

# A Retrospective Study on the Availability of Arterial Lactate Levels as a Biomarker of Mortality in Critically Ill Children

## Kritik Hasta Çocuklarda Arteriyel Laktat Düzeylerinin Mortalite Biyobelirteci Olarak Kullanılabilirliğine İlişkin Retrospektif Bir Çalışma

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### ABSTRACT

**Objective:** We aimed to determine the threshold value of lactate levels, and to analyze its availability as mortality biomarker by correlating it with scoring systems in pediatric intensive care unit (PICU).

**Material and Methods:** Observational retrospective cohort study. Our study was conducted among patients admitted to the 24-bed tertiary PICU of our hospital in 2015. All children between the ages of 1 month and 18 years were evaluated. Among 433 patients whose arterial blood gases were obtained during hospitalization, a total of 382 were included in the study. Patients with congenital metabolic disease with lactic acidosis were excluded.

The arterial blood lactate levels on admission, PIM-2, PRISM-III and PELOD scores and survival status of the patients were evaluated. Correlation between lactate levels and mortality scores, threshold values of lactate levels and the factors affecting mortality risk were the main variable of interest.

**Results:** There was a significant correlation between lactate levels and scores in patients who died ( $p < 0.001$ ). Receiver operating characteristic (ROC) curve analysis showed that blood lactate level was an effective parameter on mortality (area under the curve=AUC: 0.861;  $p < 0.001$ ) with a cut-off value of 2.55 mmol/L. The mortality risk was 1.38 fold higher in patients with higher levels of lactate.

**Conclusion:** In our series, the levels of lactate were higher in critically ill children who died. Again, lactate levels and mortality scores of these children were correlated. In our series, the levels of lactate were higher in critically ill children who died. Again, lactate levels and mortality scores of these children were correlated. We were able to establish a cut-off point with high specificity for predicting evolution. These findings should be validated in prospective and multicenter studies for their incorporation into scoring systems.

**Key Words:** Lactate, Mortality, Pediatric intensive care, PELOD, PIM-2, PRISM-III



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## ÖZ

**Amaç:** Çocuk yoğun bakım ünitesinde (ÇYBÜ) laktat düzeylerinin eşik değerini belirlemeyi ve bunun mortalite biyobelirteci olarak kullanımının skorlama sistemleriyle korelasyonunu analiz etmeyi amaçladık.

**Gereç ve Yöntemler:** Gözlemsel retrospektif bir kohort çalışmasıdır. Çalışmamız 2015 yılında hastanemizin 24 yataklı üçüncü basamak ÇYBÜ'sine başvuran hastalar arasında yapılmıştır. 1 ay-18 yaş arasındaki tüm çocuklar değerlendirildi. Yatış sürecinde takipte arteriyel kan gazı alınan 433 hastanın 382'si çalışmaya alındı. Laktik asidozlu konjenital metabolik hastalığı olan hastalar çalışma dışı bırakıldı.

Hastaların başvuru anında alınan arteriyel kan laktat düzeyleri, PIM-2, PRISM-III, PELOD skorları ve hastaların sağkalım durumları değerlendirildi. Laktat seviyeleri ile mortalite skorları arasındaki korelasyon, laktat seviyelerinin eşik değerleri ve mortalite riskini etkileyen faktörler ana değişkenlerdi.

**Bulgular:** Ölen hastaların laktat düzeyleri ile mortalite skorları arasında anlamlı bir ilişki vardı ( $p<0.001$ ). ROC eğrisi analizinde kan laktat düzeylerinin mortalite üzerinde etkili bir parametre olduğu (eğri altındaki alan=AUC: 0.861;  $p<0.001$ ) ve eşik değeri 2.55 mmol/L olarak bulundu. Laktat düzeyi yüksek olan hastalarda ölüm riski 1.38 kat daha fazlaydı.

