Is vasoactive-inotropic score associated with early lactate clearance a predictive outcome of children with septic shock?

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ABSTRACT

Background. The main goal of septic shock therapy is to keep hemodynamic parameters in the normal range for adequate tissue perfusion. Persistent lactic acidemia has increased mortality. We evaluate the association between vasoactive-inotropic score (VIS) and lactate clearance (LC) to predict mortality of septic shock in children.

Methods. This is a retrospective study of consecutive septic shock in children admitted to the pediatric intensive care unit. Vital signs, laboratory values, and VIS were obtained at admission and the 6th hour of hospitalization. LC was calculated at the 6th hour. The associations between LC and VIS were evaluated using univariate and multivariate analysis. Receiver operating characteristic analysis was used to describe the cutoff values of LC and VIS.

Results. Eighty-two children, age 82.3 ± 59.8 months, were included, with an overall lactate clearance of $29 \pm 26\%$, and a mortality rate of 25.6%. The optimal cutoff value of LC was 20%. Children with LC $\geq 20\%$ compared with LC $< 20\%$ had a lower VIS [(21.41 ± 8.36) vs. (27.48 ± 10.11) (p: 0.009)]. In multivariate comparison, PELOD score and VIS were significantly associated with 6-hour lactate clearance $< 20\%$ but VIS at 6 hours had a significant inverse relationship with LC $< 20\%$. The cutoff for VIS was ≥ 16.2 for prognosticating the 6-hour LC and the high VIS group had a significantly lower LC and higher mortality ratio than the low VIS group.

Conclusions. High VIS was associated with lower lactate clearance and has been described as a predictor of greater mortality among septic shock in children.

Key words: lactate clearance, vasoactive-inotropic score, septic shock, mortality, pediatric.

Septic shock is characterized as a subset of sepsis in which especially severe cardiovascular collapse and abnormalities of cellular metabolism are related to increased mortality risk.[1] Early identification of septic shock and effective resuscitation within the first few hours may prevent the progression of shock and organ failure.[2] Elevated serum lactic acid level is an indicator of anaerobic metabolism and is accepted to be a useful biomarker of reduced tissue perfusion in septic shock patients.[3]

Although serum lactate is commonly used to evaluate tissue perfusion in the intensive care unit, lactate clearance (LC) may be more beneficial than the baseline lactate level for assessing patient outcomes.[4,5] For adult patients with septic shock, maintaining mean arterial pressure (MAP) > 65 mm Hg is recommended.[6] In the pediatric age group, a certain MAP value has not been determined, however, the goal of MAP is suggested between the 5th and 50th percentile or higher than the 50th percentile for age.[7] It was reported that hypoperfusion was associated with increased mortality risk regardless of the concomitant hypotension.[8] In pediatric septic shock, vasoactive-inotropic scores (VIS) are utilized to improve cardiovascular dysfunction and hypotension, however, increasing VIS is

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associated with the severity of cardiovascular dysfunction and mortality risk.[9,10] The mortality rate of hypotensive children requiring vasoactive agent with lactic acid greater than 2 mmol/L was higher than children with lactate less than 2 mmol/L.[11] Multiple variables such as high serum lactate, low LC, presence of multiorgan dysfunction syndrome, and high inotropic score have been determined as mortality prognosticator factors for septic shock.[4,10] According to our knowledge, the association between VIS and early LC in septic shock children has not been researched yet. This research was performed to evaluate whether VIS might be used to predict LC of patients after sufficient resuscitation therapy in septic shock children.

