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ORIGINAL RESEARCH

The effect of lactate to albumin ratio on mortality in pediatric trauma patients

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Abstract

Background: This study aimed to examine the correlation between early-phase lactate, albumin, and lactate-to-albumin ratio (LAR) measurements and mortality in pediatric trauma patients. **Methods**: A retrospective analysis was conducted on pediatric patients with severe trauma who received treatment in the Pediatric Intensive Care Unit (PICU). We collected demographic characteristics, serum lactate and albumin levels at admission, type of trauma (falls from height, traffic accidents), medical interventions, and imaging methods performed before and after intensive care admission. The Glasgow Coma Score (GCS), Pediatric Risk of Mortality Score III (PRISM III), Pediatric Death Rate (PDR), Pediatric Trauma Score (PTS), and mortality outcomes were also documented. **Results**: A total of 184 pediatric severe trauma patients were included in this retrospective cohort study and categorized into survivors and non-survivors. The median (interquartile range (IQR)) age of survivors was 87.5 (16.25–100.50) months, while the median (IQR) age of non-survivors was 71.5 (30.75–92.75) months. Lactate, albumin, and the LAR were included in separate models, given that LAR is derived from lactate and albumin values. The regression analysis revealed that PRISM III and lactate (Odds Ratio (OR): 1.6, 95% Confidence Interval (CI) (1.03–2.62); $p = 0.039$) were independent risk factors for mortality in trauma patients. In the regression model, the LAR value was selected through the forward selection process, meeting the significance threshold (OR: 4.63, 95% CI (0.99–21.60); $p = 0.05$). **Conclusions**: LAR may serve as a valuable adjunct to other risk assessment tools in pediatric trauma patients. Its use could facilitate the early identification of patients at higher risk of mortality, thereby enhancing clinical decision-making and improving patient outcomes.

Keywords

Pediatrics; Trauma; Lactate-to-albumin ratio; Mortality

1. Introduction

Trauma is an important cause of mortality and morbidity in young populations, and it has severe physiological and economic consequences, which can have a serious negative impact, especially in countries where the number of children is already declining [1]. Due to the serious negative effects of trauma on pediatric patients, the mechanism of trauma as well as patient management in intensive care units is very significant in decreasing mortality and morbidity [2].

Conditions such as shock, sepsis, trauma, malignancy, and cardiac arrest can result in increased levels of lactate in the plasma [3]. High lactate levels in the blood have been linked to poor outcomes, including mortality [4].

Serum albumin, the most abundant plasma protein, is critical for immune modulation and maintaining intravascular balance by regulating oncotic pressure [5]. Hypoalbuminemia is defined as a serum albumin level of less than 3.5 g/dL and in critically ill patients, it occurs due to increased vascular permeability and suppressed hepatic metabolism resulting from catabolism, which subsequently increases mortality [6].

Lactate-to-albumin ratio (LAR) may strongly predict multiple organ failure and mortality in critically ill pediatric patients [7]. Increased LAR, especially in the early period, was found to be closely linked with mortality in patients with sepsis, trauma, and shock [8].

The objective of this study is to examine the correlation between early-phase lactate, albumin and LAR measurements and mortality in patients with severe trauma due to fall from height or traffic accident admitted to the PICU. If such an association is identified, the secondary aim is to predict mortality rates in pediatric trauma patients and optimize their treatment and supportive care accordingly.

2. Material and methods

A retrospective analysis was conducted of patients with severe trauma aged 1 month to 18 years who were treated in the

Pediatric Intensive Care Unit (PICU) of Batman Training and Research Hospital, a 16-bed medical center located in Batman province, between April 2021 and October 2023. Patients who had burns, electric shock, drowning, hanging, or stabbing injuries were excluded. Additionally, none of the patients who participated in the study received renal replacement therapy or plasma exchange.

Data were collected from the hospital's online data system and the records kept by the clinicians. The patients' data were obtained after getting approval from the Batman Training and Research Hospital Ethics Committee (approval date/no: 22.11.2023/369).