**Sonuç:** Mortalite olan kritik çocuklar hastalarda laktat düzeyleri daha yüksekti. Aynı çocukların laktat seviyeleri ve mortalite skorları korele edildi. Tanımladığımız eşik değerlerin üzerinde mortalitenin arttığı görüldü. Bu bulguların skorlama sistemlerine dahil edilebilmesi için prospektif ve çok merkezli daha fazla çalışma ile doğrulanması gerekmektedir.

**Anahtar Sözcükler:** Laktat, Mortalite, Pediatrik yoğun bakım, PELOD, PIM-2, PRISM-III

## INTRODUCTION

The aim of intensive care is to combat life-threatening diseases involving multiple organs and systems. This requires the provision of life support, the implementation of possible treatment options, and accurate patient care and monitoring. Disease rating and risk assessment provide early detection of treatment requirements and necessary measures. Thus, the chance of survival of patients in intensive care, whose morbidity and mortality rates are considerably higher than other patients, can be increased (1).

The comparison of patients hospitalized in one unit or in different units in terms of morbidity is quite challenging since the clinical conditions of patients admitted to intensive care units (ICU) may vary significantly. Scoring systems are used to facilitate this comparison (1). The most commonly used mortality scoring systems are 'Pediatric Risk of Mortality' (PRISM) and 'Pediatric Mortality Index' (PIM) (2,3). In addition, the best known scoring system to assess organ failure is the 'Pediatric Logistic Organ Dysfunction' (PELOD) system (4).

Although the general approach to critically ill patients has changed over the last few years, there is still no definitive indicator for predicting mortality. With the inclusion of additional parameters such as the level of lactate, which is the most important determinant of tissue perfusion and oxygenation, in the scoring systems used to determine mortality in adult patients, some previous studies have attracted attention due to their significant results (5,6).

Lactate has been used as an indicator of tissue hypoperfusion and cellular hypoxia and its relation with mortality and prognostic importance have been shown in various studies (7,8). The results of both serial lactate measurements and studies predicting mortality with a single lactate measurement taken during hospitalization are limited and controversial. Furthermore, a cut-off limit of lactate for predicting the risk of death in critically ill children has not been established (9,10).

In this study, we aimed to measure arterial blood gas lactate levels during the onset of critical illness in children and analyze its availability as a mortality-biomarker by correlating it with validated PIM-2, PRISM-III and PELOD scoring systems. We also aim to show that measuring the level of lactate within 24 hours after the onset of critical illness may contribute to the capabilities of existing predictive scoring systems.

## MATERIALS and METHODS

The study was approved by the Izmir Behçet Uz Training and Research Hospital Clinical Research Ethics Committee on February 16, 2017 (decision number: 2017/02-05). Informed consent from the parents of the patients were obtained.

The data of patients hospitalized in our pediatric intensive care unit (PICU) between January and December 2015 were obtained using the electronic database of our hospital. Patients who were hospitalized in the PICU during the study period, whose data could be accessed, and whose arterial blood gases and lactate levels were measured at the time of hospitalization were included in the study.

Patients with congenital metabolic disease with lactic acidosis and organic acidosis, patients in the neonatal period of 0-30 days, patients followed-up postoperatively, and patients who were referred to another hospital were excluded from the study. Although arterial sampling is preferred for blood gas analysis in the PICU, this is not possible in all patients. Since arterial blood samples are required to evaluate blood gas lactate levels, venous samples were not included in the study. Patients referred to the PICU from other centers were excluded from the study because it was thought that previous interventions performed on these patients may have been partially documented and these interventions may have affected the arterial blood gas lactate measurements. Since the data of our study were obtained retrospectively from the file records, cases in which the necessary data could not be accessed were also excluded.

Patients were classified according to age, gender, duration of PICU stay, etiology, C-reactive protein (CRP) and procalcitonin (PCT) levels in patients with sepsis, presence of chronic disease, duration of stay in mechanical ventilation (MV)/non-invasive mechanical ventilation (NIMV)/high-flow nasal cannula (HFNC), survival status, arterial blood gas lactate level, PIM-2, PRISM-III and PELOD scores.