Material and Methods

Patient population

This is a retrospective, observational single-center research that was performed to analyze the relationship between LC and VIS in septic shock patients who were admitted to the tertiary level pediatric intensive care unit (PICU) from March 2020 to January 2022. This study was approved by the Afyonkarahisar Health Science University Faculty Ethics Committee (date: 07.01.2022, no: 2022/1). Children aged 1 month to 18 years old who were diagnosed with septic shock enrollment. Septic shock was described based on International Consensus Conference on Pediatric Sepsis.[12] All children needed central venous catheterization for continuous inotropic infusion, medical therapy, and oxygenation monitoring. Hemodynamic support was managed according to the prescribed guidelines.[9] Restoration of tissue perfusion was defined by the following targeted resuscitation endpoints[9]:

1) Normal mental status

2) Blood pressure (systolic pressure at least fifth percentile for age): Younger than 1 month of age: 60 mmHg, children with 1 month to 10 years of age: 70 mmHg + [2 x age in years], 10 years of age or older: 90 mmHg

3) Quality of central and peripheral pulses (strong, distal pulses equal to central pulses)

4) Sufficient skin perfusion (warm, and capillary refill <2 seconds)

5) Urine output >1 mL/kg/h (after efficient circulating volume is restored)

Broad-spectrum antibiotics were administered after blood cultures were taken. Children were supported by mechanical ventilation as needed.

Exclusion criteria

The study exclusion criteria were: 1) patients aged > 18 years or < 1 month 2) patients with serious hepatic disease 3) disease of inborn errors of metabolism 4) missing lactate data 5) staying for <24 hours in the Pediatric Intensive Care Unit 6) patients requiring renal replacement therapy within the first 6 hours of PICU admission.

Collection of blood samples

The baseline clinical and demographic information including age, sex, initial vital signs (heart rate, mean arterial pressure, and temperature), peripheral oxygen saturation, and the need for mechanical ventilation, the length of intensive care unit, outcome, and laboratory values at the time of admission were noted. The Pediatric Logistic Organ Dysfunction Score (PELOD) and Pediatric Risk of Mortality III score (PRISM III score) were calculated to determine the severity of the disease on admission. Lactate level in the blood was measured on admission to PICU and was accepted as the initial (0th) lactate level. More than two serum lactate values may be obtained within 6 hours, but only the initial and lactate at 6-hour values were analyzed. VIS contains dopamine, dobutamine, epinephrine, norepinephrine, vasopressin, and milrinone defines the amount of cardiovascular support required by patients (Fig. 1).[13] Data were acquired from patient files and an electronic hospital data management system.

$$\begin{aligned}
\textbf{VIS} = \; & \text{dopamine dose } (\mu g/kg/min) + \\
& \text{dobutamine dose } (\mu g/kg/min) + \\
& 100 \times \text{epinephrine dose } (\mu g/kg/min) + \\
& 100 \times \text{norepinephrine dose } (\mu g/kg/min) + \\
& 10{,}000 \times \text{vasopressin dose } (unit/kg/min) + \\
& 10 \times \text{milrinone dose } (\mu g/kg/min)
\end{aligned}$$

Fig. 1. Formula of Vasoactive-Inotropic Score (VIS)

Biochemical analysis

Lactate measurements were done by Radiometer Copenhagen ABL 555 blood gas analyzer. Lactate clearance (%) was calculated as follows: lactate at admission minus lactate at 6 hours, divided by lactate at admission, and then multiplied by 100. A positive result shows a reduction of LC, whereas a negative result shows an increase of LC after 6 hours.

Statistical analysis

In the univariable analysis, continuous parameters are described as mean ± standard deviation (SD) for normal distribution, median and interquartile range (IQR) for skewed distribution, and nonparametric data. Categorical parameters were evaluated by using the Chi-square test. Mann Whitney-U test was used for non-parametric parameters and the Student t-test was performed for normally distributed data. The significant parameters in the univariate comparison were then included in a multivariate logistic regression model. Cutoff levels of the VIS and LC were calculated by using the receiver operating characteristic curves (ROC curves). For all results, a p-value < 0.05 was regarded as the significance level. SPSS Statistics 22 software was used for the analysis of data.

Results

During the study period, a total of eighty-six children with septic shock were recorded. According to the exclusion criteria, four

Table I. Baseline characteristics and clinical data of the patients.

