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**Brief Report** 

# Prognostic value of neglected biomarker in sepsis patients with the old and new criteria: predictive role of lactate dehydrogenase



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# ABSTRACT

*Objectives*: This study examined the pH, lactate dehydrogenase (LDH), and heart rate values on the first day of hospitalization in patients with a prediagnosis of sepsis and biomarkers that may predict mortality. *Methods*: Patients hospitalized in an emergency intensive care unit with a diagnosis of systemic inflammatory response syndrome were classified as having sepsis (n = 28), septic shock (n = 8), or severe sepsis (n = 8) according to International Sepsis Guidelines (old criteria). Forty-four patients were classified as having sepsis (n = 4), septic shock (n = 30), or infection (n = 10) according to The Third International Consensus Definitions for Sepsis and Septic Shock (new criteria). The effects of these patients' laboratory values on survival between groups were

compared. Significant values were evaluated by  $\chi^2$  automatic interaction detection analysis. *Results:* When the patients were categorized according to the new classification criteria, there was an increase in the number of septic shock patients and a decrease in the number of septis patients. In addition, 10 patients were removed from the sepsis category. There was a significant difference between ex and discharged patients in terms of heart rate, pH, sodium bicarbonate, lactate, and LDH (*P*= .007, *P*= .002, *P*= .034, *P*= .009, and *P*= .002, respectively). Based on a  $\chi^2$  automatic interaction detection analysis of the significant values, pH, LDH, and heart rate were prominent predictors of prognosis.

*Conclusions:* Systemic pH, LDH, and heart rate values may be used to determine the best time to discharge patients from intensive care to other, more affordable hospital units.

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# 1. Introduction

Sepsis is a common condition with a large global effect on health resources and expenditures [1]. It is defined as the presence of infection combined with evidence of associated systemic manifestations; thus, sepsis is also known as systemic inflammatory response syndrome [2]. Although *severe sepsis* is defined as sepsis combined with sepsisinduced organ dysfunction or tissue hypoperfusion, *septic shock* is defined as prolonged sepsis-induced hypotension despite adequate fluid resuscitation [2]. Data from studies conducted in mainly developed countries show that the incidence of severe sepsis (up to 300 cases per 100 000 adults) is increasing [3–5].

Cases of sepsis may be identified from pH, lactate dehydrogenase (LDH), and heart rate values. Blood pH values can be used to determine whether bicarbonate is required as an emergency treatment for sepsis and the necessity of intubation in patients with respiratory problems [6,7]. Increasing serum LDH levels can reveal the extent of tissue injury,

\* Corresponding author. Tel.: +90 532 483 38 81 (Mobile). *E-mail address:* drturkdogan@gmail.com (K.A. Turkdogan). necrosis, and hypoxia. A patient's 24-hour heart rate is a useful prognostic tool; in previous studies, a heart rate of 106 beats per minute was the only cardiac parameter that predicted a favorable outcome [8,9].

The purpose of this study was to examine the pH, LDH, heart rate, and lactate values on the first day of hospitalization in patients with a prediagnosis of systemic inflammatory response syndrome at our intensive care unit and biomarkers that may predict mortality.

#### 2. Materials and methods

Overall, 44 of 585 patients who received follow-up care in our emergency intensive care unit were diagnosed with sepsis; at our hospital, approximately 80 000 patients were hospitalized each year between January 1, 2014, and December 31, 2014. Ethics approval was received from the relevant local ethics committee (approval no. 2015/626).

The patients were classified as having sepsis, severe sepsis, or septic shock according to International Sepsis Guidelines (old criteria) [2]. The same patients were classified as having sepsis and septic shock, as shown below, according to the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3; new criteria) [10]. Sepsis:

- respiratory rate of 22 breaths per minute,
- altered mentation, and
- systolic blood pressure of 100 mm Hg.

## Septic shock:

- sepsis diagnosis;
- vasopressor therapy needed to elevate the mean arterial pressure to greater than or equal to 65 mm Hg, and
- lactate greater than 2 mmol/L (18 mg/dL) despite adequate fluid resuscitation.

The arterial blood gas, hemogram, and biochemical test results of the patients were reviewed retrospectively. The significance of these values between groups and their effect on mortality were compared.

#### 2.1. Statistical analysis

Descriptive statistics for categorical variables are shown as percentages; the  $\chi^2$  test was used to compare groups. The fit of continuous variables to a normal distribution was investigated using the Kolmogorov-Smirnov test; descriptive statistics are presented as the median (25%-75%) because none of the variables displayed a normal distribution. The Mann-Whitney *U* test was used for group comparisons. A  $\chi^2$  automatic interaction detection (CHAID) analysis was performed to determine the effective factors for sepsis status and the correlation between these factors. *P*<.05 was accepted as significant.

