 month to 15 years, who were admitted to the Pediatric Intensive Care Unit (PICU) at Khon Kaen Hospital with severe sepsis and septic shock between July 2021 and October 2023, were identified from the electronic medical record.

Inclusion criteria involved pediatric patients who were diagnosed with severe sepsis and septic shock following international pediatric sepsis consensus conference (IPSCC)<sup>5</sup>. Exclusion criteria consisted of patients with incomplete medical records, patients who were discharged against medical advice within 48 hours of initial diagnosis.

Clinical data were collected retrospectively through electronic medical records. The information included general patient data, diagnostic details, treatment history, vital signs, as well as outcomes recorded on case record forms (Appendix a). The treatment history included fluid therapy, vasoactive medication which was calculated into vasoactive-inotropic score as described by Gaies et al<sup>6</sup>, hydrocortisone, mechanical ventilation, and vascular access.

The shock index was obtained from the heart rate and systolic blood pressure recorded hourly on the graphic sheet by experienced PICU nurses. It was calculated at the time of diagnosis (SI<sub>0</sub>). Patients with normal shock index were excluded, while those with abnormal shock index were included and assessed for the shock index at 6 hours after diagnosis (SI<sub>6</sub>). Subsequently, patients with abnormal shock index at the time of diagnosis (abnormal SI<sub>0</sub>) were classified into the group with resolution of abnormal shock index (normal SI<sub>6</sub>) and the group with persistent abnormal shock index (abnormal SI<sub>6</sub>) at 6 hours, based on age-specific shock index cut-offs<sup>4</sup>. Mortality at 48 hours was the primary outcome, while in-hospital mortality was the secondary outcome.

## Definition

- Severe sepsis defined as sepsis plus one of the following: cardiovascular organ dysfunction or acute respiratory distress syndrome or two or more other organ dysfunctions<sup>5</sup>

- Septic shock defined as sepsis and cardiovascular organ dysfunction<sup>5</sup>

- Vasoactive-inotropic score was calculated by dopamine dose (mcg/kg/min) + dobutamine dose (mcg/kg/min) + 100 x epinephrine dose (mcg/kg/min) + 100 x norepinephrine dose (mcg/kg/min) + 10,000 x vasopressin dose (U/kg/min) + 10 x milrinone dose (mcg/kg/min)<sup>6</sup>

## Sample Size

To investigate the association between shock index and mortality at 48 hours after diagnosis, the sample size for this study was determined using hypothesis testing (two independent proportions) with reference to previous research by Gupta and Alam<sup>4</sup>. According to their findings, patients with persistent abnormal shock index both at the time of diagnosis and 6 hours after diagnosis (abnormal SI0 and abnormal SI6) exhibited a mortality rate of 78.4%. In contrast, the group with resolution of abnormal shock index after 6 hours (abnormal SI0 and normal SI6) had a lower mortality rate of 27.3%. The calculated sample size (n) required for this study is at least 42, aiming for 80% power and an alpha error of 0.01.

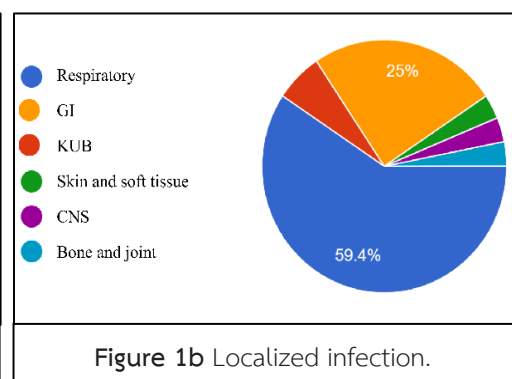
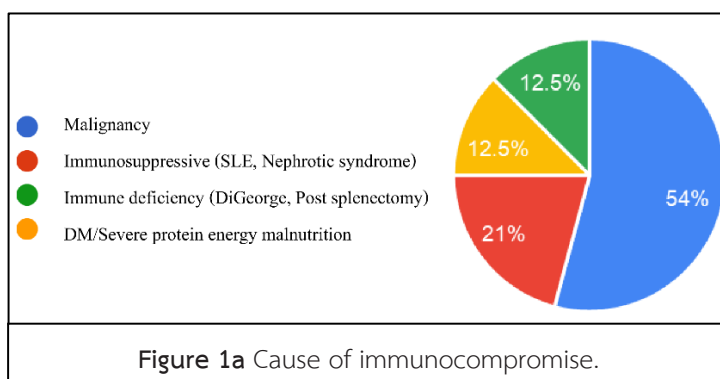
## Statistical Analysis