In our pediatric intensive care unit, all trauma patients aged between 1 month and 18 years, irrespective of trauma type, were included. The inclusion was based on clinical evaluation supported by Pediatric Trauma Score and PRISM III scores, both of which were routinely recorded and used in decision-making.

Several parameters were recorded, such as the patient's demographic characteristics, and laboratory findings, (serum lactate, and albumin levels (at admission), White Blood Cell (WBC), Hemoglobin (HGB), Platelet (PLT), Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), International normalized ratio (INR), base excess (BE), creatinine, glucose), type of trauma (falling from a height, traffic accident), medical interventions, and imaging methods before and after intensive care. In the PICU, serum albumin is routinely measured in all trauma patients as part of the standard admission panel. Therefore, albumin data were consistently available for all included patients, despite the retrospective nature of the study. Also, Glasgow coma score (GCS), Pediatric Risk of Mortality Score III (PRISM III), Pediatric Death Rate (PDR), Pediatric Trauma Score (PTS), Vasoactive Inotropic Score (VIS) (at 6th hour), and mortality were recorded.

PRISM score and PDR were calculated via the website of scoring systems for intensive care units and surgical patients by filling in obligatory data [9]. PTS was calculated from the medical calculator system used by patients' weight, airway status, systemic blood pressure, and system findings [10]. VIS was calculated as follows: dopamine dose (μg/kg/min) + dobutamine dose (μg/kg/min) + 100 $\times$ epinephrine dose (μg/kg/min) + 100 $\times$ norepinephrine dose (μg/kg/min) + 10 $\times$ milrinone dose (μg/kg/min) + 10,000 $\times$ dose of vasopressin (U/kg/min) [11].

The primary outcome measures of this study were serum albumin and lactate levels. We hypothesize that elevated serum lactate levels, decreased serum albumin levels, and higher LAR values are associated with a poorer prognosis. Additionally, survival, defined as being alive at the time of discharge, was considered a key outcome measure.

2.1 Statistical analysis

Statistical analysis was performed by SPSS Statistics 22 software (IBM, Armonk, NY, USA). Baseline characteristics of the survivor and non-survivor samples were compared. Normal distributions were assessed by using a histogram and a Q-Q plat test. Continuous variables with normal distribution were tested by Student's *t*-test and presented as the mean $\pm$ standard deviation (SD), whereas non-normal distributed continuous variables were tested by Mann-Whitney U-test and presented as the median with interquartile range (median (IQR)). Categorical variables were tested by chi-square analysis or Fisher's exact test and described as numbers (percentage, %).

Independent risk factors for in-hospital mortality were identified using univariable and multivariable regression analyses. Potential risk factors with p values < 0.05 in the univariable analysis were included in a multivariable regression analysis. Multiple logistic regression models with forward selection were performed to analyze the risk factors and mortality association. Multicollinearity was tested by examining the variance inflation factor (VIF), the values for each variable are less than 5 taking no similarity.

MedCalc for Windows, version 22.030 (MedCalc Software, Ostend, Belgium) was used to plot receiver operating characteristic (ROC) curves, calculate the area under the ROC curve (AUC), and determine cutoff values. A comparison of the AUC of different variables was performed using the DeLong *et al.* [12] method.

2.2 Outcomes

A total of 184 pediatric severe trauma patients were included in this retrospective cohort study. These patients were categorized into two groups: survivors and non-survivors. The median (IQR) age of the surviving patients was 87.5 (16.25–100.50) months, while the median (IQR) age of the non-surviving patients was 71.5 (30.75–92.75) months (Table 1). Statistical analysis revealed no significant difference between these two groups ($p = 0.877$).

Among the survivors, 112 patients (66.7%) were male, compared to 12 (75%) in the non-surviving group. This difference was not statistically significant ($p = 0.497$).

Of the total patient cohort, 71% (132 patients) sustained injuries from falling from a height, whereas 29% (52 patients) were *involved* in traffic accidents. Comparative analysis of mortality rates indicated that traffic accidents were associated with a significantly higher mortality rate compared to falls ($p = 0.017$).

