

# The Lactate/Albumin Ratio is an Effective Predictor for Mortality in Critically Ill Children

## Laktat / Albümin Oranı, Kritik Hasta Çocuklarda Mortalite İçin Etkili Bir Belirleyicidir

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### ABSTRACT

**Objective:** Many predictive biomarkers were developed to evaluate the prognosis and mortality of critically ill children. Serum lactate level is a common biomarker because hyperlactatemia is associated with mortality in these patients. Previous studies have shown that serum albumin level is also a useful biomarker. Several recent articles suggested that the combination of serum lactate and albumin is a more effective predictor of mortality in critically ill patients. This study aimed to determine whether the lactate/albumin (L/A) ratio was a better prognostic factor than serum lactate level alone.

**Material and Methods:** Thus, we retrospectively investigated the relationship between L/A ratio and lactate, and their relationship with invasive mechanical ventilation, noninvasive mechanical ventilation support, inotropic drug need, acute renal kidney injury, continuous renal replacement therapy, mortality, and duration of pediatric intensive care unit stay.

**Results:** A total of 379 patients with a mean age of 4.8±5.3 years (range, 1 month to 18 years) were included in this study. The average duration of stay in the paediatric intensive care unit was 7.4±11.5 days, and the median L/A ratio was 0.46 (range, 0.11–10.0). Our findings indicate that the L/A ratio and serum lactate level were associated with mortality in critically ill children. However, our analysis also suggested that an L/A ratio of >0.5 upon admission is an overall better predictor of mortality.

**Conclusion:** We conclude that the L/A ratio is a useful and effective predictor of mortality in critically ill children.

**Key Words:** Albumin, Intensive care unit, Lactate, Paediatric, Prognosis

### ÖZ

**Amaç:** Kritik hasta çocukların prognozunu ve mortalitesini değerlendirmek için birçok öngörücü biyobelirteç geliştirilmiştir. Hiperlaktateminin kritik hastalarda mortalite ile ilişkili olması nedeniyle serum laktat seviyesi yaygın bir biyobelirteçtir. Önceki çalışmalar, serum albümin seviyesinin de faydalı bir biyobelirteç olduğunu göstermiştir. Bazı yeni makaleler, serum laktat ve albümin kombinasyonunun kritik hastalardaki ölüm oranlarını daha etkili bir belirleyicisi olduğunu ileri sürdü. Bu çalışmada laktat / albümin (L / A) oranının tek başına serum laktat seviyesinden daha iyi bir prognostik faktör olup olmadığını belirlemeyi amaçladık.

**Gereç ve Yöntemler:** Bu nedenle bu biyobelirteçler ile invaziv mekanik ventilasyon, invaziv olmayan mekanik ventilasyon desteği, inotropik ilaç ihtiyacı, akut böbrek hasarı, sürekli renal replasman tedavisi, mortalite ve çocuk yoğun bakım yatış süresi arasındaki ilişkiyi geriye dönük olarak inceledik.

**Bulgular:** Çalışmaya yaş ortalamaları 4.8 ± 5.3 yıl (1 ay ile 18 ay arasında değişen) 379 hasta dahil edildi. Pediatrik yoğun bakım ünitesinde ortalama kalış süresi 7.4 ± 11.5 gün, ortalama L / A oranı 0.46 (dağılım, 0.11-10.0)'di. Bulgularımız kritik



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hasta çocuklarda L / A oranı ve serum laktat seviyesinin mortalite ile ilişkili olduğunu göstermektedir. Bununla birlikte, analiz sonuçlarımız > 0.5 L / A oranının genel olarak daha iyi bir mortalite belirleyicisi olduğunu düşündürmektedir.

**Sonuç:** L / A oranının kritik hasta çocuklarda mortalitenin yararlı ve doğru bir belirleyicisi olduğu sonucuna vardık.

**Anahtar Sözcükler:** Albumin, Yoğun bakım ünitesi, Laktat, Prognoz, Pediatrik

## INTRODUCTION

Many predictive biomarkers were developed to evaluate the prognosis and mortality in critically ill children(1). Serum lactate concentration is a commonly used biomarker (2,3). Specifically, it has been used as an indicator of tissue hypoperfusion and cellular hypoxia in patients (3–5). Hyperlactatemia is also associated with short-term mortality in critically ill children (2,4,5). Many studies have reported that hyperlactatemia is an independent predictor of mortality in critically ill patients (6,7). Furthermore, serum lactate concentration at the paediatric intensive care unit (PICU) admission predicts mortality (8).

