ORIGINAL ARTICLE

Relationship between Lactate Levels and Shock Index in Pediatric Patients with Sepsis at a Tertiary Care Hospital in Karachi, Pakistan

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ABSTRACT

Objective: To determine the relationship between lactate levels and shock index (SI) in pediatric patients with sepsis at tertiary care Hospital in Karachi, Pakistan

Study Design: Cross-sectional Study

Place and Duration of Study: Department of Pediatrics, Civil Hospital, Dow University of Health Sciences, Karachi. 6 months after the approval from the Institutional Review Board

Material and Methods: This study was conducted at Civil Hospital Karachi on children aged 1 to 60 months with septic shock. Heart rate, Systolic blood pressure, and lactate levels were recorded at 0, 2, 4, and 6 hours after admission to calculate SI. The outcome (death or survival) was documented, and Pearson correlation (r) between SI and lactate was calculated. Sensitivity and specificity of both markers in predicting mortality were evaluated using the area under the curve (AUC).

Results: The study included 153 children with septic shock, showing a 63.4% mortality rate. Survival rates varied significantly by age, particularly between 1-2 years and 2-4 years ($p=0.049$). A strong correlation between serum lactate levels and SI was observed ($r=0.910$ to 0.942, $p<0.001$), with both markers demonstrating high sensitivity and specificity for predicting mortality. SI showed strong diagnostic performance across all age groups, making it a reliable prognostic tool for pediatric septic shock.

Conclusions: In pediatric septic shock, SI was a significant, simple predictor of mortality, offering better hemodynamic assessment than heart rate or blood pressure alone for early sepsis detection.

Key Words: *Sepsis, Severe sepsis, Septic shock, Shock index, Lactate level*

INTRODUCTION:

Pediatric sepsis, characterized by a cluster of abnormalities disrupting the normal physiological and biochemical homeostasis of the human body due to infection, remains a significant global health issue. This condition is typically associated with a dysfunction involving multiple organs due to

an uncontrolled systemic response by the immune response to infection, leading to critical illness and high mortality rates worldwide.[1,2] Severe sepsis and septic shock (Sepsis-3) are particularly prevalent in the children , exhibiting high mortality and morbidity rates.[3] Severe sepsis, which involves organ dysfunction, can escalate to septic shock and persistent hypotension despite sufficient fluid replacement.[4] Among children, severe sepsis-3 are common and are linked to high death and morbidity rates.[5,6] While rapid and aggressive treatment of severe sepsis leads to better outcomes,[7] only a small percentage of children receive prompt and effective care.[8] Global studies report a the frequency of pediatric severe sepsis at a specific point in time at 8.2%, with regional variations such as a 15.3% prevalence in Asia. Alarmingly, an estimated 25% of children with severe sepsis die in hospitals worldwide.[9]

Infections caused by viruses, bacteria, parasites, fungi, or toxins are the usually responsible for triggers of sepsis in children and young adults. Successful management of sepsis-3 within the l initial hours following admission to the pediatric ICU is crucial for improving outcomes.[10]

Traumatic injuries continue to be the primary cause of mortality among individuals aged1 to 44 years, The National Center for Health Statistics reports that shock is responsible for 46% of all deaths in children aged 5 to 14 years and 73% of mortality in young adults aged 15 to 24 years. Trauma patients are currently categorized and prioritized in emergency departments using definite triage criteria, including blood pressure, respiratory status, Glasgow Coma Score, and the mechanism of injury.[11] Sepsis-3 definitions are derived from the American College of Chest Physicians/Society of Critical Care Medicine consensus conference criteria.[12,13]

Suspected or confirmed infected patients, along with meeting at least two systemic inflammatory response syndrome (SIRS) criteria, are classified as sepsis. SIRS is identified by specific clinical signs, including a body temperature >38°C or <36°C, a heart rate (HR) 90 beats per minute, a respiratory rate > 20 breaths per minute or a P_aCO_2 level below 32 mm Hg, and a white blood cell count exceeding 12,000/mm³.[12]