The surviving and non-surviving patients were evaluated using various scoring systems. The Pediatric Trauma Score (PTS) was higher in the non-surviving patient group ($p < 0.001$). Similarly, the PRISM III score was elevated in the non-surviving group ($p < 0.001$). Additionally, examination of the VIS at the 6th hour revealed higher values in the non-surviving group compared to the surviving group ($p < 0.001$). All scoring system results demonstrated statistically significant differences between the two groups.

The inotrope requirement status was compared between the two groups, revealing that 12 (75%) of the non-surviving patients required inotropic support, a statistically significant difference ($p < 0.001$). Additionally, the number of patients who needed invasive mechanical ventilation (MV) support was higher in the non-surviving group, with 13 patients (81.3%) requiring MV ($p < 0.001$). The length of MV support, measured as the median (IQR) number of days, was 13 (4–18) days in the non-surviving group, also demonstrating statistical significance ($p = 0.003$). Similarly, the median length of stay

TABLE 1. Comparison of clinical and laboratory variables of survivor and non-survivors.

Variables	Survivor (n = 168)	Non-survivor (n = 16)	*p* value
Demographics			
Age (mon)*	87.5 (16.25–100.50)	71.5 (30.75–92.75)	0.877
Gender (Male), %	112 (66.70)	12 (75.00)	0.497
Scores			
PTS*	3.00 (2.25–6.75)	12.00 (9.25–12.00)	**<0.001**
PRISM*	11 (0)	20 (13.25–26.25)	**<0.001**
VIS (at 6th hour)*	0 (0)	27.2 (5–27.5)	**<0.001**
Trauma type, %			
Falling from height	125 (74.4)	7 (43.8)	**0.017**
Traffic accident	43 (25.6)	9 (56.3)	
Treatments			
Inotropic requirement, %	11 (6.5)	12 (75)	**<0.001**
Invasive MV, %	14 (8.3)	13 (81.3)	**<0.001**
Length of MV, d*	2 (1–4)	13 (4–18)	**0.003**
Length of PICU stay, d*	7.5 (2–3)	13 (2.75–15.50)	**<0.001**
Laboratory variables			
Lactate (mmol/L)*	2.85 (1.00–2.30)	5.35 (4.82–7.07)	**<0.001**
Albumin (g/dL)**	4.10 ± 0.39	3.09 ± 0.68	**<0.001**
LAR*	0.77 (0.30–0.6)	1.98 (1.40–3.0)	**<0.001**
WBC (10^9/L)**	14.15 ± 7.22	13.60 ± 6.85	0.772
HGB (g/dL)**	11.62 ± 1.59	10.83 ± 2.31	0.205
PLT × 10^3/µL	352.68 ± 120.93	330.62 ± 137.80	0.492
ALT (U/L)*	34.50 (16.25–42.00)	49.50 (20.75–89.25)	**0.047**
AST (U/L)*	91.50 (34–82.75)	107.00 (40–121)	**0.030**
INR*	1.22 (1.10–1.32)	1.29 (1.21–1.88)	**0.001**
BE (mmol/L)*	−3.70 (−3.6–2)	−7.55 (−7.67–−5.85)	**<0.001**
Creatinine (mg/dL)*	0.39 (0.27–0.45)	0.37 (0.32–0.48)	0.510
Glucose (mg/dL)*	142.00 (101–145)	182.00 (137–271)	**<0.001**

**Median (IQR), Mann Whitney U test, **mean (±SD).*
PTS: Pediatric Trauma Score; PRISM: Pediatric Risk of Mortality; VIS: Vasoactive Inotropic Score; MV: Mechanical Ventilatory; PICU: Pediatric Intensive Care Unit; LAR: Lactate-to-albumin Ratio; WBC: White Blood Cell; HGB: Hemoglobin; PLT: Platelet; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; INR: International Normalized Ratio; BE: base excess.
p values are significant for statistical analyse important and they bolded.

in the pediatric intensive care unit (PICU) was significantly higher in the non-surviving group, at 13 (2.75–15.50) days ($p < 0.001$).