The lactate levels of the patients were obtained from the first arterial blood gas samples collected during the first interventions at the time of admission to the pediatric intensive care unit. The survival rate of the patients was determined according to their mortality in the first 28 days after hospitalization.

In our clinic, the diagnosis of organ dysfunction is made according to the criteria reported by Pediatric Sepsis International pediatric sepsis consensus conference in 2005 (11). According to these diagnostic criteria, arterial blood lactate levels of hemodynamically unstable patients with cardiovascular dysfunction were also evaluated.

Mortality calculations of scoring systems were performed logarithmically in a digital environment (12,13).

According to the definitions of the National Center for Health Statistics (NCHS) and the World Health Organization (WHO), we considered a disease as chronic if it lasts longer than 3 months, progresses slowly, cannot be completely cured, and prevents the person from maintaining daily life and activities (14, 15). In accordance with this definition, cerebral palsy, severe congenital cardiopathy, metabolic diseases, bronchiolitis obliterans, bronchopulmonary dysplasia, malignancy, renal failure and multiple congenital anomalies are considered as chronic diseases.

Blood lactate levels were measured in our hospital laboratory using ABL90 series blood gas device (Radiometer Medical ApS, Åkadej 21, DK-2700brønshøj, Denmark). Blood samples were transported in cold chain with heparinized syringes. Normal lactate level, hyperlactatemia, and lactic acidosis were defined as 0.5-2.50 mmol/L, 2.5-50 mmol/L, and >5 mmol/L, respectively (16-18).

For descriptive statistical evaluation, percentage (%) and frequency values were used for categorical variables; median (minimum (min) and maximum (max)); and interquartile range (IQR) or mean and standard deviation (SD) values were used for numerical variables. Chi-square or Fisher's exact test was used for categorical variables and Mann-Whitney U test was used for numerical variables that were not normally distributed to compare the deceased and surviving patient groups. Pearson correlation analysis was performed between lactate levels and mortality scores of deceased patients.

Receiver operating characteristics (ROC) curve analysis was used to determine a lactate threshold value to predict mortality and calculate predictive power. The parameter was assumed to be discriminative if the area under the curve (AUC) was above

0.50. After constructing the ROC curve, the AUC value was used to show that lactate is a predictor of mortality risk. Then, the coordinates of the ROC curve and the sensitivity and specificity values for each coordinate were determined. The coordinate with the highest sensitivity and specificity was selected as the cut-off value and then positive and negative predictive values were calculated by cross-tabulation by using this cut-off value. Furthermore, Youden's index was calculated to determine whether the cut-off values were suitable for diagnostic use and values above 50% were considered significant.

One-way analysis of variance (ANOVA) was performed to determine whether there was a difference in lactate levels between etiologic groups and if there was a difference, to determine where the difference originated from.

Logistic regression analysis was performed to determine the factors affecting mortality risk and to create a model.

Statistical analyses were performed using SPSS 22.0 Microsoft for Windows. P value less than 0.050 was considered significant.

## RESULTS

A total of 433 patients were evaluated. Among the 382 patients included in the study, 170 (44.50%) were female and 212 (55.50%) were male. The mean age was 18 months (min:2, max:300; IQR 54). The mean follow-up period was 5 days (min: 1, max: 372; IQR 10). Forty-nine (12.80%) patients died (Table I).

The most common etiology for hospitalization was respiratory diseases (n=140, 36.60%). In 201 patients (52.60%), an underlying chronic disease was identified. Respiratory support was needed in 147 (38.50%) cases and invasive mechanical ventilation was applied in 85 (57.90%) patients. The median duration of respiratory support was 5 days (min: 1, max: 230; IQR: 18). The median arterial blood gas lactate level of all patients was 1.8 mmol/L (min: 5, max: 18; IQR: 1.6) and hyperlactatemia and lactic acidosis were detected in 29.8% (n=114) of these patients. The median values of PRISM 3, PIM 2 and PELOD scores were 5, 0.90 and 1, respectively (Table I).