Serum albumin can be an indicator of systemic inflammation (9). Several studies have suggested that albumin is a biomarker of mortality and prognosis (9,10). More recently, it was reported that the combination of lactate and albumin is a better predictor of mortality in critically ill patients. Our study showed a significant association between the lactate/albumin (L/A) ratio and mortality (11–13).

In this study, we evaluated the efficacy of the L/A ratio to more accurately predict mortality in critically ill children compared to that of only serum lactate levels.

## MATERIALS and METHODS

Healthcare provision for children aged from one month to 18 years admitted to PICU equipped with seven beds, seven ventilators, and two isolation rooms. Data was collected and extracted from medical records (in accordance with the ethical principles for medical research) for all patients admitted for various critical illnesses in the PICU between January 2014 and February 2019. All patients who were admitted for <24 hours, died on the first day of admission, had missing medical data, or diagnosed with metabolic/liver disease were excluded from the study (Figure 1). Approval was obtained according to World Medical Association Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subject from the Ethics Committee of the institution in which the study was conducted (Ethical committee, no: 29430533-903.99-109967, December 13, 2018). We have recorded all materials, data, computer codes, and protocols associated with the publication for readers.

Demographic data were recorded upon the admission to the intensive care unit. The sex, age, invasive mechanical ventilation (IMV), noninvasive mechanical ventilation (NIV), duration of pediatric intensive care unit stay., mortality, inotropic drug need,

acute kidney injury (AKI), Paediatric Risk of Mortality (PRISM III) score, continuous renal replacement therapy (CRRT), red blood cell (RBC) transfusion were recorded for all patients. The laboratory values were obtained from the first blood withdrawal following admission to the intensive care unit (ICU).

AKI was defined as oliguria (urine output: <0.5 ml per kg of body weight per hour) and an elevated serum creatinine concentration for the patient's age, or a 1.5-fold increase in serum creatinine concentration in 24 hours.

The PRISM III score was calculated with an online calculator (available at: <https://kalite.saglik.gov.tr/>). Blood pressure (systolic and diastolic) was recorded in the first 24 hours for each patient. Heart rate and the respiratory rate per minute, partial arterial oxygen pressure to fraction of inspired oxygen (ie, PaO<sub>2</sub>/FIO<sub>2</sub>), partial arterial pressure of oxygen (i.e., PaCO<sub>2</sub>), prothrombin to partial thromboplastin time, serum total bilirubin, calcium, potassium, glucose, bicarbonate, pupillary response, and Glasgow coma score were used to determine the PRISM III score.

Initial blood gases and serum albumin concentration were recorded. Blood was collected into vacutainer tubes, processed and analysed (Beckman Coulter, Brea, California, US). The measurement of blood gasses was done using a standard gas injector (Radiometer ABL 700, Brønshøj, Denmark). Hypoalbuminaemia was classified as a serum albumin concentration of <3.0 g/dL.

SPSS (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY) was used for statistical analysis. Continuous variables were expressed as mean±standard deviation; whereas, categorical variables were expressed as frequency. Pearson chi-square and analysis of variance (ANOVA) were used for the comparison of categorical data between groups. The relationship between lactate and the L/A ratio was examined using receiver operating characteristic (ROC) curve analysis. Multivariate binary logistic regression models were employed to calculate the odds ratios (ORs) with 95% confidence interval (CIs) for L/A ratio. For all data, A P value of <0.05 was considered statistically significant.

## RESULTS

The medical records of 486 patients were evaluated. A total of 18 patients were excluded because of early discharge from the ICU (<24 hours of admission) or missing medical data. An additional 89 patients were excluded from the study because of metabolic disease. There were 379 patients included in the study. The demographic characteristics of these patients are

**Table I:** Demographic Characteristics of Patients in the Paediatric Intensive Care Unit Between January 2014 and February 2019.