The data analysis and statistics for the research utilized both descriptive and comparative approaches. Descriptively, the methods included percentage and

measures such as mean with standard deviation (for normally distributed data) or median with interquartile range (for non-normally distributed data). For comparative analysis, a combination of parametric statistics, including t-tests, and non-parametric statistics, such as Mann-Whitney U tests for comparing continuous variables between independent groups, Chi-square tests for assessing association between categorical variables, and Fisher's Exact test for small sample sizes or violated assumptions, were applied. Statistical significance with  $p < 0.05$  was considered. The association between variables was assessed through multiple logistic regression analysis. The entire analysis was conducted using IBM SPSS Premium V.28 for Windows.

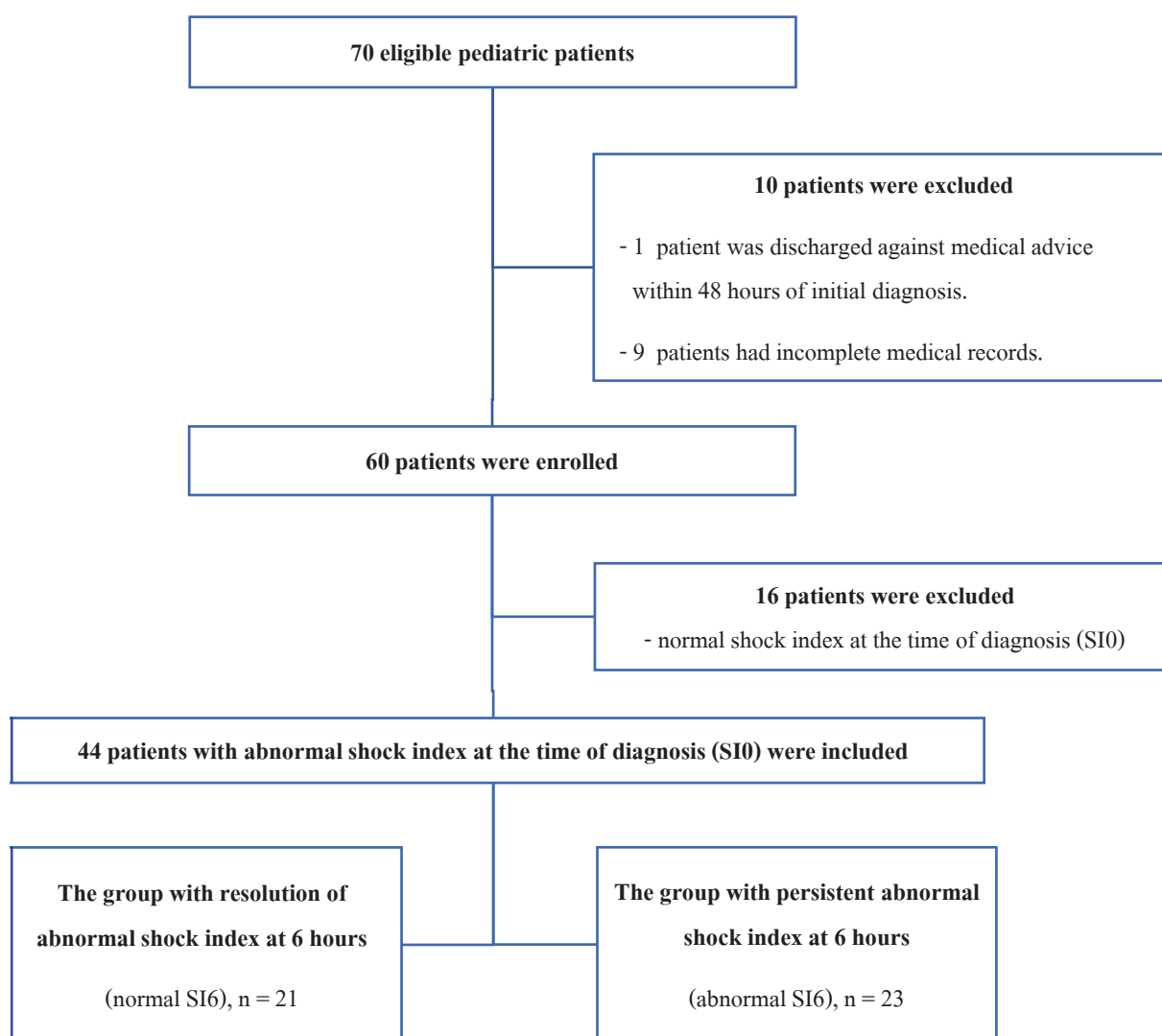
## Results

A total of 70 patients with severe sepsis and septic shock were eligible by the inclusion criteria. Ten patients were excluded due to incomplete medical records or discharge against medical advice within 48 hours of initial diagnosis. Sixty patients were then enrolled in the study, all of whom were diagnosed with severe sepsis, with 93.3% manifesting septic shock. Malignancy was found to be the major cause of immunocompromise (Figure 1a). The most common localized infection occurred in the respiratory system (59.4%), followed by the gastrointestinal system (25%) (Figure 1b). The mortality at 48 hours was 8.3%, and in-hospital mortality was 30%. The median time before death is 108 hours (30.5-384.5).



All 60 patients were assessed for the shock index at the time of diagnosis. Sixteen patients with normal shock index were excluded; subsequently, the remaining 44 patients with abnormal shock index were assessed for the shock index at 6 hours after diagnosis. Of these, 21 patients were in the group with resolution of abnormal shock index (normal SI6) and 23 patients were in the group with persistent abnormal shock index (abnormal SI6) at 6 hours (Figure 2).

The baseline characteristics of the patients with abnormal shock index at the time of diagnosis were shown in Table 1. The median age was 10.8 years old (3.3-12.8). There was no significant difference between the group with resolution of abnormal shock index and the group with persistent abnormal shock index, except the vasoactive-inotropic score and central venous access, which were found to be higher in the group with persistent abnormal shock index.