Total number	82
Age, months	82.3 ± 59.8
Gender (female/male)	29/53
Length of PICU stay (days)	8.3 ± 3.3
Mechanical ventilation (days)*	5 (4)
VIS	26.6 ± 9.5
Source of infection (%)	
Pneumonia	44 (53.7%)
Urosepsis	15 (18.3%)
Intra-abdominal	14 (17.1%)
Others	9 (11%)
Vital signs and hemodynamic parameters	
Heart rate (beats per minute)*	138 (32)
Respiratory rate (beats per minute)	34.6 ± 6.2
Temperature (C°)	37.6 ± 1.4
MAP (mmHg)	38.9 ± 6.2
Peripheral oxygen saturation, %*	94 (6)
Laboratories data	
Hemoglobin (g/dl)*	11.3 (1.7)
White blood cells (x10³ per mm³)	16.07 ± 5.9
Thrombocyte count (x10³ per mm³)	194 ± 105
Creatinine (mg/dl)*	0.37 (0.4)
Albumin (g/dl)*	3 (0.4)
Total bilirubin (mmol/L)	1.6 ± 0.84
D-dimer (ug/mL)	4 ± 1.9
Prothrombin Time (seconds)*	26.2 (23.4)
pH*	7.32 (0.09)
Base deficit (mmol/L)*	-2.8 (6.6)
Lactate (mmol/L)*	3.6 (2.1)
Lactate clearance (%)	29 ± 26
Organ dysfunction / Mortality risk score	
PELOD score	8.3 ± 3.3
PRISM III score	16.6 ± 3.5
Outcome (%)	
28-day mortality rate (%)	21 (25.6%)

*Median (IQR)
PICU: pediatric intensive care unit, PRISM III score: pediatric risk of mortality III score, PELOD: pediatric logistic organ dysfunction score, IQR: interquartile range, VIS: Vasoactive-inotropic score, MAP: Mean Arterial Pressure

patients were excluded. Baseline characteristics, vital signs of the patients, and initial laboratory data are demonstrated in Table I. Mean patient age was 82.3 ± 59.8 months, and 29 (35%) were

male. The total PICU length of stay was 8.3 ± 3.3 days. The baseline hemodynamic variables included mean arterial pressure of 38.9 ± 6.2 mm Hg, heart rate of 138 per min (IQR, 32), and peripheral oxygen saturation of 94 % (IQR, 6). The patient's total mechanical ventilation day was 5 days (IQR, 4). The predominant admission diagnoses were respiratory infection 53.7%. The mean VIS was 26.6 ± 9.5 for admission. Patients had a mean baseline PELOD score of 8.3 ± 3.3, and a PRISM III score of 16.6 ± 3.5. Overall, 61 patients survived and 21 patients died, a primary outcome of the 28-day mortality rate was 25.6%. The median admission serum lactate level was 3.6 mmol/L (IQR, 2.1), and the mean LC was 29 ± 26% at the 6th hour. After 6 hours of resuscitation, an optimal cutoff value of LC was determined as the LC ≥ 20% with the highest specificity of 38.1% and sensitivity of 75.4% for prediction of mortality. Based on the LC cutoff value patients were divided into two groups: LC ≥ 20% (high clearance group), and LC < 20% (low clearance group) (Fig. 2). Comparisons of both the LC groups in terms of age, gender, vital signs, laboratory data, metabolic factors, fluid volume received in the PICU, VIS, PRISM III, and PELOD score were performed (Table II). There was no significant difference between the low clearance group and the high clearance group for initial vital signs, white blood cells, hemoglobin, pH, base deficit, fluid therapy, length of mechanical ventilation, PRISM III score, and duration of