Characteristics	Total no. of patients, n=379 (%) / Mean $\pm$ SD
<b>Sex</b>	
Male	208 (54.9 %)
Female	171 (45.1%)
<b>Reason for hospitalisation</b>	
Respiratory system disease	122 (32.2%)
Neurologic disease	59 (15.6%)
Sepsis	50 (13.2%)
Post-operation	50 (13.2%)
Nephrology	41 (10.9%)
Cardiovascular disease	17 (4.5%)
Haematology-oncology	15 (4.0%)
Endocrinology	12 (3.2%)
Other	13 (3.4%)
<b>Age</b>	4.76 $\pm$ 5.31 years (range, 1 month to 18 years)
<b>Acute kidney injury</b>	67 (17.7%)
<b>Inotropic medication</b>	81 (21.4%)
<b>CRRT</b>	40 (10.6%)
<b>IMV</b>	154 (40.6%)
<b>Duration of stay in the PICU, days</b>	7.35 $\pm$ 11.51
<b>Central venous catheter</b>	190 (50.1%)
<b>Red Blood Cell Transfusion</b>	168 (44.3%)
<b>PRISM III</b>	15.20 $\pm$ 14.12
<b>NIV</b>	128 (33.8%)
<b>Mortality</b>	27 (7.1%)

**CRRT:** continuous renal replacement therapy, **IMV:** invasive mechanical ventilation, **PICU:** paediatric intensive care unit, **PRISM:** Paediatric Risk of Mortality score, **NIV:** non-invasive mechanical ventilation

**Table II:** Comparison of Prognostic Factors for Lactate/albumin ratio.

	Lactate/Album Ratio		p
	$\leq 0.5$ (n=221)	$> 0.5$ (n=158)	
<b>Sex</b>			
Male	119 (53.8%)	89 (56.3%)	0.354
Female	102 (46.2%)	69 (43.7%)	
<b>Age, years</b>	4.49 $\pm$ 4.89	5.14 $\pm$ 5.83	0.238
<b>IMV support</b>	80 (36.2%)	74 (46.8%)	0.038
<b>Inotropic drug usage</b>	24 (10.9%)	57 (36.1%)	<0.001
<b>Acute kidney injury</b>	29 (13.1%)	38 (24.1%)	0.006
<b>Continuous renal replacement therapy</b>	19 (8.6%)	21 (13.3%)	0.143
<b>NIV support</b>	68 (30.8%)	60 (37.9%)	0.144
<b>Mortality</b>	5 (2.3%)	22 (13.9%)	<0.001
<b>Duration of stay in PICU</b>	8.09 $\pm$ 12.39	6.82 $\pm$ 10.82	0.288
<b>PRISM III</b>	14.10 $\pm$ 13.46	17.88 $\pm$ 16.39	<0.001
<b>Sepsis</b>	19 (8.6%)	31 (19.6%)	0.002
<b>Heart failure</b>	13 (5.9%)	28 (17.7%)	<0.001
<b>RBC transfusion</b>	83 (37.6%)	85 (53.8%)	<0.001

**IMV:** invasive mechanical ventilation, **NIV:** noninvasive mechanical ventilation, **PICU:** paediatric intensive care unit, **PRISM:** paediatric Risk of Mortality score

**Table III:** Analysis of Prognostic Factors by Roc Analysis for Lactate/Albumin Ratio.

Parameter	95% CI							
	AUC	SE	Specificity	Lower Bound	Upper Bound	Cut-off Value	Sensitivity	p
<b>NIV</b>	0.552	0.031	55.0%	0.491	0.613	0.485	51.6%	0.097
<b>CRRT</b>	0.584	0.054	55.2%	0.479	0.689	0.495	55.0%	0.082
<b>IMV</b>	0.574	0.031	52.2%	0.514	0.634	0.495	50.6%	0.074
<b>AKI</b>	0.625	0.041	44.6%	0.545	0.705	0.475	65.7%	<0.001
<b>Sepsis</b>	0.645	0.046	41.9%	0.555	0.736	0.415	70.0%	<0.001
<b>Inotropic drugs usage</b>	0.726	0.034	66.8%	0.660	0.792	0.505	71.6%	<0.001
<b>Heart failure</b>	0.735	0.044	57.7%	0.649	0.821	0.505	70.7%	<0.001
<b>Mortality</b>	0.792	0.050	57.3%	0.694	0.890	0.495	85.2%	<0.001