Examining laboratory variables at admission revealed significant changes in several parameters within the non-surviving group. These parameters included lactate, albumin, lactate-to-albumin ratio (LAR), base excess (BE), hyperglycemia, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and the International Normalized Ratio (INR). The median (IQR) lactate value (mmol/L) in the non-surviving group was 5.35 (14.82–7.07), whereas in the surviving group, it was 2.85 (1.0–2.3) ($p < 0.001$). The Lactate/Albumin Ratio (LAR) was 1.98 (1.40–3.0) in the non-surviving group and 0.77 (0.30–0.60) in the surviving group ($p < 0.001$). Alanine aminotransferase (ALT) levels (U/L) were 49.50 (20.75–89.25) in the non-surviving group and 34.50 (16.25–42.00) in the surviving group ($p = 0.047$). Aspartate aminotransferase (AST) levels (U/L) were 107.00 (40–121) in the non-surviving group and 91.50 (34–82.75) in the surviving group ($p = 0.030$). The International Normalized Ratio (INR) was 1.29 (1.21–1.88) in the non-surviving group and 1.22 (1.10–1.32) in the surviving group ($p = 0.001$). Base excess (BE) (mmol/L) was −7.55 (−7.67—5.85) in the non-surviving group and −3.70 (−3.6–2) in the surviving group ($p < 0.001$). Finally, glucose levels (mg/dL) were 182.00 (137–271) in the non-surviving group and 142.00 (101–145) in the surviving

group ($p < 0.001$). The mean (±SD) albumin levels (g/dL) were 3.09 ± 0.68 in the non-surviving group and 4.10 ± 0.39 in the surviving group ($p < 0.001$).

In univariable analyses, higher PTS and PRISM III scores, a history of traffic accidents, elevated VIS (at 6th hour), and the requirement for invasive mechanical ventilation were all linked to heightened risk of mortality. Additionally, admission lactate and albumin levels, lactate-albumin ratio (LAR), INR ratio, base excess (BE), and glucose levels were found to contribute to an elevated odds ratio in univariable analyses. A forward selection multivariable logistic regression analysis was performed to identify the variables that serve as independent risk factors for mortality. For the multivariable logistic regression analysis, nine variables (PRISM III, PTS, type of trauma, VIS (at 6th hour), invasive ventilation, lactate, albumin, LAR, BE) were incorporated into the model. INR and glucose were excluded from the model, as the PRISM III score inherently accounts for these parameters. Lactate, albumin, and the LAR were included in separate models, given that LAR is derived from lactate and albumin values. The regression analysis revealed that PRISMIII and lactate (OR: 1.6, 95% CI (1.03–2.62); $p = 0.039$) were the independent risk factors for mortality in trauma patients. In the regression model, the LAR value was selected through the forward selection process, meeting the significance threshold (OR: 4.63, 95% CI (0.99–21.60); $p = 0.05$) (Table 2).

When comparing the AUC values for each variable, none of the variables demonstrated superiority over the others ($p > 0.05$). However, PRISM III score, lactate, and LAR for predicting mortality exhibited high sensitivity and specificity (Table 3). Although the AUC of LAR was higher than others, this difference was not statistically significant (Fig. 1).

In the research, 12 patients were excluded from the study: 4 with burns, 2 with electric shock, 2 with drowning, 1 with hanging, and 3 with stabbing injuries. Additionally, 7 patients who received renal replacement therapy or plasma exchange were excluded.

3. Discussion

This research contributes to the expanding body of evidence suggesting that LAR may be a crucial predictor of adverse outcomes, particularly in pediatric trauma patients. The findings demonstrate that lactate, LAR, PTS, and PRISM III scores are significantly associated with mortality in cases of severe pediatric trauma and serve as independent risk factors. Furthermore, non-surviving patients had significantly higher VIS scores, greater need for MV support, and longer PICU stays compared to survivors.

It was shown that patients with serum lactate levels ≥4.3 mmol/L demonstrated a significantly higher mortality risk compared to those with levels <4.3 mmol/L. Although no official recommendation has been issued regarding the classification of lactate values as indicative of low or high

TABLE 2. Univariable and multivariable logistic regression of variables.