In sepsis patients, septic shock is identified when the systolic blood pressure (SBP) drops from the usual level, even after receiving enough fluids. Treatment for pediatric sepsis is typically based on the severity of blood loss and variations in hemodynamic factors, including HR, SBP, and central venous pressure (CVP). While resuscitation can lead to noticeable improvements in HR and SBP, some patients may continue to experience hidden inadequate blood flow (occult hypoperfusion).[11,14]

In the general population, the SI, computed as the ratio of pulse rate to SBP, is considered a more sensitive early indicator of hemodynamic instability compared to traditional vital signs.[15] (15) While normal adult SI ranges from 0.5 to 0.7.[16] there is limited research evaluating SI within pediatric populations, particularly in LMIC.

In Pakistan, there is a significant lack of understanding about how the SI can predict the progression of pediatric septic shock. Addressing this gap, the current study seeks to determine the relationship between lactate levels and SI in a pediatric population. This research aims to provide insights that could enhance the early identification and management of septic shock in children.

MATERIAL AND METHODS

This was a cross sectional study, conducted at Civil Hospital Karachi. After approval from Ethical Review Board with IRB number IRB-2816/DUHS/Approval/2022-20232. The data was collected after taking parental consent of pediatric patients aged 5 years and below, visiting the Pediatric emergency department of The Civil Hospital, meeting the eligibility criteria were enrolled in the research. The information regarding the patient's age, weight, gender, blood pressure (BP), pulse rate (PR), lactate levels and outcome were recorded. SI were documented for every 2-hour interval from "0" to 6 hours. Anonymity and confidentiality of the patients was protected by assigning the codes to the data sets, instead of name by keeping the data password protected.

Statistical analysis: Data was analyzed by using SPSS version 26. Continuous variables were presented as median (IQR) values were given for non normally distributed variables. Normality was

assessed through the Shapirowilk test. Mann-Whitney U-test was applied to see the difference of quantitative variable used for comparison of two groups. Categorical variables were reported by frequencies and percentages. Association between two categorical variables were assessed by Pearson Chi-square test . Evaluation and comparison of diagnostic markers were evaluated by Receiver operating characteristics (ROC). The correlation test was applied between SI and lactate level. The significance level was taken as $\alpha = 0.05$.

RESULTS

A total of 153 admitted children were enrolled in the study. The distribution of male and female were almost same. Results showed majority (32%) of the patients were having age 12-24 years followed by less than 12 month and 24 to 60 months, (table 1). Mortality rate in our study was 97(63.4%), fig 1. The results showed a statistically significant difference in age group distribution. A higher proportion of survivors(improved) were observed among children aged 1 to 2 years, whereas a greater number of deceased patients were found in the 2 to 4 years age group, p value was showed statistically significant (p=0.049, table-1). It was observed that 51 (33.3%) patients had diagnosis of gastro-enteritis followed by myocarditis 38 (24.8%), bronchiolitis 31 (20.3%) and meningitis 21 (13.7%), it was observed that majority of the patients who deceased had higher proportion of myocarditis. p value was observed statistically significant (p<0.0001 table-1. There was no significant association of gender with survival status was seen (p=0.520, table-1).

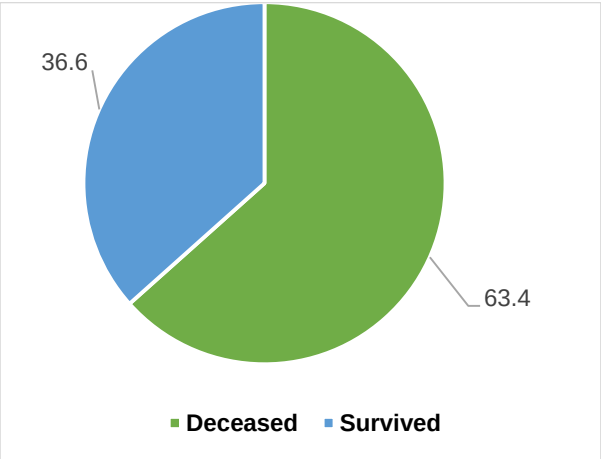

Fig 1: Final outcome of patients

Table 1: Characteristics of children presenting with sepsis at a tertiary care hospital (N=153)