**SE:** Standard error, **CI:** confidence interval

**Table IV:** Analysis of Lactate Value by ROC Analysis for Prognostic Factors in PICU Patients.

Parameter	95% CI							
	AUC	SE	Specificity	Lower Bound	Upper Bound	Cut-off Value	Sensitivity	p
<b>NIV</b>	0.546	0.031	49.8%	0.485	0.607	1.65	56.7%	0.148
<b>CRRT</b>	0.513	0.057	47.3%	0.402	0.623	1.65	50.0%	0.795
<b>IMV</b>	0.530	0.031	47.5%	0.468	0.591	1.65	52.3%	0.330
<b>AKI</b>	0.557	0.044	38.1%	0.470	0.643	1.45	65.2%	0.149
<b>Sepsis</b>	0.587	0.048	42.3%	0.492	0.682	1.55	62.0%	0.048
<b>Inotropic drugs usage</b>	0.672	0.037	52.8%	0.600	0.744	1.65	69.1%	<0.001
<b>Heart failure</b>	0.693	0.047	49.6%	0.602	0.784	1.65	68.3%	<0.001
<b>Mortality</b>	0.770	0.055	62.6%	0.662	0.877	1.95	81.5%	<0.001

**SE:** Standard error, **CI:** confidence interval

**Table V:** Logistic Regression Analysis of the Lactate/albumin Ratio (>0.5) for Prognostic Factors in the PICU.

RISK	95% confidence, interval	Odds Ratio	p
<b>Mechanical Ventilation</b>	0.573-1.491	0.925	0.747
<b>Noninvasive Mechanical Ventilation</b>	0.814-2.102	1.308	0.267
<b>Heart failure</b>	0.475-2.721	1.136	0.774
<b>Blood product transfusions</b>	0.686-1.929	1.151	0.595
<b>Acute Kidney Injury</b>	0.460-2.594	1.092	0.842
<b>Continuous Renal Replacement Therapy</b>	0.300-2.249	0.832	0.703
<b>Sepsis</b>	0.594-2.563	1.234	0.573
<b>Inotropic drug usage</b>	1.513-6.285	3.084	0.002
<b>Mortality</b>	1.018-7.417	2.257	0.047

shown in Table I. Two hundred eight (54.9 %) of the patients were male, and 171 (45.1%) were female. The mean patient age was  $4.76 \pm 5.31$  years (range, one month to 18 years). The mean body weight was  $11.10 \pm 9.71$  (range 2.2–77) kg. The most frequent cause of hospitalisation was respiratory disorders ( $n=122$ , 32.2%), followed by neurological disease ( $n=59$ , 15.6%), sepsis ( $n=50$ , 13.2%) and post-operation ( $n=50$ , 13.2%). The mean duration of stay in the PICU was  $7.35 \pm 11.51$  days. IMV was used in 154 (40.6%) patients, and NIV was used in 128 (33.8%) patients. AKI developed in 67 (17.7%) patients during PICU stay, and 40 (10.6%) of these patients underwent CRRT. There were a total of 27 (7.1%) patients lost during pediatric intensive care unit stay.

In this study, the median L/A ratio was 0.46 (range, 0.11–10.0). Thus, we separated patients into two groups: (1) L/A ratio: <0.5; and (2) L/A ratio: >0.50). There was a statistically significant relationship between patients with an L/A ratio of >0.5 and the following (Table II): IMV support ( $p=0.038$ ), inotropic drug use

**Table VI:** Correlation Between Lactate, Lactate/Albumin Ratio, And Prism III Score in the Study Group.

Risk factors	Lactate		Lactate / albumin ratio		PRISM <sup>1</sup> III score	
	r	p	r	p	r	p
Lactate	-	-	0.932	<0.001	0.357	<0.001
Lactate / albumin ratio	0.932	<0.001	-	-	0.429	<0.001
PRISM1 III score	0.357	<0.001	0.429	<0.001	-	-

**PRISM<sup>1</sup>:** pediatric risk of mortality

( $p < 0.001$ ), mortality ( $p < 0.001$ ), AKI ( $p = 0.006$ ), PRISM III score ( $p < 0.001$ ), sepsis ( $p = 0.002$ ), heart failure ( $p < 0.001$ ), and RBC transfusion ( $p < 0.001$ ).