	Univariable analysis			Multivariable analysis		
	OR	95% CI	*p*	OR	95% CI	*p*
PTS	0.49	0.38–0.63	<**0.001**	0.5	0.24–1.03	0.061
PRISM III	1.34	1.21–1.49	<**0.001**	1.24	1.10–1.40	**0.01**
Trauma type %						
Falling from height	Ref	Ref	Ref	Ref	Ref	Ref
Traffic accident	3.74	1.31–10.64	**0.010**	3.47	0.45–26.69	0.23
VIS at 6th hour	1.23	1.14–1.32	<**0.001**	0.87	0.67–1.11	0.26
Invasive MV	47.66	12.12–187.47	<**0.001**	8.05	0.91–70.97	0.06
Length of MV	1.13	0.99–1.29	0.061	-	-	-
Lactate	3.059	1.96–4.77	<**0.001**	1.6	1.03–2.62	**0.039**
Albumin	0.033	0.009–0.12	<**0.001**	0.52	0.31–8.73	0.65
LAR	23.64	7.4–75.07	<**0.001**	4.63	0.99–21.60	**0.05**
ALT	1.00	0.99–1.01	0.18	-	-	-
AST	1.00	0.99–1.00	0.27	-	-	-
INR	65	6.43–660.57	<**0.001**	8.13	0.23–277.67	0.24
BE	0.35	0.22–0.56	<**0.001**	0.66	0.33–1.31	0.23
Glucose	1.01	1.00–1.02	**0.002**	1.00	0.99–1.01	0.58

PTS: Pediatric Trauma Score; PRISM: Pediatric Risk of Mortality; VIS: Vasoactive Inotropic Score; MV: Mechanical Ventilatory; LAR: Lactate-to-albumin Ratio; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; INR: International Normalized Ratio; BE: base excess; OR: Odds Ratio; CI: Confidence Interval; Ref: Reference group.
For the multivariable logistic regression analysis, nine variables (PRISM III, PTS, type of trauma, VIS at 6th hour, invasive ventilation, lactate, albumin, LAR, BE) were incorporated into the model. Lactate, albumin, and the LAR were included in separate models, given that LAR is derived from lactate and albumin values.

TABLE 3. Results of the receiver operating curve statistics.

Variables	AUC	95% CI	Cut-off value	Sensitivity	Specificity	Youden's index
LAR	0.922	0.873–0.956	1.035	87.50	97	0.84
Lactate	0.921	0.872–0.955	4.3	87.50	98.2	0.85
PRISM III	0.922	0.873–0.956	7	87.50	94	0.81
PTS	0.886	0.831–0.928	8	81.25	96.43	0.77

LAR: Lactate-to-albumin Ratio; PRISM: Pediatric Risk of Mortality; PTS: Pediatric Trauma Score; AUC: Area under the Curve; CI: Confidence Interval.