	Deceased	Survived	Total	p value
Age groups				
< 12-months	30(30.9)	18 (32.1)	48 (31.4)	
12 - < 24 months	25(25.8)	25 (44.6)	50 (32.7)	
24 - < 48 months	29(29.9)	09 (16.1)	38 (24.8)	0.049*
48 – 60 months	13(13.4)	04 (7.1)	17 (11.1)	
Total	97(100)	56 (100)	153 (100)	
Gender				
Male	45(46.4)	29 (51.8)	74 (48.4)	
Female	52(53.6)	27 (48.2)	79 (51.6)	0.520□
Total	97(100)	56 (100)	153 (100)	
Provisional diagnosis				
Bronchiolitis	11(11.3)	20 (35.7)	31 (20.3)	
Gastroenteritis	36(37.1)	15 (26.8)	51 (33.3)	
Meningitis	12(12.4)	09 (16.1)	21 (13.7)	0.000**
Myocarditis	37(38.1)	01 (1.8)	38 (24.8)	
Others*	1(1)	11 (19.6)	12 (7.8)	
Total	97(100)	56 (100)	153 (100)	
Sepsis Severity				
Multiorgan dysfunction	55(56.7)	05 (8.9)	60 (39.2)	
Sepsis	-	45 (80.4)	45 (29.4)	0.000**ǂ
Septic Shock	42(43.3)	06 (10.7)	48 (31.4)	
Total	97(100)	56 (100)	153 (100)	

** p<0.0001, * <0.05, ǂ Fischer exact test, □ Chi square test

With regards of severity, 60(39.2%) showed multiorgan dysfunction, 48(31.4%) showed septic shock and 45(29.4%) showed sepsis, it was observed that higher proportion of multiorgan dysfunction and septic shock was observed in those patients who expired. Median weight of the patients was 10 kg with interquartile range,[7-12] with minimum weight 3 kg and maximum 16 kg table 2. Furthermore we observed, median duration of pediatric intensive care unit (PICU) stay was 4 days with min and max days (1-12 days) and overall median duration of hospital stay was 6 days with interquartile range 3.5- 9 years with minimum one day and maximum 15 days, table-2.

TABLE 2: Characteristics of children presenting with sepsis at a tertiary care hospital (N=153)

		Deceased n=97	Survived n=56	Total 153	p value
Weight (kg)	Median (IQR)	10 (7-12)	8 (7-11)	10 (7-12)	0.094ǂ
	Min-Max	3-16	3-16	3-16	
Duration of PICU stay	Median (IQR)	4(2-6)	3 (2-6)	4 (2-6)	0.673ǂ
	Min-Max	1-12	1-10	1-12	
Duration of hospital stay	Median (IQR)	4 (2.5-6)	9 (8-12)	6 (3.5-9)	0.000**ǂ
	Min-Max	1-15	4-14	1-15	
	Ho				
	Median (IQR)	2.4(2.2-2.7)	1.6(1.5-1.8)	2.2(1.7-2.5)	0.000**ǂ
	Min-Max	2-3	1.2-2.9	1.2-3.0	
	H2				
SI (HR/SBP)	Median (IQR)	2.4(2.3-2.7)	1.5(1.5-1.6)	2.3(1.6-2.5)	0.000**ǂ
	Min-Max	2.1-3.1	1.2-2.9	1.2-3.1	
	H4				
	Median (IQR)	2.5(2.4-2.7)	1.5(1.4-1.6)	2.4(1.6-2.6)	
	Min-Max	2.2-3.1	1.2-2.9	1-3	0.000**ǂ
	H6				
	Median (IQR)	2.5(2.4-2.7)	1.5(1.4-1.6)	2.4(1.5-2.6)	0.000**ǂ
	Min-Max	2.2-3.1	1.2-3	1.2-3.1	
	Ho				
	Median (IQR)	7.1(6.1-8.2)	3.5(2.9-4)	6.1(3.8-7.6)	0.000**ǂ
	Min-Max	5.2-10.7	2.2-8.4	2.2-10.7	
	H2				
Lactate (mmol/L)	Median (IQR)	7.2(6.2-8.4)	3.2(2.7-3.8)	6.2(3.7-7.6)	0.000**ǂ
	Min-Max	2.3-10.8	2.1-8.6	3.1-10.8	
	H4				
	Median (IQR)	7.3(6.5-8.4)	3.1(2.6-3.8)	6.5(3.5-7.8)	0.000**ǂ
	Min-Max	2.1-10.6	2-8.8	2.0-10.6	
	H6				
	Median (IQR)	6.4(11-7.3)	2.6(8.7-3)	6.4(3.5-7.9)	0.000**ǂ
	Min-Max	2.2-11.0	1.8-8.7	1.8-11.0	