**Figure 2** Flow diagram illustrates the enrollment process of children in the study.

**Table 1** Baseline characteristics of the patients with abnormal shock index at the time of diagnosis (SI0)

Characteristics	Total patients (n=44)	The group with resolution of abnormal shock index (normal SI6) (n=21)	The group with persistent abnormal shock index (abnormal SI6) (n=23)	p-value
Age in years, median (interquartile range)	10.8 (3.3-12.8)	11.3 (7.1-13.1)	9.4 (3.1-12.6)	0.397 <sup>a</sup>
Sex (male), n (%)	24 (54.5)	12 (57.1)	12 (52.2)	0.741 <sup>b</sup>
Body weight in kilograms, median (interquartile range)	29.5 (12.3-40.8)	37.0 (21.5-43.5)	20.0 (11.0-40.0)	0.128 <sup>a</sup>
Immunocompromise, n (%)	24 (43.2)	7 (33.3)	12 (52.2)	0.208 <sup>b</sup>
Underlying disease, n (%)	40 (72.7)	14 (66.7)	18 (78.3)	0.388 <sup>b</sup>
<b>Nature of infections</b>				
- Community acquired infection, n (%)	22 (50.0)	13 (61.9)	9 (39.1)	0.131 <sup>b</sup>
- Nosocomial infection, n (%)	22 (50.0)	8 (38.1)	14 (60.9)	
<b>Source of infection</b>				
- Systemic infection, n (%)	18 (40.9)	8 (38.1)	10 (43.5)	0.717 <sup>b</sup>
- Localized infection, n (%)	26 (59.1)	13 (61.9)	13 (56.5)	
<b>Diagnosis of severe sepsis</b>				
- Cardiovascular dysfunction (Septic shock), n (%)	43 (97.7)	20 (95.2)	23 (100.0)	0.477 <sup>c</sup>
- Acute respiratory distress syndrome (ARDS), n (%)	6 (13.6)	3 (14.3)	3 (13.0)	1.000 <sup>c</sup>
- Dysfunction in 2 or more other organ systems, n (%)	27 (61.4)	12 (57.1)	15 (65.2)	0.583 <sup>b</sup>
<b>Treatment</b>				
Fluid resuscitation volume in 1 hours, mL/kg, median (interquartile range)	33.4 (20.0-43.2)	37 (20.0-42.7)	30 (10.0-44.4)	0.925 <sup>a</sup>
Fluid resuscitation volume in 6 hours, mL/kg, mean (standard deviation)	43.1 (23.4)	41 (20.0)	45 (26.3)	0.588 <sup>a</sup>
Vasoactive medication use, n (%)	42 (95.5)	19 (90.5)	23 (100.0)	0.222 <sup>c</sup>
vasoactive-inotropic score, median (interquartile range)	28.0 (10.0-131.3)	20.0 (9.5-50.0)	68.0 (20.0-302.5)	<u>0.010</u> <sup>a</sup>
Hydrocortisone use, n (%)	24 (54.5)	11 (52.4)	13 (56.5)	0.783 <sup>b</sup>
Mechanical ventilation use, n (%)	28 (63.6)	11 (52.4)	17 (73.9)	0.138 <sup>b</sup>
Central venous access, n (%)	32 (72.7)	12 (57.1)	20 (87.0)	<u>0.027</u> <sup>b</sup>
Arterial-line access, n (%)	27 (61.4)	13 (61.9)	14 (60.9)	0.944 <sup>b</sup>

a = Mann-Whitney Test, b = Pearson Chi-Square, c = Fisher's Exact Test, \_\_\_\_ = statistically significant

The mortality at 48 hours between the group with resolution of abnormal shock index and the group with persistent abnormal shock index was not significantly different, however there was a significant difference for in-hospital mortality (Table 2).

The factors associated with in-hospital mortality are shown in Table 3. Among children with severe sepsis and septic shock, significant associations with in-hospital mortality were observed for

immunocompromise, underlying disease, nosocomial infection, mechanical ventilation use, central venous access, and persistent abnormal shock index at 6 hours after diagnosis. The results of multiple logistic regression analysis found that immunocompromise, nosocomial infection, and persistent abnormal shock index at 6 hours after diagnosis were significantly associated with in-hospital mortality (Table 4).

**Table 2** The mortality between the group with resolution of abnormal shock index (normal SI6) and the group with persistent abnormal shock index (abnormal SI6).