It was determined that there was a significant difference in the level of lactate between all etiologic groups and this difference was due to the sepsis group (p<0.001 post hoc test: Bonferroni). The mean lactate value was higher in the sepsis group compared to the other groups [5.10 ± 4.14 mmol/L (min: 0.70, max: 18)].

Sepsis (n=19, 38.80%) was the most common diagnosis among 49 patients who died. When sepsis cases were evaluated in terms of CRP and PCT values, there was no difference in PCT values between survivors and non-survivors, while CRP values were higher in non-survivors (p = 0.245; p = 0.024, respectively).

The prevalence of chronic disease (81.60%) and respiratory support therapy (95.90%) was higher in patients who died

**Table I: Comparison of patients who died and were alive.**

	Patients who died	Patients who were alive	Total	p
Number and percentage of patients	49/12.8	333/87.2	382	-
Etiology*				
Respiratory tract diseases	14/28.6	126/37.8	140/36.6	0.032
Neurologic disorders	4/8.2	61/18.3	65/17	
Intoxication and trauma	1/2	50/15	51/13.4	
Sepsis	19/38.8	18/5.4	37/9.7	
Cardiovascular diseases	7/14.3	24/7.3	31/8.1	
Dehydration	1/2	19/5.7	20/5.2	
Renal diseases	2/4.1	14/4.2	16/4.2	
Diabetic ketoacidosis	-	12/3.6	12/3.2	
Others	1/2	9/2.7	10/2.6	
CRP value in patient with sepsis (mg/dl) <sup>†</sup>	11.7; 2.42-49.04; 9,66	5.8; 2.05-24.2; 6.83	7.6; 2.05-49.04; 9.03	0.024
Procalcitonin value in patient with sepsis (ng/ml) <sup>†</sup>	2.1; 0.14-7.16; 4.4	1.2; 0.02-9.6; 3.03	1.44; 0.02-9.6; 3.64	0.245
Presence of chronic disease*	40/81.6	161/48.3	201/52.6	<0.001
Lactate values in patients with cardiovascular dysfunction (mmol/L) <sup>†</sup>	5.35; 0.8-18; 9.7	2.3; 0.7-16; 2.4	3.1; 0.7-18; 3.6	<0.001
Need for respiratory support*	47/95.9	100/30	147/38.5	
Invasive mechanical ventilation	46/97.8	39/39	85/57.9	<0.001
Non-invasive mechanical ventilation	0/0	9/9	9/6.1	<0.001
High flow nasal cannula	1/ 2.2	52/52	53/36	
Duration of respiratory support (days) <sup>†</sup>	7, 1-180, 24	5, 1-230, 13	5, 1-230, 18	0.413
Blood lactate level (mmol/L) <sup>†</sup>	5.1, 0.8-18, 9.4	1.7, 0.5-16, 1.3	1.8, 0.5-18, 1.6	
Hyperlactatemia*	15/30.6	66/19.8	81/21.2	<0.001
Lactic acidosis*	25/51	8/2.4	33/8.6	<0.001
Normal level*	9/18.4	259/77.8	268/70.2	
PRISM III score <sup>†</sup>	21; 2-45; 18	3; 2-35; 5	5; 2-45; 7	<0.001
PIM 2 score <sup>†</sup>	52.9; 24-99; 51.6	0.8; 0.5-80; 2	0.9; 0.6-99; 8.7	<0.001
PELOD score <sup>†</sup>	23; 12-52; 20	1; 0-32; 10	1; 0-52; 11	<0.001
PELOD mortality <sup>†</sup>	26; 13-100; 83.4	0.1; 0-87.7; 1	0.1; 0-100; 1	<0.001

\*: n(%), †: median, min-max, IQR, ‡: median, **PRISM III**: Pediatric risk of mortality score III, **PIM 2**: Pediatric index of mortality – 2, **IQR**: interquartile range, **PELOD**: Pediatric logistic organ dysfunction