** p value <0.0001, * p value <0.05, ǂ MannWhitney U test

The consistently high Pearson Correlation coefficients (ranging from 0.910 to 0.942) indicated a strong positive correlation between serum lactate levels and shock indexes at all observed time intervals (0,2, 4 and 6 hours). The p-values being less than 0.001 suggested that these correlations were statistically significant, table 3 and fig 2.

TABLE 3: Correlation of serum lactate levels and shock indexes at 0, 2, 4 and 6-hours in children presenting with sepsis at a tertiary care hospital (N=153)

Time interval	Pearson correlation (r)	p-value
0-hours	0.942	< 0.001
2-hours	0.942	< 0.001
4-hours	0.910	< 0.001
6-hours	0.939	< 0.001

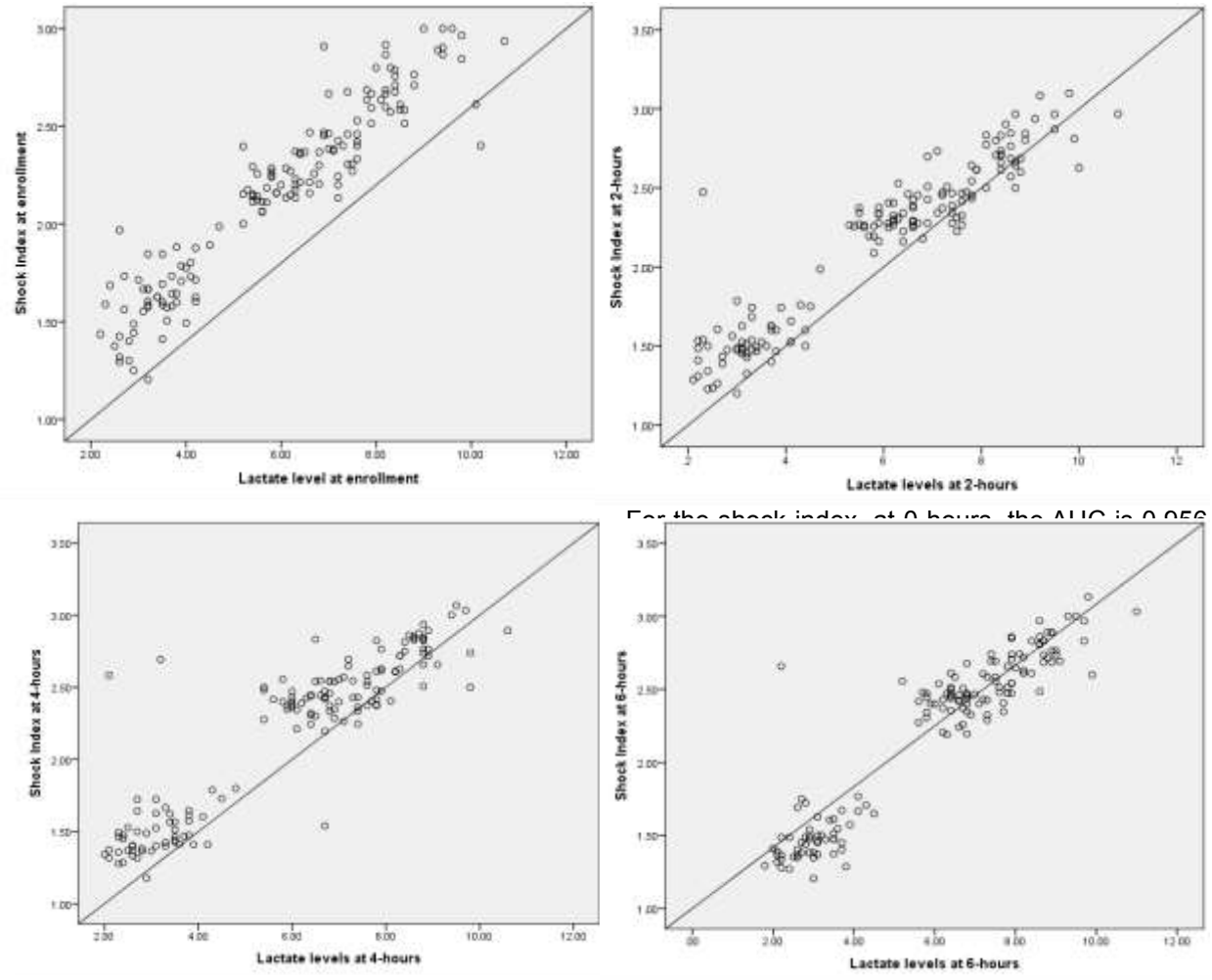

TABLE 4: ROC analysis for serum lactate levels at 0, 2, 4 and 6 hours in predicting mortality among children presenting with sepsis at a tertiary care hospital (N=153)

Time Interval	Area under Curve	95 % CI AUC	p-value	Cutoff	Sensitivity (%)	Specificity (%)
Serum Lactate Levels						
0-hour	0.955	0.91 – 1.0	< 0.001	4.95	100	92.9
2-hour	0.944	0.89 – 0.99	< 0.001	5.00	99	92.9
4-hour	0.932	0.88 – 0.98	< 0.001	5.10	97.9	91.1
6-hour	0.945	0.90 – 0.99	< 0.001	4.85	99	92.9