Analysis of ROC curves (Table III) for mortality (area under curve [AUC], 0.792) showed that an L/A ratio with a cut-off value of 0.495 has a sensitivity of 85.2% and a specificity of 57.3%. Heart failure (AUC, 0.735) showed 70.7% sensitivity and 57.7% specificity; inotropic drugs use (AUC, 0.726) showed 71.6% sensitivity and 66.8% specificity; sepsis (AUC, 0.645) showed 70.0% sensitivity and 41.9% specificity; and AKI (AUC, 0.625) showed 65.7% sensitivity and 44.6% specificity. NIV, CRRT, and IMV all exhibited low sensitivity and specificity (Table III). The relationships between the L/A ratio and prognostic factors are presented in Table I.

Analysis of ROC curves for mortality (AUC, 0.770) showed that a lactate concentration with a cut-off value of 1.95 has a sensitivity of 81.5% and a specificity of 62.6% (Table IV). Heart failure (AUC, 0.693) showed 68.3% sensitivity and 49.6% specificity; inotropic drugs use (AUC, 0.672) showed 69.1% sensitivity and 52.8% specificity; sepsis (AUC, 0.587) showed 62.0% sensitivity and 42.3% specificity. AKI, NIV, CRRT, and IMV all exhibited low sensitivity and specificity (Table IV). The relationships between the lactate values and prognostic factors are presented in Figures II.

The relationship between the prognostic factors and an L/A ratio of  $>0.5$  were calculated using logistic regression models (Table V). The OR (95% CI) for prognostic factors were as follows: mortality was 2.257 (1.018–7.417); inotropic drug use was 3.084 (1.513–6.285); sepsis was 1.234 (0.594–2.563); CRRT was 0.832 (0.300–2.249); and AKI was 1.092 (0.460–2.594).

There were statistically significant correlations between PRISM III score and lactate ( $r = 0.357$ ,  $p < 0.001$ ), and L/A ratio ( $r = 0.429$ ,  $p < 0.001$ ) (Table VI).

## DISCUSSION

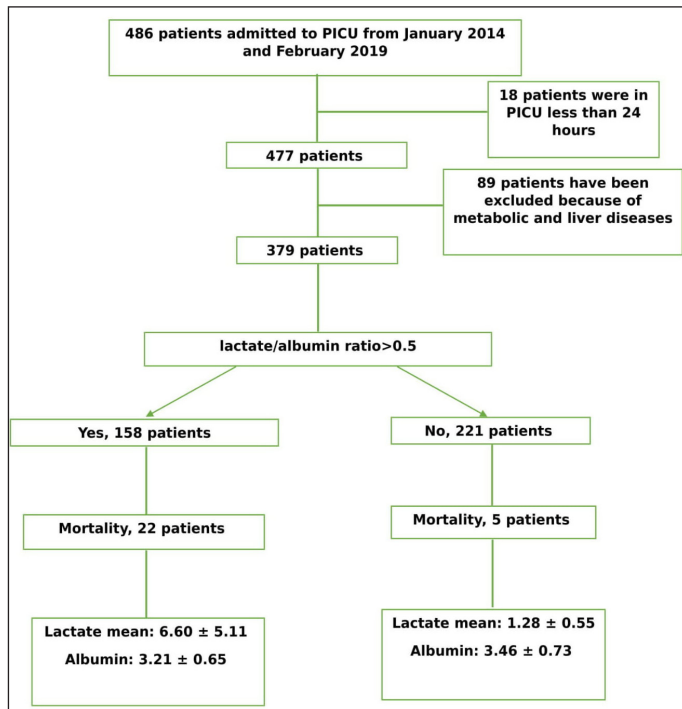
In this study, we examined if the L/A ratio was a better prognostic factor than serum lactate. Assessment of the L/A ratio is straightforward and measured using a routine test. Herein, we showed that an L/A ratio of  $>0.5$ , as well as serum lactate, could predict mortality in critically ill children at admission.