**Table II: Results of correlation analysis between lactate levels and scoring systems.**

Pearson correlation analysis	PRISM-III score		PIM-2 score		PELOD score	
	r	p	r	p	r	p
Lactate level	0.658	<0.001	0.693	<0.001	0.557	<0.001

r: correlation coefficient, **PRISM III**: pediatric risk of mortality score III, **PIM 2**: pediatric index of mortality – 2, **PELOD**: pediatric logistic organ dysfunction

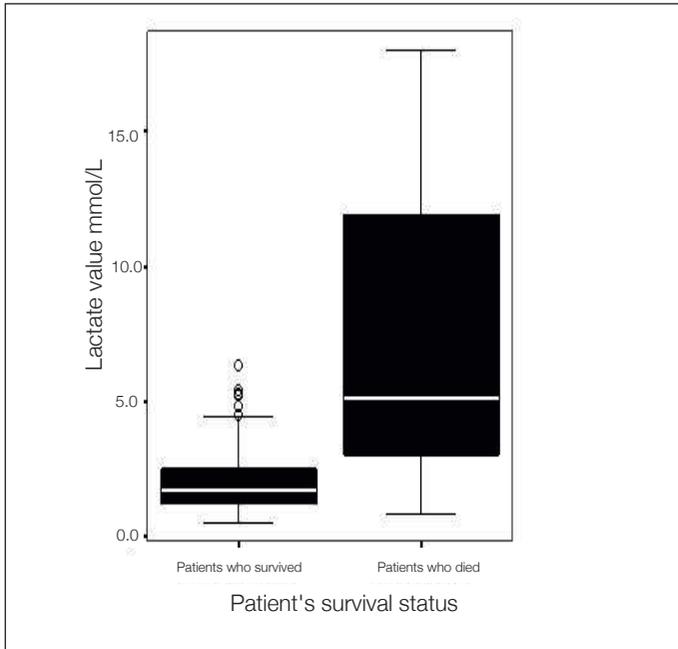
compared to those who were alive ( $p < 0.001$ ,  $p < 0.001$ , respectively). Invasive mechanical ventilation was the most commonly used respiratory support therapy in patients who died (97.80%). The need for respiratory support therapy was higher in patients who died compared to those who were alive ( $p < 0.001$ ). While there was no difference in the duration of respiratory support therapy between the two groups, arterial blood level of lactate (median: 5.10; min:0.8, max:18; IQR:9.40) was higher in patients who died compared to those who were alive (median: 1.70; min:0.50, max:16; IQR:1.30) ( $p < 0.001$ ) (Figure 1). As expected, the median PRISM3, PIM2 and PELOD scores were significantly higher in patients who died ( $p < 0.001$ ,  $p < 0.001$  and  $p < 0.001$ , respectively) (Table I).

The most common organ dysfunction in our patient group was respiratory system dysfunction with a rate of 38.40% (147/382). Cardiovascular dysfunction was detected in 26.40% (101/382) of the patients. This group had a higher median arterial blood gas lactate (median 3.10mmol/L, min 0.70-max 18, IQR 1.30) than the group of patients without cardiovascular dysfunction (median 1.60mmol/L, min 0.50-max 13.70, IQR 1.30) ( $p < 0.001$ ). Furthermore, mortality was observed in 37.60% (38/101) of patients with cardiovascular dysfunction compared to 3.90% (11/281) in the other group ( $p < 0.001$ ). Arterial blood gas lactate levels were higher in patients with cardiovascular dysfunction, who died, compared to patients with cardiovascular dysfunction who were alive ( $p < 0.001$ ) (Table I).