Shock Index						
0-hour	0.956	0.91 – 1.0	< 0.001	1.99	100	92.9
2-hour	0.961	0.92 – 1.0	< 0.001	2.04	100	92.9
4-hour	0.959	0.91 – 1.0	< 0.001	2.00	100	92.9
6-hour	0.962	0.92 – 1.0	< 0.001	1.98	100	92.9

The table-5 presents the diagnostic performance of the Shock Index across different age groups and time intervals. For children aged 1 to less than 12 months, the AUC ranges from 0.908 to 0.917, with high sensitivity (100%) but moderate specificity (89%) at various cutoff points between

2.01 and 2.08. For the 1 to less than 2 years age group, the AUC is higher, ranging from 0.976 to 0.986, with both sensitivity and specificity being 100% and 92%, respectively, at cutoff points between 1.92 and 2.02. In children aged 2 to less than 4 years, the AUC is perfect at 1.000 across all time intervals, with sensitivity at 100% and specificity at 88.9% at cutoff points between 2.03 and 2.08. Lastly, for children aged 4 to 6 years, the AUC is also perfect at 1.000, with both sensitivity and specificity being 100% at cutoff points between 1.78 and 1.83. These results indicate that the Shock Index is a highly sensitive marker across all age groups, with specificity varying slightly by age group and time interval.