hospital stay. Although the low clearance group had significantly higher VIS, PELOD score, and prothrombin time, the high clearance group had lower baseline and 6th-hour lactate values (all p < 0.05). Variables were added to the multivariate logistic regression model via a forward stepwise technique that was statistically significant in the univariate model. In multivariate comparison, PELOD score and VIS scores at baseline was significantly associated with 6 hour LC < 20% but VIS at 6 hour had a significant inverse relationship with LC < 20% (95% CI: 1.10-1.53, p: 0.002; 95% CI: 1.34-2.93, p:0.001; 95% CI: 0.27-0.66, p: <0.001, respectively) (Table III). The cutoff value of VIS was ≥ 16.2 (sensitivity: 85.7%; 55% specificity) for prognosticating LC after adequate intravenous fluid resuscitation and application of vasoactive medications. When used ROC area under the curve (AUC), the estimation of LC was 0.75 (Fig. 3). Based on the VIS score cutoff value patients were divided into two groups: VIS ≥ 16.2 (high VIS group) and VIS < 16 (low VIS group). Although there was no significant differentiation between initial and 6th-hour lactate values, the high VIS group had significantly lower LC than the low VIS group (p: 0.01). Thrombocyte count was higher in the low VIS group (p: 0.01). The base deficit at the 6th hour was more negative in the high VIS group after resuscitation (p: 0.02). The high VIS score group had a significantly higher 28-day mortality rate (p: 0.02) (Table IV).
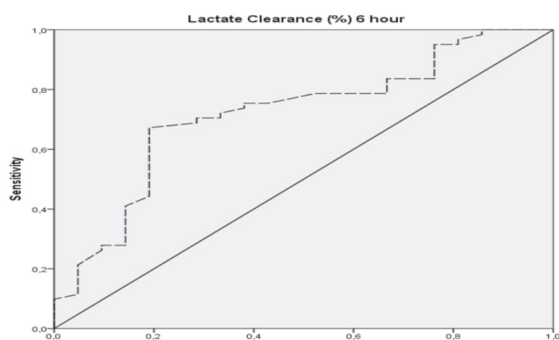

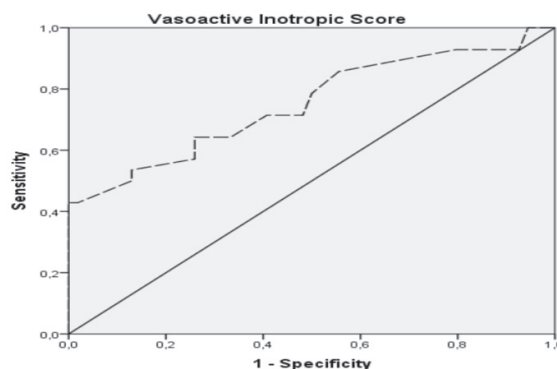**Fig. 2.** ROC curve of Lactate Clearance (%) 6 hour

Fig. 3. ROC curve of VIS 6 hour for predicting 6nd Lactate Clearance

Table II. Baseline characteristics, therapy, and outcome comparisons between LC < 20% and LC ≥ 20% groups.