Outcomes	The group with resolution of abnormal shock index (normal SI6) (n=21)	The group with persistent abnormal shock index (abnormal SI6) (n=23)	Crude OR (95% CI)	p-value
The mortality at 48 hours, n (%) (Primary outcome)	1 (4.8)	3 (13.0)	0.33 (0.03-3.48)	0.609
In-hospital mortality, n (%) (Secondary outcome)	2 (9.5)	14 (60.9)	0.07 (0.01-0.36)	<0.001

**Table 3** The factors associated with in-hospital mortality.

Variables		Non-survivor, n (%)	Crude OR (95%CI)	p-value
Characteristics, n (%)				
Immune status	Immunocompromise, n=19	12 (63.2)	9.00	0.001 <sup>b</sup>
	Immunocompetent, n= 25	4 (16.0)	(2.18-37.18)	
Underlying disease	Yes, n=32	15 (46.9)	9.71	0.032 <sup>c</sup>
	No, n =12	1 (8.3)	(1.12-84.30)	
Nature of infections	Nosocomial infection, n=22	14 (63.6)	17.50	≤0.001 <sup>b</sup>
	Community acquired, n=22	2 (9.1)	(3.22-95.16)	
Source of infection	Localized infection, n=26	8 (30.8)	0.56	0.354 <sup>b</sup>
	Systemic infection, n=18	8 (44.4)	(0.16-1.94)	
Diagnosis of severe sepsis				
Cardiovascular dysfunction (Septic shock)	Yes, n=43	16 (37.2)	N/A	
	No, n=1	0 (0.0)		
Acute respiratory distress syndrome (ARDS)	Yes, n=6	3 (50.0)	1.92	0.652 <sup>c</sup>
	No, n=38	13 (34.2)	(0.34-10.90)	
Dysfunction in 2 or more other organ systems	Yes, n=27	9 (33.3)	0.71	0.598 <sup>b</sup>
	No, n=17	7 (41.2)	(0.20-2.50)	
Treatment				
Fluid resuscitation volume ≥ 30 ml/kg	Yes, n=28	10 (35.7)	0.93	0.906 <sup>b</sup>
	No, n=16	6 (37.5)	(0.26-3.31)	
Vasoactive medication use	Yes, n=42	16 (38.1)	N/A	
	No, n=2	0 (0.0)		
Hydrocortisone use	Yes, n=24	11 (45.8)	2.54	0.153 <sup>b</sup>
	No, n=20	5 (25.0)	(0.70-9.24)	
Mechanical ventilation use	Yes, n=28	14 (50)	7.00	0.013 <sup>b</sup>
	No, n=16	2 (12.5)	(1.34-36.69)	



**Table 3** The factors associated with in-hospital mortality. (cont.)

Variables		Non-survivor, n (%)	Crude OR (95%CI)	p-value
Central venous access	Yes, n=32	15 (46.9)	9.71	0.032 <sup>c</sup>
	No, n=12	1 (8.3)	(1.12-84.30)	
Arterial-line access	Yes, n=27	9 (33.3)	0.71	0.598 <sup>b</sup>
	No, n=17	7 (41.2)	(0.20-2.50)	
SI at 6 hours after diagnosis (SI6)	Persistent abnormal SI, n=23	14 (60.9)	14.78	<0.001 <sup>b</sup>
	Resolution of abnormal SI, n=21	2 (9.5)	(2.75-79.33)	

b = Pearson Chi-Square, c = Fisher's Exact Test, \_\_\_\_ = statistically significant, N/A = not applicable

**Table 4** Multiple logistic regression analysis of the factors associated with in-hospital mortality.

Variables		Non-survivor, n (%)	Adjust OR (95%CI)	p-value
<b>Characteristics, n (%)</b>				
Immune status	Immunocompromise, n=19	12 (63.2)	23.88	0.032
	Immunocompetent, n= 25	4 (16.0)	(1.32-431.31)	
Nature of infections	Nosocomial infection, n=22	14 (63.6)	45.21	0.012
	Community acquired, n=22	2 (9.1)	(2.28-898.55)	
SI at 6 hours after diagnosis (SI6)	Persistent abnormal SI, n=23	14 (60.9)	86.59	0.009
	Resolution of abnormal SI, n=21	2 (9.5)	(3.01-2491.98)	