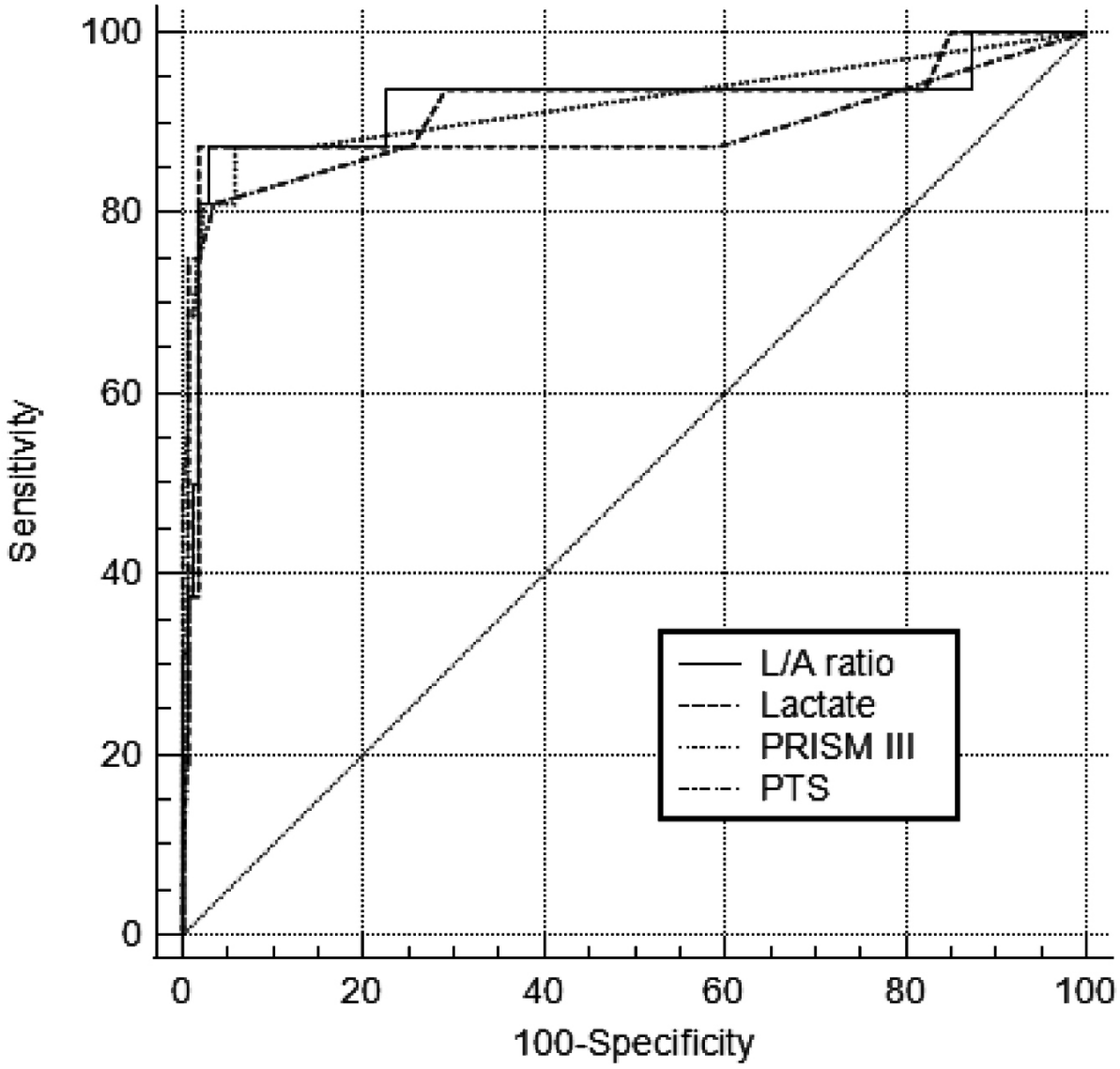

FIGURE 1. Receiver operating characteristic (ROC) curves for predictors related to in-hospital mortality index. PRISM: Pediatric Risk of Mortality; PTS: Pediatric Trauma Score; L/A: Lactate/Albumin.

risk in the management guidelines for septic shock and sepsis-associated organ dysfunction in children, lactate levels are routinely measured in clinical practice [13]. Numerous studies have consistently demonstrated that hyperlactatemia is closely associated with increased mortality [14, 15].

Hypoalbuminemia is prevalent among critically ill patients, and numerous studies have indicated that serum albumin levels upon admission are correlated with mortality [16, 17]. Albumin constitutes two-thirds of plasma proteins, contributes approximately 80% of plasma osmotic pressure, and plays a crucial role in molecular transport and binding. Post-traumatic hypoalbuminemia can occur due to factors such as hemorrhage, disruption of the blood-brain barrier, increased vascular permeability from neuroinflammation, and elevated albumin consumption [18]. In an adult study conducted by Wang *et al.* [19], serum albumin levels were found to be lower in the non-

survivor group. Similarly, in this research, serum albumin levels were significantly lower in non-survivor patients compared to the survivor group. A correlation has also been observed between hypoalbuminemia and poor outcomes, cognitive impairment, increased intracranial pressure, and brain edema in patients with traumatic brain injury (TBI) [20].