Variables	LC < 20% (n:28)	LC ≥ 20% (n:54)	p value
Age, months	105.86 ± 57.17	79.81 ± 58.73	0.06
Length of PICU stay (days)	7.32 ± 3.59	8.62 ± 2.74	0.07
Mechanical ventilation (days)*	6 (5)	5 (5)	0.09
Fluid therapy ml/kg during first 6 hour	65 ± 22.02	65.18 ± 19.4	0.97
Heart rate (rate/minute) 0 hour	135.46 ± 18.88	139.96 ±19.51	0.31
Heart rate (rate/minute) 6 hour	133.52 ± 17.63	135.81 ±18.43	0.38
Respiratory rate (rate/minute) 0 hour	33.64 ± 5.08	34.31 ± 6.29	0.62
Respiratory rate (rate/minute) 6 hour	33.52 ± 4.76	34.26 ± 5.74	0.56
Temperature (C°) 0 hour	37.75 ± 1.41	37.61 ± 1.45	0.67
Temperature (C°) 6 hour	36.86 ± 1.28	36.70 ± 1.29	0.73
MAP (mmHg) 0 hour	37.54 ± 5.82	39.2 ± 6.31	0.24
MAP (mmHg) 6 hour	44.71 ± 7.23	47.35 ± 8.33	0.16
Peripheral oxygen saturation, % 0 hour*	94.5 (5)	96 (3)	0.08
Peripheral oxygen saturation, % 6 hour*	96 (4)	97 (5)	0.12
Hemoglobin (g/dl) 0 hour*	10.95 (2.35)	11.45 (1.7)	0.35
Hemoglobin (g/dl) 6 hour*	9.82 (2.51)	10.25 (1.3)	0.42
White blood cells (x10³ per mm³)	15.94 ± 7.06	15.77 ± 5.5	0.90
Thrombocyte count (x10³ per mm³)	190 ± 119	193 ± 97	0.89
Creatinine (mg/dl)*	0.42 (0.52)	0.36 (0.34)	0.11
Albumin (g/dl)*	3.01 (0.51)	3.01 (0.42)	0.79
ALT (U/L)	130.71 ± 119.06	108.84 ± 208.3	0.16
Total bilirubin (mmol/L)	1.8 ± 0.83	1.5 ± 0.76	0.08
D-dimer (ug/mL)	3.93 ± 2.23	3.70 ± 2.04	0.63
Prothrombin Time (seconds)*	25.15 (23.17)	26.25 (23.1)	0.03
pH 0 hour*	7.34 (0.08)	7.35 (0.07)	0.34
pH 6 hour	7.34 ± 0.13	7.36 ± 0.04	0.42
Base deficit (mmol/L) 0 hour*	-2.8 (4.23)	-1.2 (6.60)	0.28
Base deficit (mmol/L) 6 hour	-1.6 ± 3.3	-1.37 ± 3.19	0.21
Lactate (mmol/L) 0 hour*	3.8 (2)	3.4 (2.1)	0.006
Lactate (mmol/L) 6 hour*	3.75 (2.2)	1.7 (1.25)	0.003
Lactate Clearance (%) 6 hour	2.6 ± 13.14	45.41 ± 13.86	>0.001
VIS 0 hour	27.48 ± 10.11	21.41 ± 8.36	0.009
VIS 6 hour	29.07 ± 9.55	20.94 ± 7.71	>0.001
PRISM III score	16.54 ± 3.86	15.24 ± 3.8	0.15
PELOD score	22.17 ± 4.52	27.31 ± 6.95	0.001
28-day mortality rate %	8 (46.4%)	13 (14.8%)	0.002

*Median (IQR)
LC: Lactate clearance, PICU: pediatric intensive care unit, PRISM III score: pediatric risk of mortality III score, PELOD: pediatric logistic organ dysfunction score, IQR: interquartile range, VIS: Vasoactive-inotropic score, MAP: Mean Arterial Pressure, ALT: alanine aminotransferase
(The Formula of Lactate clearance (%) was calculated as follows: lactate at admission minus lactate at 6 hours, divided by lactate at admission and then multiplied by 100)

Table III. Statistically significant univariate variables associated with 6 h Lactate Clearance <20% were analyzed using multivariate logistic regression modeling.

Variables	Odds Ratio	Confidence Interval	p value
PELOD score	1.3	1.10-1.53	0.002
VIS 0 hour	1.98	1.34-2.93	0.001
VIS 6 hour	0.42	0.27-0.66	>0.001
Prothrombin Time	1.01	0.95-1.07	0.67

PELOD: pediatric logistic organ dysfunction score, VIS: Vasoactive-inotropic score, CI: Confidence Interval

Table IV. Baseline characteristics, therapy, and outcome comparisons between VIS < 16.2 and VIS ≥ 16.2 groups.