## Discussion

In this study, we found that the persistent abnormal shock index at 6 hours after diagnosis was not significantly associated with mortality at 48 hours. However, there was a significant difference in in-hospital mortality. Our results indicated that the persistent abnormal shock index at 6 hours after diagnosis was significantly associated with increased risk of in-hospital mortality, consistent with previous findings by Lopez-Reyes et al<sup>7</sup>, which highlighted the utility of a high shock index at 6 hours post-resuscitation as a predictor of mortality. Corroborating the study by Gupta and Alam<sup>4</sup>, resolution of the abnormal shock index after hemodynamic resuscitation within 6 hours was associated with better outcomes. Conversely, a persistently high shock index over 6 hours was associated with a higher risk of early mortality, defined as mortality within 48 hours of admission. Despite these findings, our study did not identify a significant difference in mortality at 48 hours between the group with resolution of abnormal shock

index and the group with persistent abnormal shock index. The median time before death in our setting was 108 hours (30.5-384.5), suggesting that mortality at 48 hours might not be a reliable early mortality indicator in our specific context.

The concept of initiating early goal-directed therapy (EGDT) within the first 6 hours in sepsis was largely influenced by the landmark study known as the "Rivers protocol." This study suggested that a bundle of interventions, including central venous pressure (CVP) monitoring and specific targets for resuscitation, could significantly reduce mortality in patients with severe sepsis and septic shock. The goal was to promptly initiate resuscitation measures and achieve specific hemodynamic targets within this timeframe. However, some hemodynamic targets, such as central venous pressure (CVP), central venous oxygen saturation (ScvO<sub>2</sub>), or lactate clearance, may have limitations in children<sup>8</sup>.



The shock index serves as a critical indicator of hemodynamic instability, often resulting in compromised tissue perfusion and oxygen delivery. By considering both heart rate and blood pressure, the shock index offers insight into the balance between cardiac output and perfusion pressure, which is crucial for maintaining tissue viability<sup>9</sup>. Yasaka et al<sup>10</sup> suggested that an elevated shock index correlates with increased mortality in patients with septic shock, thus rendering it a valuable prognostic tool for identifying individuals at heightened risk of adverse outcomes.

Gupta and Alam<sup>11</sup> found that high age-adjusted shock-index was associated with vasopressor use, mechanical ventilation, elevated arterial lactate levels, and early mortality (within 48 hours). Similarly, our study revealed a higher vasoactive-inotropic score in the group with persistent abnormal shock index, suggesting a potential need for more frequent central venous access, in line with recommendations advocating for central venous access in cases of high-dose inotrope use and prolonged infusions<sup>12</sup>.

Furthermore, results from multiple logistic regression analysis revealed that immunocompromise (predominantly malignancy), nosocomial infection and persistent abnormal shock index at 6 hours after diagnosis were associated with an increased risk of in-hospital mortality. These findings were corroborated by a systematic review, which identified several clinical variables associated with increased mortality in children with severe sepsis and septic shock, including chronic conditions, oncologic diagnosis, use of vasoactive medication, elevated vasoactive-inotropic score, mechanical ventilation, hypotension, increased shock index, and decreased level of consciousness<sup>13</sup>.

### Limitation

First, it is important to note that this study is a single-center retrospective observational study. Although the statistical significance is present, the wide 95% confidence interval suggests that a larger sample size may be necessary for more precise conclusions.

Second, the objective was to explore the association between abnormal shock index and elevated blood lactate for guiding hemodynamic

resuscitation. However, the inability to assess blood lactate in all patients resulted in insufficient data. A prospective study conducted across multiple centers may be essential to validate the use of shock index as a bedside hemodynamic monitoring tool, akin to blood lactate.

### Conclusion

After hemodynamic resuscitation, the resolution of abnormal shock index within 6 hours was associated with a significantly decreased risk of in-hospital mortality. Conversely, a persistent abnormal shock index at 6 hours after diagnosis (SI6) was significantly associated with increased in-hospital mortality, indicating potential inadequate hemodynamic resuscitation and the need for additional stabilization.

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