**Table III: Receiver operating characteristic (ROC) analysis showing that arterial blood gas lactate values were effective on the mortality risk.**

Lactate level (mmol/L)	
Cut-off value	2.55
Sensitivity*	81.6
Spesifity*	77.8
Positive predictive value*	35.1
Negative predictive value*	96.6

\*(%)

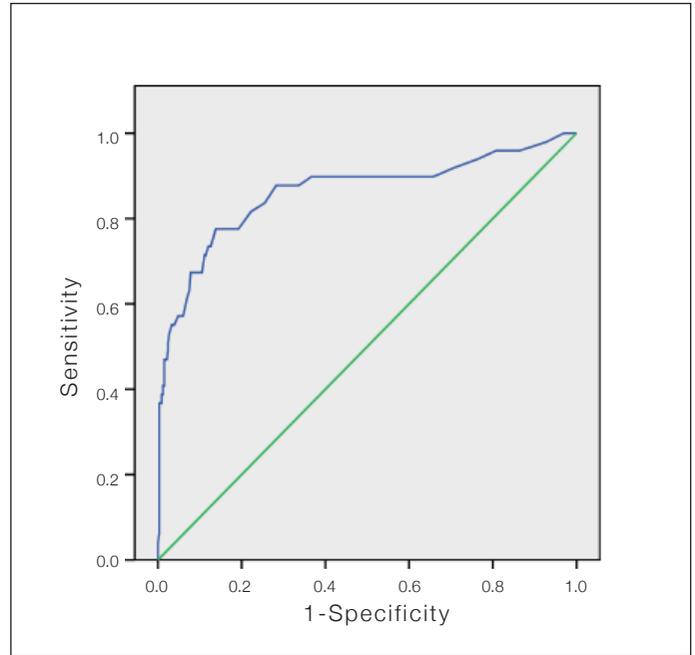


**Figure 1:** Box plot graph showing lactate levels of patients who died and were alive.

There was a good and significant correlation between the levels of lactate and mortality scoring systems in patients who died (Table II).

ROC analysis revealed that the arterial blood gas lactate level was an effective parameter on mortality risk (AUC: 0.861 (95% confidence interval (CI): 0.79-0.93;  $p < 0.001$ )) and the cut off value was 2.55 mmol/L (sensitivity 81.6%, specificity 77.8%, positive predictive value: 35.10%, negative predictive value: 96.60%) (Table III). This cut-off value had a low value for predicting a high risk of mortality in patients with a lactate level  $>2.55$  mmol/L (positive predictive value: 35.10%) and a high value for predicting a low risk of mortality in patients with a lactate level  $\leq 2.55$  mmol/L (negative predictive value: 96.60%) (Figure 2). After determining the coordinates of the curve obtained by ROC analysis, the lactate level with the highest sensitivity and specificity was selected as the cut-off level and the Youden index of this value was found to be 59.40, which was statistically significant ( $p < 0.001$ ).

The lactate value was  $>2.55$  mmol/L in 40 (81.60%) of 49 patients who died, while it was below the limit value in 259



**Figure 2:** Receiver operating characteristic (ROC) analysis showed that the arterial blood gas lactate values were effective on mortality risk.

(77.80%) of 333 patients who survived ( $p < 0.001$ ). Furthermore, 11 of 13 patients (84.60%) with sepsis and lactate levels  $>2.5$  mmol/L died, while only 8 of 24 patients (33.30%) with sepsis and lactate levels  $\leq 2.50$  mmol/L died ( $p = 0.003$ ).

Logistic regression analysis was performed to determine the factors affecting mortality risk. As a result, the mortality risk was 1.38-fold higher in patients with lactate levels above the threshold (Odds ratio: 1.38;  $p < 0.001$ ; 95% CI: 1.1-1.6).

## DISCUSSION

Standard mortality scoring systems are systems used to identify risky patients in ICUs, to determine the treatment plan early, and to ensure quality control of ICUs. In order to improve these systems, they should be applied in different units and patient groups and their validity should be tested. The systems should be updated over time, taking into account changes in health care quality and treatment practices. Ideal scoring systems are those that have successfully passed reliability and validity tests (19, 20).

According to the consensus decision of the ethics committee of the intensive care association, it is not appropriate to use scoring systems as the sole source for making the decision to start and continue intensive care treatment (20). Therefore, in addition to scoring systems developed for early recognition of mortality, parameters that will give rapid and effective results should also be used.