Variables	VIS < 16.2 (n:28)	VIS ≥ 16.2 (n:54)	p value
Age, months	82.54 ± 56.63	91.91 ± 60.71	0.49
Length of PICU stay (days)	8.71 ± 2.66	7.90 ± 3.29	0.26
Mechanical ventilation (days)*	7 (6)	5 (5)	0.11
Fluid therapy ml/kg during first 6 hour	67.5 ± 18.58	63.88 ± 21.04	0.42
Heart rate (rate/minute) 0 hour	139.11 ± 16.51	138.07 ±20.74	0.82
Heart rate (rate/minute) 6 hour	138.25 ± 15.67	137.92 ±19.66	0.76
Respiratory rate (rate/minute) 0 hour	34.0 ± 6.11	34.13 ± 5.82	0.35
Respiratory rate (rate/minute) 6 hour	33.25 ± 5.36	33.67 ± 4.76	0.43
Temperature (C°) 0 hour	37.86 ± 1.35	37.55 ± 1.46	0.67
Temperature (C°) 6 hour	36.74 ± 1.28	36.43 ± 1.37	0.71
MAP (mmHg) 0 hour	38.75 ± 5.11	38.57 ± 6.69	0.89
MAP (mmHg) 6 hour	46.79 ± 7.05	46.28 ± 8.54	0.78
Peripheral oxygen saturation, % 0 hour*	95 (3)	94 (5)	0.23
Peripheral oxygen saturation, % 6 hour*	96 (4)	95(5)	0.27
Hemoglobin (g/dl) 0 hour*	11.6 (1.0)	11.0 (2.7)	0.14
Hemoglobin (g/dl) 6 hour*	10.8 (1.2)	10.7 (2.2)	0.22
White blood cells (x10³ per mm³)	14.45 ± 5.37	16.54 ± 6.28	0.12
Thrombocyte count (x10³ per mm³)	230 ± 111	172 ± 96	0.01
Creatinine (mg/dl)*	0.32 (0.32)	0.38 (0.46)	0.81
Albumin (g/dl)*	2.99 (0.42)	3.01 (0.5)	0.39
ALT (U/L)	139.42 ± 279.61	130.53 ± 209.22	0.99
Total bilirubin (mmol/L)	1.57 ± 0.71	1.71 ± 0.84	0.45
D-dimer (ug/mL)	3.35 ± 1.53	4.0 ± 2.32	0.13
Prothrombin Time (seconds)*	26.2 (18.90)	23.30 (19)	0.20
pH 0 hour*	7.34 (0.05)	7.32 (0.06)	0.09
pH 6 hour	7.37 ± 0.04	7.33 ± 0.06	0.11
Base deficit (mmol/L) 0 hour*	-0.34 (3.27)	-2.5 (3.64)	0.09
Base deficit (mmol/L) 6 hour	0.26 ± 2.75	-1.7 ± 3.17	0.02
Lactate (mmol/L) 0 hour*	3.8 (2.4)	3.6 (2)	0.98
Lactate (mmol/L) 6 hour*	2.4 (2)	2.5 (2.3)	0.20
Lactate Clearance (%) 6 hour	39.6 ± 18.77	26.22 ± 26.0	0.01
VIS 0 hour	13.35 ± 1.79	28.74 ± 7.13	>0.001
VIS 6 hour	13.51 ± 1.76	29.0 ± 6.63	>0.001
PRISM III score	14.61 ± 4.04	16.24 ± 3.66	0.06
PELOD score	25.82 ± 5.46	25.42 ± 7.26	0.80
28-day mortality rate %	3 (10.7%)	18(33.3%)	0.02

*Median (IQR)

PICU: pediatric intensive care unit, PRISM III score: pediatric risk of mortality III score, PELOD: pediatric logistic organ dysfunction score, IQR: interquartile range, VIS: Vasoactive-inotropic score, MAP: Mean Arterial Pressure, ALT: alanine aminotransferase

Discussion

The present research is a retrospective clinical research that analyzes the relationship between vasoactive-inotropic score and lactate clearance of septic shock children after resuscitation. The main results of this research are as follows. Firstly, some septic shock patients had high lactate levels and poor lactate clearances after resuscitation of intravenous fluid therapy and vasoactive medications. Mean arterial pressure, hemoglobin concentration, peripheral oxygen saturation, and temperature, which are essential for perceiving of production and consumption of lactate were not sufficient to accurately predict LC after resuscitation. Secondly, VIS was associated with LC closely and had high sensitivity and specificity for the prediction of 6th hour LC after resuscitation in pediatric patients with septic shock. Finally, LC was found as inversely associated with hospital mortality in pediatric septic shock and patients with higher VIS had an increased mortality rate.