TABLE 5: ROC analysis for serum lactate levels at 0, 2, 4 and 6 hours in predicting mortality among children with different age group (N=153)

Age groups	Time Interval	Area under Curve	95 % CI AUC	p-value	Cutoff	Sensitivity (%)	Specificity (%)
			Shock Index				
1 to <12 months	0-hour	0.915	0.80 – 1.0	< 0.001	2.01	100	89
	2-hour	0.917	0.81 – 1.0	< 0.001	2.08	100	89
	4-hour	0.913	0.80 – 1.0	< 0.001	2.03	100	89
	6-hour	0.908	0.80 – 1.0	< 0.001	2.04	100	89
1 to < 2 years	0-hour	0.976	0.94 – 1.0	< 0.001	2.02	100	92
	2-hour	0.986	0.96 – 1.0	< 0.001	1.92	100	92
	4-hour	0.981	0.95 – 1.0	< 0.001	1.99	100	92
	6-hour	0.985	0.96 – 1.0	< 0.001	1.98	100	92
2 to <4 years	0-hour	1.000	1.0 – 1.0	< 0.001	2.06	100	88.9
	2-hour	1.000	1.0 – 1.0	< 0.001	2.08	100	88.9
	4-hour	1.000	1.0 – 1.0	< 0.001	2.03	100	88.9
	6-hour	1.000	1.0 – 1.0	< 0.001	2.04	100	88.9
4 to 6 years	0-hour	1.000	0.91 – 1.0	0.003	1.78	100	100
	2-hour	1.000	0.92 – 1.0	0.003	1.81	100	100
	4-hour	1.000	0.91 – 1.0	0.003	1.83	100	100
	6-hour	1.000	0.92 – 1.0	0.003	1.8	100	100

DISCUSSION

This study sought to compare conventional vital signs, specifically HR and SBP, with the SI, a ratio of HR to SBP, given the limited ability of vital signs to accurately assess the need for vasopressors and mechanical ventilation (MV). Our research showed that the cut off value of SI was 1.99 at 0 hour, 2.04 at 2 hour, 2.00 at 4 hour, and 1.98 at 6 hours with sensitivity of 100% and specificity of 92.9% for all four time intervale. while an study conducted at India in 2022 reported the SI cutoff 2.16 at 0 hour and 1.77 at 6 hours a sensitivity of 57.14 percent and a specificity of 75 percent was observed.[10]

Previous research has shown that HR and blood pressure alone are not reliable predictors of outcomes in critically harmed patients. It is widely recognized that HR is the earliest vital sign to change in response to hemorrhagic shock, increasing in cases of class II shock (15–30% blood loss). Studies have also linked an elevated SI to worse outcomes and a greater need for medical resources. Allgower and Burri were the first to report that an SI of 1.0 or higher was associated with a 40% death rate. Similarly, Oestern et al., in a small study on trauma patients, found that an SI of 1.0 or higher correlated with increased mortality.[11] Our study showed the median (IQR) SI at 0 hour was 2.4 (2.2-2.7) of those patients who had deceased as outcome. While median (IQR) of survived patients at 0 hour was observed 1.5 (1.5-1.6) was much lesser to deceased patients. As a higher SI was observed in deceased patients those patients may have experienced shock or hemodynamic instability, indicating that the body was under more stress.

This could be due to various conditions, such as hemorrhage, sepsis, or other forms of cardiovascular compromise. Similarly, In 2007, Nakasone et al. found that a higher SI was strongly linked to an increased likelihood of detecting contrast extravasation on an arteriogram, indicating active bleeding.[11]

The results from our analysis revealed that the cutoff values for the SI vary significantly across different pediatric age groups, with younger age groups displaying higher cutoff values. For instance, in the 1 to <12 months age group, the cutoff values ranged from 2.01 to 2.08 across different time intervals. This is consistent with existing literature that suggests younger children, especially infants, tend to have higher heart rates relative to their blood pressure, leading to a naturally higher SI. As children grow older, the cutoff values decrease slightly, as seen in the 4 to 6 years age group, where the cutoff ranged from 1.78 to 1.83. This trend is likely due to the maturation of cardiovascular physiology, where heart rate decreases and blood pressure increases with age, resulting in a lower SI.