In the study, it was found that the discrimination of mortality was higher for LAR, which was identified as an independent risk factor in severe trauma patients. Similarly, LAR was found to be significantly associated with poor neurological outcomes and discharge in cases of sepsis, multi-organ dysfunction syndrome, and cardiac arrest [19]. In the current study, patients with a LAR cut-off value of 1.035 (CI: 0.873–0.956) and above were significantly associated with mortality. Similarly, in the study conducted by Skaansar *et al.* [21], a positive correlation between LAR and mortality was observed among traumatic brain injury patients. Another study that investigated the association of LAR with mortality in severe TBI patients, indicated that LAR is a significantly worse prognostic factor [19]. In a prospective study conducted by Bou Chebl R *et al.* [22], the Lactate/Albumin Ratio (LAR) was found to be a better prognostic factor than lactate in patients with cancer, diabetes, and those over the age of 65. Although there was no significant difference in patients with septic shock, LAR was identified as a parameter indicating increased hospital mortality. Retrospective studies assessing the significance of LAR as a prognostic indicator generally have limitations. However, in a retrospective study by Gharipour *et al.* [23] evaluating 6000 septic patients, LAR was found to be significantly superior to lactate alone in predicting 28-day mortality.

PTS is a scoring system designed for patients under the age of 18, incorporating parameters such as weight (in kilograms), systolic blood pressure (in mmHg), airway maintenance, mental status, skeletal fractures, and open wounds [24]. In the study, PTS was identified as an independent risk factor for mortality in trauma patients. In a comparable study evaluating the efficacy of PTS in the emergency department, no significant association was observed between PTS and mortality, likely attributed to the study's limitation of a low mortality rate, however, an increased duration of hospitalization was noted [25]. In the study, patients with higher PTS scores had a significantly higher mortality rate.

The study found that a PRISM III score of 7 or above was associated with mortality. PRISM III score, comprising multiple variables, is a scoring system designed to predict the risk of mortality in patients with various diagnoses upon admission to the PICU [26]. In a study examining the prognostic factors in pediatric trauma patients, Durak *et al.* [27] reported that a PRISM III score cut-off value of 18.5 and above was associated with mortality. Numerous studies have demonstrated the effectiveness of the PRISM III score in predicting mortality, thereby confirming its utility as a prognostic tool in the PICU.

When evaluating the laboratory parameters of patients, hyperglycemia, and coagulopathy were found to be significantly more prevalent in the non-survivor group compared to the survivor group. Similarly, in the randomized controlled observational study on traumatic outcomes conducted by Van Beek *et al.* [28], hyperglycemia and coagulopathy were reported to be significant predictors of poor outcomes.

4. Limitations

This research has some limitations; it was conducted in a single tertiary pediatric trauma center with a limited number of pediatric patients suffering from severe trauma. The investigation focused on 28-day mortality and did not include long-term mortality. Research that requires a greater example volume with multiple centers would be the suitable next step to better estimate the prognostic utility of the LAR ratio and decide the ideal threshold that differentiates between non-survivors and survivors. Unfortunately, the factors such as ED overcrowding, holiday-related variations, and lack of universal PICU admission criteria, may have influenced admission decisions and contributed to selection bias.

5. Conclusions

This current study contributes to the increasing research proof demonstrating that albumin-to-lactate may have unfortunate impacts, mainly for pediatric patients with trauma. After assessing the outcomes of this investigation, it may be concluded that there has been increased notice in the interpretation of the result of LAR on poor results; there appears to be an association between LAR and negative outcomes; it can be accepted that lower lactate with physiologic albumin level should be maintained; and the development of higher LAR ratio should be reflected as a prognostic indicator, considering the severity of the pediatric trauma patient. It can also help identify those at higher risk for early period mortality, thereby improving the management and outcomes of pediatric traumatic patients.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

SY—contributed to the study's conceptualization and design.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Batman Training and Research Hospital Ethics Committee (approval date/no: 22.11.2023/369). The study was conducted by the principles stated in the Declaration of Helsinki. I have obtained all subjects' consent to participate.

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CONFLICT OF INTEREST

The author declares that he has no conflict of interest that may have affected the conduct or presentation of the research.

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