In critical illness, the benefit of evaluation of the lactate level has demonstrated that measurement of serum lactate values has an important role in the understanding of mortality risk.[14] During the early stage of resuscitation, values of lactate appear to be more nearly interested in mortality than hemodynamic variables.[15] Several types of research have emphasized that increased lactate values are a powerful sign to predict a high probability of mortality and morbidity ratio in critically ill patients, furthermore increasing LC decreases the odds of mortality at 24 hour.[16] Numerous septic shock patients who still have hyper lactic acidemia after completion of effective fluid resuscitation have a poor prognosis.[17] The significance of monitoring of lactate trend from high lactate value to normal lactate levels has been highlighted in Surviving Sepsis Campaign Guideline in 2016.[2] In this present study has a convenient outcome to previous research such as mortality was significantly higher among patients with lower LC.

Inotropic agents are routinely used to ensure cardiovascular support for adequate delivery of oxygen and tissue perfusion in septic shock children.[10] VIS is a clinical instrument that is used to understand the inotropic requirement of the cardiovascular system and can be utilized to predict morbidity and mortality.[18] VIS is independently associated with outcomes including ventilator days, length of hospital stay, and mortality in patients with sepsis.[19] Nguyen et al.[20] showed that hemodynamic parameters were similar between groups in patients with septic shock, while vasopressor dosage was significantly higher in the low LC group. Nazir et al.[16] presented that mean arterial pressure, central venous pressure, and VIS in the first 72 hours were not significantly different between high and low LC groups. Another previous study demonstrated that hemodynamic variables including mean arterial pressure, central venous pressure, central venous oxygen saturation, and central venous-to-arterial CO_2 difference were not useful to predict LC after resuscitation, but norepinephrine dose was better for prediction of LC.[21] We found that hemodynamic measurements were not useful to predict the early LC in this study, whereas VIS > 16.2 can predict early LC with high sensitivity and specificity after 6-hour resuscitation. Additionally, VIS was positively associated with increased mortality.

Walker et al.[19] reported that an optimal cutoff level of 6th hour LC was found at 36% which was independently associated with hospital mortality and also greater than the previously reported value. In another study, the Cutoff value of LC was calculated at 10% which predicted hospital mortality with maximum sensitivity and specificity.[5] In this research, we found an optimal cutoff of LC < 20% that is consistent with other research related to LC in septic shock patients, and also LC was inversely associated with risk of mortality.

Our research has some limitations. Firstly, this study was a retrospective clinical investigation

and there was a risk of bias due to the limited number of cases. Secondly, it was a single-center study and institution-specific parameters may have affected the outcomes. Furthermore, one could discuss that all patients did not receive a similar antibiotic regimen that might affect lactate production.

As a conclusion, this is the first study to assess the association between LC and VIS to predict mortality among pediatric patients with septic shock. We perceived that some children with septic shock still had poor tissue oxygen metabolism after ensuring normal hemodynamic parameters. A high VIS may be associated with deterioration of tissue oxygen metabolism. After sufficient resuscitation, vasoactive inotropic drug doses should be withdrawn without causing permanent impairment in tissue oxygen metabolism in septic shock. Further prospective research is fundamental to better understand the relationship between lactate clearance and vasoactive-inotropic score in pediatric septic shock.

Ethical approval

Approval was obtained from the ethics committee (date: 07.01.2022, no: 2022/1).

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: KÇ; data collection: MÇ; analysis and interpretation of results: KÇ, MÇ; draft manuscript preparation: KÇ, MÇ. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

6. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). Jama 2016; 315: 801-810. https://doi.org/10.1001/jama.2016.0287

7. Rhodes A, Evans LE, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. Intensive Care Med 2017; 43: 304-377. https://doi.org/10.1007/s00134-017-4683-6

8. Mikkelsen ME, Miltiades AN, Gaieski DF, et al. Serum lactate is associated with mortality in severe sepsis independent of organ failure and shock. Crit Care Med 2009; 37: 1670-1677. https://doi.org/10.1097/CCM.0b013e31819fcf68

9. Marty P, Roquilly A, Vallee F, et al. Lactate clearance for death prediction in severe sepsis or septic shock patients during the first 24 hours in Intensive Care Unit: an observational study. Ann Intensive Care 2013; 3: 3. https://doi.org/10.1186/2110-5820-3-3