Lactate has been used as an indicator of tissue hypoperfusion and cellular hypoxia and its relation with mortality has been shown in several studies (7,8). Lactate values can be obtained

quickly and easily in arterial blood gas which is used in the first step in diagnosis and treatment at ICUs. Hyperlactatemia is a predictive marker in determining the risk of death in adult patients admitted to ICUs. Hyperlactatemia has been proven to increase the ability of prognostic scoring systems in predicting mortality when included (5,6). In children, lactate levels are not included in standard scoring systems. In our study, we aimed to find a cut-off value for lactate obtained from blood arterial gas at hospitalization that predicts mortality, to determine the relationship between lactate and mortality and survival, and to prove its efficacy by correlation with the validated PIM-2, PRISM-III and PELOD scoring systems.

Lactate is a by-product of anaerobic cellular metabolism. Anaerobic metabolism becomes dominant to provide energy in the absence of tissue perfusion and in cases such as hemorrhagic shock or septic shock where tissues are provided with insufficient oxygen. This leads to increased lactate metabolism in the liver and kidneys and elevated lactate levels in the blood (9,21). In this study, the median lactate value in all patients was 1.8 mmol/L (min:0.5, max:18; IQR:1.6). In 29.80% of these patients, lactate levels were above 2.50 mmol/L. In a study conducted on 140 patients admitted to PICU, lactate levels in the first 24 hours after hospitalization were shown to have higher sensitivity and specificity in predicting mortality risk (22). El-Mekawy et al. (9) reported that hyperlactatemia persisting 24 hours after hospitalization was associated with mortality. In a single-center study including a large number of patients, a significant correlation was found between serum lactate levels during hospitalization and mortality (21). In another study, patients with lactate levels > 2 mmol/L obtained within 48 hours of hospitalization had poor neurological outcomes as well as mortality (23). In another study in which serum lactate level was examined as an indicator of mortality, mortality rate was 24% in 79 patients and serum lactate levels were found to be 0.79-17.17 mmol/L in survivors and 1.14-24.50 mmol/L in those who died. The relationship between lactate levels in deceased and surviving patients was significant ( $p<0.050$ ) (24). In our study, lactate levels during hospitalization were shown to be a significant indicator of mortality ( $p<0.001$ ).

Several studies have shown that blood lactate levels can be considered as a useful indicator in determining the severity of diseases and mortality rates (21,25,26). On the other hand, there are also studies showing that the initial lactate level measured at the time of hospitalization is a poor predictor of mortality. Mortality studies with a single lactate value at the time of hospitalization as well as studies with serial lactate measurements are still controversial (10,22,27).

However, there is no acceptable lactate cut-off value for predicting mortality in critically ill children. In our study, we calculated the cut-off value of blood lactate level for predicting in-hospital mortality. ROC curve analysis revealed that the lactate cut-off value for predicting mortality was 2.55 mmol/L

(sensitivity 81.60%, specificity 77.80%, positive predictive value: 35.10%, negative predictive value: 96.60%). The low positive predictive value but high negative predictive value of this cut-off suggested that the mortality rate would be lower in patients with lactate levels below 2.55 mmol/L. In a similar study, the lactate cut-off value for in-hospital mortality was 5.50 mmol/L. The sensitivity, specificity, positive and negative predictive values of this cutoff value were found to be 61%, 86%, 84% and 66%, respectively (21).

While the adjusted probability of death in patients with a lactate value between 2.50-4 mmol/L is 2.20 (1.10-4.20), there is a 7.10 (3.60-13.90) fold higher probability of death in patients with lactate $\geq$ 4.0 mmol/L (28). In a study conducted by Anil et al. on pediatric patients admitted to the emergency department, it was shown that high lactate levels during hospitalization could predict mortality ( $p<0.001$ ) and the lactate cut-off value was calculated as 5.10 mmol/L (sensitivity 93.30%, specificity 80.60%, positive predictive value 70%, negative predictive value 96.20%) (29). In another study conducted in 1299 children with sepsis, it was emphasized that lactate levels above 36 mg/dL ( $\approx$ 3.60 mmol/L) on admission were associated with 30-day mortality (odds ratio, 3.26; 95% CI: 1.16-9.16) (30).