However, the L/A ratio was a better predictor of mortality than serum lactate concentration. This relationship between the L/A ratio ( $>0.5$ ) and mortality was further supported by ROC and logistic regression analysis. Therefore, the L/A ratio might be a useful tool for determining the prognosis of critically ill children.

Some variables have been developed to determine the response to treatment and prognosis in critically ill patients such as serum lactate, PRISM, and serum albumin. However, the most commonly used tool is serum lactate. The Surviving Sepsis Campaign and early goal-directed therapy recommend following lactate concentration (14,15). For this reason, many studies have examined the relationship with lactate and prognosis of patients in intensive care. Hyperlactatemia is reported to be an independent predictor of mortality in critically ill patients (4–8,16). Most studies on lactate have focused on septic shock patients (1,3,5). Previous studies have shown similar findings to ours in critically ill patients (6,7). In our study, hyperlactatemia was associated with mortality, heart failure, inotropic drug use, and sepsis. The most common area in the ROC curve for lactate was mortality.

Serum albumin is suggested to be a useful biomarker for critically ill patients. As a negative acute phase reactant, its concentration, normally 3.5–5.0 g/dl, is decreased with sepsis and metabolic disease (9,10). Furthermore, the half-life of albumin (i.e., ~20 days) can be significantly reduced by systemic inflammation, malnutrition, and liver disease (17). One large population study, demonstrated that serum albumin is an important marker of mortality and morbidity (18). In another study, serum albumin was the laboratory value that was most closely associated with mortality in adult patients with sepsis (19). However, the efficacy of albumin as a prognostic factor can be negatively affected by health conditions that directly reduce the concentration of serum albumin (i.e., chronic malnutrition and inflammation). Similarly, confounding factors, associated with hepatic and kidney insufficiency, reduce the prognostic value of serum lactate (20). Based on these limitations, patients with metabolic or liver diseases were excluded from this study. Moreover, we only measured initial serum lactate and albumin concentration.

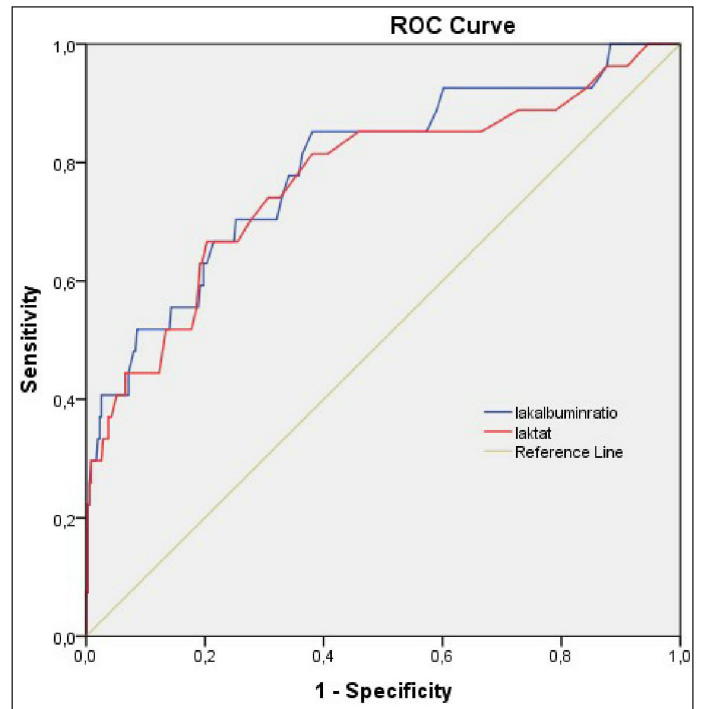
In a large pediatric study, Leite and et al. (21) reported that serum albumin was associated with mortality, duration of mechanical ventilation, clinical severity score, malnutrition, and serum



**Figure I:** Cohort Flow

lactate. This study showed that albumin and lactate levels were related each others. Therefore, combination of these laboratory values (the L/A ratio) may be a more valuable prognostic factor. Already, it was the aim of our study, too.