Our analysis showed that the sensitivity of SI as a predictive marker for shock was consistently high (100%) across all age groups and time intervals, highlighting its utility as a screening tool. However, specificity varied slightly between age groups. The specificity was highest (100%) in the 4 to 6 years age group, suggesting that SI is particularly effective in this age range for ruling out shock. In contrast, the 1 to <12 months and 1 to <2 years age groups exhibited slightly lower specificity (89% and 92%, respectively), indicating a higher rate of false positives in these younger children. This is consistent with prior research that has emphasized the challenges of using SI in younger populations, where physiological variations may contribute to less specific predictions.

Interestingly, our study found that the AUC for SI remained high across all time intervals (0-hour to 6-hour), with values typically above 0.9, demonstrating the robustness of SI as a diagnostic tool over time. This consistency over time intervals suggests that SI can be used not only for initial assessment but also for ongoing monitoring of pediatric patients at risk for shock. A study conducted in the UK from 2009 to 2012 demonstrated that the Shock Index (SI) is a highly effective predictor of mortality, showing excellent discrimination with an AUC of 0.87 (95% CI: 0.85–0.89).[17]

A previous study found that age-specific shock index (SI) was significantly higher among non-survivors during the first six hours across three different ages. This aligns with another pediatric study, which reported that elevated SI was linked to increased mortality at three time points: 0, 4, and 6 hours. However, after adjusting for age, only children with higher SI at 0 and 6 hours had a significantly greater relative risk of death compared to those with a normal age-adjusted SI.[7,8,18] Research has indicated that children who did not survive within the first 48 hours of admission had significantly elevated SI values compared to those who either survived or succumbed after the 48-hour mark.[8,19] Furthermore, The SI can aid in early triage by identifying higher acuity without waiting for lab results. An SI greater than one is linked to higher mortality.[20]

At the 0-hour mark, serum lactate levels displayed an outstanding diagnostic performance with an AUC of 0.955 (95% CI: 0.91 – 1.0) and a p-value of <0.001. The cutoff value of 4.95 mmol/L achieved a sensitivity of 100% and a specificity of 92.9%, indicating its strong predictive power for early identification of shock. These findings are consistent with previous research, such as the study by Fuernau et al., in 2020 at Germany which highlighted the utility of arterial lactate as an indicator of patients prognosis in cardiogenic shock. That study identified lactate as a crucial laboratory marker for predicting outcomes in critically ill patients. Its significance, especially in septic shock, has been extensively validated through large cohort studies.[21,22]

Serum lactate measurement has long been recognized as a key tool for risk stratification and predicting in-hospital morbidity and mortality, particularly in identifying high-risk patients in the emergency department. As the focus on timely recognition and management of sepsis continues to grow, driven by increasing demands and limited resources, there is a critical need for fast and reliable screening tools.[23] Literature suggests that patients with a SI below 0.7 are 95% less likely to exhibit elevated levels of established sepsis severity markers, such as serum lactate. As a

result, a normal SI could serve as an effective alternative to SIRS criteria, helping prioritize patients who need lactate level assessments for diagnosing or monitoring the progression of sepsis.[23]

CONCLUSION

In children Shock Index (SI) could be a valuable predictor of fatality risk. SI is a simple, non-invasive, cost-effective, and rapid bedside clinical tool that can help us identify children at high risk. Elevated SI values indicate a higher risk of mortality, suggesting that these patients may benefit from more aggressive resuscitation and intensive care. Further research is needed to explore the use of SI before hospital admission, its role as a marker of response to treatment, and its relationship with organ dysfunction, in order to establish more sensitive and specific cutoff values.

Conflict of Interest: There is no conflict of interest in this study

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