10. Nguyen HB, Rivers EP, Knoblich BP, et al. Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. Crit Care Med 2004; 32: 1637-1642. https://doi.org/10.1097/01.ccm.0000132904.35713.a7

11. Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med 2021; 47: 1181-1247. https://doi.org/10.1007/s00134-021-06506-y

12. Weiss SL, Peters MJ, Alhazzani W, et al. Surviving sepsis campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. Pediatr Crit Care Med 2020; 21: e52-e106. https://doi.org/10.1097/PCC.0000000000002198

13. Jentzer JC, Burstein B, Van Diepen S, et al. Defining shock and preshock for mortality risk stratification in cardiac intensive care unit patients. Circ Heart Fail 2021; 14: 84-96. https://doi.org/10.1161/CIRCHEARTFAILURE.120.007678

14. Brierley J, Carcillo JA, Choong K, et al. Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine. Crit Care Med 2009; 37: 666-688. https://doi.org/10.1097/CCM.0b013e31819323c6

15. Haque A, Siddiqui NR, Munir O, Saleem S, Mian A. Association between vasoactive-inotropic score and mortality in pediatric septic shock. Indian Pediatr 2015; 52: 311-313. https://doi.org/10.1007/s13312-015-0630-1

16. Thompson K, Hammond N, Eastwood G, et al. The Australian and New Zealand Intensive Care Society Clinical Trials Group point prevalence program, 2009-2016. Crit Care Resusc 2017; 19: 88-93. PMID: 28215137.

17. Goldstein B, Giroir B, Randolph A; International Consensus Conference on Pediatric Sepsis. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. Pediatr Crit Care Med 2005; 6: 2-8. https://doi.org/10.1097/01.PCC.0000149131.72248.E6

18. McIntosh AM, Tong S, Deakyne SJ, Davidson JA, Scott HF. Validation of the vasoactive-inotropic score in pediatric sepsis. Pediatr Crit Care Med 2017; 18: 750-757. https://doi.org/10.1097/PCC.0000000000001191

19. Zhang Z, Xu X. Lactate clearance is a useful biomarker for the prediction of all-cause mortality in critically ill patients: a systematic review and meta-analysis*. Crit Care Med 2014; 42: 2118-2125. https://doi.org/10.1097/CCM.0000000000000405

20. Jansen TC, van Bommel J, Woodward R, Mulder PG, Bakker J. Association between blood lactate levels, Sequential Organ Failure Assessment subscores, and 28-day mortality during early and late intensive care unit stay: a retrospective observational study. Crit Care Med 2009; 37: 2369-2374. https://doi.org/10.1097/CCM.0b013e3181a0f919

21. Nazir M, Wani W, Dar SA, et al. Lactate clearance prognosticates outcome in pediatric septic shock during first 24 h of intensive care unit admission. J Intensive Care Soc 2019; 20: 290-298. https://doi.org/10.1177/1751143719855202

22. Husain FA, Martin MJ, Mullenix PS, Steele SR, Elliott DC. Serum lactate and base deficit as predictors of mortality and morbidity. Am J Surg 2003; 185: 485-491. https://doi.org/10.1016/s0002-9610(03)00044-8

23. Gaies MG, Gurney JG, Yen AH, et al. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. Pediatr Crit Care Med 2010; 11: 234-238. https://doi.org/10.1097/PCC.0b013e3181b806fc

24. Walker CA, Griffith DM, Gray AJ, Datta D, Hay AW. Early lactate clearance in septic patients with elevated lactate levels admitted from the emergency department to intensive care: time to aim higher?. J Crit Care 2013; 28: 832-837. https://doi.org/10.1016/j.jcrc.2013.02.004

25. Ryoo SM, Lee J, Lee YS, et al. Lactate level versus lactate clearance for predicting mortality in patients with septic shock defined by Sepsis-3. Crit Care Med 2018; 46: e489-e495. https://doi.org/10.1097/CCM.0000000000003030

26. Yu C, Fan W, Shao M. Norepinephrine dosage is associated with lactate clearance after resuscitation in patients with septic shock. Front Med (Lausanne) 2021; 8: 761656. https://doi.org/10.3389/fmed.2021.761656