To date, there are only a few articles that examined the L/A ratio in critically ill children. These mostly reported that serum lactate concentration was related to prognosis (11–13). The L/A ratio has been suggested to be a more sensitive predictor than the individual biomarkers. Serum lactate and albumin are categorised as positive and negative acute phase reactants, respectively. Thus, an increase in the L/A ratio would more accurately reflect a pro-inflammatory condition (i.e., high lactate, low albumin). The L/A ratio is also suggested to be a better predictor of mortality. One adult study, reported that the L/A ratio was associated with mortality in patients with septic shock (11). This article was different from our study, in that the sample size was smaller, and the participants were all in septic shock. More recently, Lichtenauer et al. (22) reported that the L/A ratio at admission was associated with poor outcome in patients. In our study, the L/A ratio was associated with short-term mortality, and the ROC curves showed that the L/A ratio was a better predictor of mortality than serum lactate. Pearson correlation analysis also showed the that L/A ratio was better of the PRISM III score than serum lactate. However, as these correlations were weak ( $r < 0.500$ ), the L/A ratio could not be considered a better predictor than serum lactate. In the largest adult study that included the ten centers, Shin and et al reported that the prognostic performance of the L/A ratio was better than a single lactate measurement for predicting 28-day mortality in critically ill septic patients (23). Similar to our study, initial L/A



**Figure II:** Analysis of ROC curves of correlation between mortality and biomarkers (lactate, lactate/albumin ratio).

ratio was associated with mortality in this study. In contrast, most of the patients had an underlying chronic disease such as diabetes, cardiovascular disease, etc.

There have been many articles that focused on the relationship between inotropic drug use and poor prognosis. In the literature, Belletti and et al. (24) suggested that delayed inotrope initiation is associated with increased mortality. In our study, there was a significant relationship between the L/A ratio ( $>0.5$ ) and the need for inotropic drugs (36.1%). Our analysis also showed that patients with L/A ratio  $>0.5$  had over three times more inotrope drugs use. Based on these findings, we can say a high L/A ratio is associated with increased inotropic drug use. Our data also indicated that the L/A ratio was a better predictor of inotropic drug use than serum lactate alone (AUC, 0.726 vs 0.672). Furthermore, we showed that sepsis and heart failure were associated with both the L/A ratio and serum lactate; however, the L/A ratio was a better predictor of sepsis (AUC, 0.645 vs 0.587) and heart failure (AUC, 0.735 vs 0.693) than serum lactate concentration. Finally, our results showed that AKI was associated with the L/A ratio ( $p < 0.001$ ), but not serum lactate alone ( $p = 0.149$ ).

A limitation of the current study was its retrospective design. In addition, it was conducted at a single centre. Although this approach yielded valuable data, our findings may not be easily applied to other clinics or facilities because of the potential variability. Our study was the first to use a large sample size ( $n = 379$ ) to determine if the L/A ratio was a better prognostic factor for patients admitted to the PICU. However, to address the limitations of our study, additional investigation will be required. We think that there are needing more specifically,

large-scale prospective and multi-centre studies for support our findings. On the other hand, the fact that such a study evaluating the L/A ratio as a prognostic factor in PICU has not been done before in the literature makes our study valuable.

In conclusion, our study showed that the L/A ratio of patients upon admission to the PICU was associated with mortality in critically ill children. Furthermore, the L/A ratio was a better predictor of mortality than serum lactate, which is the currently recommended biomarker for patients with a critical illness. The serum L/A ratio as a clinical biomarker of mortality can be used in critical illness.