Patients with high lactate levels are critically ill patients at risk of developing multiple organ failure. Lactate concentrations and mortality rates increase almost linearly. Patients with high lactate levels (>2 mmol/L) beyond the first 24 hours have a higher mortality rate (31). In our study, we found that the mortality rate increased significantly (81.60%) in patients with lactate levels above the cut-off value (>2.55 mmol/L) ( $p<0.001$ ).

In our study, the median value of arterial blood gas lactate in patients who did not survive in the cardiovascular dysfunction group was found to be above the cut-off value (5.35 mmol/L) and below the cut-off value (2.30 mmol/L) in the surviving group.

In this study, it was found that lactate levels were higher in patients with sepsis compared to other etiologies and mortality was higher in patients with sepsis. Andre et al. found that the initial lactate value measured in the emergency service was associated with mortality in patients (32). In our study, lactate levels were >2.55 mmol/L in 84.6% of patients who died due to sepsis. We emphasize the necessity of early initiation of targeted treatment in such patients.

Many studies on human lactate levels have shown that an increase in lactate level from 2.10 to 8 mmol/L decreased survival from 90% to 10% (33). In our study, arterial blood gas lactate level was found to be higher in patients who died. There was a significant correlation between blood lactate levels and mortality scores of the dead patients. Patients with lactate levels above the lactate cut-off value of 2.50 mmol/L had a 1.38-fold increased risk of mortality. Bai et al. reported that a 1 mmol/L increase in lactate levels resulted in a 1.38-fold increase in the risk of death (21).

In our study, we found a high correlation between lactate levels during hospitalization and PRISM-III, PIM-2 and PELOD scores of patients admitted to the PICU ( $p < 0.001$ ). In a previous study, the combined assessment of PRISM-III scores and lactate levels during hospitalization was shown to better in predicting mortality ( $p = 0.018$ ) (21). In another study, lactate level during hospitalization was shown to predict mortality independently of PIM-2 scores in patients admitted to the PICU (10). In their study in patients with sepsis, Scott et al. showed that the median lactate level obtained from venous catheters was 2.26 (IQR: 1.76-3.63) mmol/L in patients with a PELOD score  $\geq 10$  and 2.02 (IQR: 1.44-2.83) in patients with a PELOD score  $< 10$  (34).

As known, mortality scoring systems are calculated by using laboratory and clinical parameters predicting the risk of mortality and give a mortality rate predicted by logarithmic method in terms of the score obtained (20). We think that if arterial blood gas lactate level measurement, which is an important tissue perfusion marker and was shown to be effective in determining the mortality risk in our study, is added to the laboratory parameters in the currently used scoring systems, this may increase the predictive power of the scoring systems.

The most important limitation of our study is that it was retrospective. Reflecting the experience of a single center is another limitation of our study. Another limitation is the uncertainty of the duration of arterial blood gas analysis. We could not accurately measure the time between admission and arterial blood gas sampling. In addition, the lactate value used in the study is the baseline value, not the patient's worst lactate level. In our observational study, patient-specific clinical decisions may also have an impact on the prognosis of patients. However, the adequacy of the number of patients and the threshold value determined for lactate levels are positive aspects of our study. In addition, the results of future studies may contribute to the inclusion of lactate levels in pediatric intensive care mortality scoring systems, which will increase the value of our study.

In conclusion, we found that measuring lactate level in arterial blood gas analysis is useful in predicting mortality in patients admitted to PICUs. We also found a significant correlation between arterial blood gas lactate measurements and mortality scores. We showed that the risk of mortality is increased in patients with lactate levels above the determined cut-off value. In our study, we showed that lactate is a good indicator of mortality. Measurement of lactate levels in PICUs may be useful in early mortality risk classification.

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