## REFERENCES

- Lanziotti VS, Póvoa P, Soares M, Silva JR, Barbosa AP, Salluh JI. Use of biomarkers in pediatric sepsis: literature review. *Rev Bras Ter Intensiva* 2016;28:472–82.
- 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; 42:2118–25.
- Gibot S. On the origins of lactate during sepsis. *Crit. Care* 2012;16:151.
- Martin J, Blobner M, Busch R, Moser N, Kochs E, Lupp PB. Point-of-care testing on admission to the intensive care unit: lactate and glucose independently predict mortality. *Clin Chem Lab Med* 2013; 51: 405-12.
- Kim YA, Ha EJ, Jhang WK, Park SJ. Early blood lactate area as a prognostic marker in paediatric septic shock. *Intensive Care Med* 2013; 39:1818–23.
- Haas SA, Lange T, Saugel B, Petzoldt M, Fuhrmann V, Metschke M, et al. Severe hyperlactatemia, lactate clearance and mortality in unselected critically ill patients. *Intensive Care Med* 2016;42: 202–10.
- Bai Z, Zhu X, Li M, Hua J, Li Y, Pan J, et al. Effectiveness of predicting in-hospital mortality in critically ill children by assessing blood lactate levels at admission. *BMC Pediatr* 2014;14: 83.
- Morris KP, McShane P, Stickley J, Parslow RC. The relationship between blood lactate concentration, the Paediatric Index of Mortality 2 (PIM2) and mortality in paediatric intensive care. *Intensive Care Med* 2012;38:2042–6.
- Gatta A, Verardo A, Bolognesi M. Hypoalbuminemia. *Intern Emerg Med* 2012;7: S193–9.
- Jellinge ME, Henriksen DP, Hallas P, Brabrand M. Hypoalbuminemia is a strong predictor of 30-day all-cause mortality in acutely admitted medical patients: a prospective, observational, cohort study. *PLoS One* 2014; 9: e105983.
- Wang B, Chen G, Cao Y, Xue J, Li J, Wu Y. Correlation of lactate/albumin ratio level to organ failure and mortality in severe sepsis and septic shock. *J Crit Care* 2015; 30:271–5.
- Choi SJ, Ha EJ, Jhang WK, Park SJ. Association between the lactate/albumin ratio and mortality in pediatric septic shock patients with underlying chronic disease: Retrospective pilot study. *Minerva Pediatr* 2016.
- Shin J, Hwang SY, Jo IJ, Kim WY, Ryoo SM, Kang GH, et al. Prognostic value of the lactate/albumin ratio for predicting 28-day mortality in critically ill sepsis patients. *Shock* 2018; 50: 545–50.
- Dellinger RP, Lev MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock. *Crit Care Med* 2013;41:580–637.
- Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001; 345: 1368–77.
- Jansen TC, Van BJ, Schoonderbeek FJ, Sleswijk Visser SJ, van der Klooster JM, Lima AP, et al. Early lactate-guided therapy in intensive care unit patients: a multicenter, open-label, randomized controlled trial. *Am J Respir Crit Care Med* 2010; 182: 752–61.
- Taverna M, Marie, AL, Mira, JP, Guidet, B. Specific antioxidant properties of human serum albumin. *Ann Intensive Care* 2013; 3: 4.
- Gibbs J, Cull W, Henderson W, Daley J, Hur K, Khuri SF. Preoperative serum albumin level as a predictor of operative mortality and morbidity: results from the National VA Surgical Risk Study. *Arch Surg* 1999; 134: 36–42.
- Artero A1, Zaragoza R, Camarena JJ, Sancho S, González R, Nogueira JM. Prognostic factors of mortality in patients with community-acquired bloodstream infection with severe sepsis and septic shock. *J Crit Care* 2010; 25: 276–81.
- Scheiner B, Lindner G, Reiberger T, Schneeweiss B, Trauner M, Zauner C, et al. Acid-base disorders in liver disease. *J Hepatol* 2017; 67:1062–73.
- Leite HP, Rodrigues da Silva AV, de Oliveira Iglesias SB, Koch Nogueira PC. Serum Albumin Is an Independent Predictor of Clinical Outcomes in Critically Ill Children. *Pediatr Crit Care Med* 2016;17:e50-7.
- Lichtenauer M, Wernly B, Ohnewein B, Franz M, Kabisch B, Muessig J, et al. The Lactate/Albumin Ratio: A Valuable Tool for Risk Stratification in Septic Patients Admitted to ICU. *Int J Mol Sci* 2017;18: E1893.
- Shin J, Hwang SY, Jo IJ, Kim WY, Ryoo SM, Kang GH, et al. Prognostic Value of The Lactate/Albumin Ratio for Predicting 28-Day Mortality in Critically ILL Sepsis Patients. *Shock* 2018;50:545-50.
- Belletti A, Castro ML, Silveti S, Greco T, Biondi-Zoccai G, Pasin L, et al. The Effect of inotropes and vasopressors on mortality: a meta-analysis of randomized clinical trials. *Br J Anaesth* 2015;115: 656–75.