## 3. Results

The average age of the 44 patients included in the study was 78.0 years (69.0-83.7) Fourteen (31.8%) of the patients were women. The mean duration of hospitalization was 6.5 days (3.0-12.75). Twenty-four (54.5%) of the patients died during the follow-up period.

The average systolic blood pressure of the patients was 90.0 mm Hg (80.0-110.0), the average diastolic blood pressure was 50.0 mm Hg

(46.2-63.7), the average heart rate was 100.0 beats per minute (90.0-118.0), the average respiratory rate was 24.0 breaths per minute (18.5-28.0), and the average body temperature was  $36.5^{\circ}$ C ( $36.0^{\circ}$ C- $37.1^{\circ}$ C).

Tables 1 and 2 show the demographic data and laboratory results of the patients, who were classified according to International Sepsis Guidelines (old criteria) and the Sepsis-3 (new criteria).

When the new sepsis criteria were applied, 10 of the 28 sepsis patients were excluded, whereas 14 were added to the septic shock group and included in the evaluation of lactate (Table 3).

Table 4 shows the demographic data and vital and laboratory results of the patients, classified according to survival. Significant differences were detected between the exitus and discharged patients in terms of heart rate, pH, formate, lactate, and LDH (P= .007, P= .002, P= .034, P= .009, and P= .002, respectively).

Based on the CHAID analysis, which was conducted to determine the status of the discharged the patients according to mortality without classifying them as having sepsis or septic shock, pH, LDH, and heart rate were the most prominent of the 5 values (Figure). The rate of exitus was 92.3% in patients who had a pH value less than or equal to 7.32 and 38.7% in patients who had a pH value greater than 7.32. In patients who had a pH value greater than 7.32. In patients who had a pH value greater than 7.32. In patients who had an LDH value less than or equal to 265 U/L and 81.8% in patients who had an LDH value greater than 265 U/L. The rate of exitus was 0% in patients who had an LDH value less than 265 U/L and a heart rate of less than or equal to 105 beats per minute, whereas the rate of exitus was 50% in patients who had a heart rate greater than 105 beats per minute. The cross-validation error of our model was 0.07, the sensitivity was 87.5%, and the specificity was 85.0%.

## 4. Discussion

The reported inhospital mortality ratio for patients with severe sepsis or septic shock is between 20% and 50% [4,11–14]. The intensive care mortality ratio in our study was 54.5%, which is slightly higher than the

Table 1

Demographic data, vital findings, and laboratory results of all patients according to International Sepsis Guideline

	Sepsis $(n = 28)$	Septic shock $(n = 8)$	Severe sepsis $(n = 8)$	Р
Characteristics				
Age (v)	79.5 (70.2-84.0)	71.5 (57.7-82.7)	73.5 (61.2-79.5)	.181
Female sex	6 (21.4%)	3 (37.5%)	5 (62.5%)	.110
Hospitalization duration	7.0 (4.0-15.0)	3.5 (1.0-5.5)	8.5 (3.5-11.7)	.131
Ex	13 (46.4%)	5 (62.5%)	6 (75.0%)	.386
Vital findings				
Systolic blood pressure	110.0 (90.0-120.0)	70.0 (66.2-70.0)	82.5 (80.0-90.0)	<.001
Diastolic blood pressure	60.0 (50.0-70.0)	40.0 (40.0-45.0)	50.0 (41.2-50.0)	<.001
Heart rate	100.0 (90.0-110.0)	117.0 (92.5-135.0)	112.5 (85.0-127.5)	.181
Respiratory rate	25.0 (18.5-28.0)	22.0 (18.5-27.0)	24.0 (19.5-28.7)	.635
Fever	36.7 (36.1-38.0)	36.1 (35.0-37.9)	36.2 (36.1-36.6)	.120
Laboratory results				
рН	7.42 (7.37-7.48)	7.3 (7.20-7.4)	7.33 (7.25-7.47)	.125
po <sub>2</sub>	81.3 (55.8-116.5)	73.6 (63.8-94.6)	50.1 (46.8-88.4)	.308
pco <sub>2</sub>	35.4 (28.8-41.9)	30.4 (27.4-41.5)	34.4 (27.0-72.5)	.645
Hco <sub>2</sub>	21.7 (19.4-25.5)	15.7 (13.9-23.0)	18.9 (14.5-24.9)	.107
Lactate	2.0 (1.4-3.1)	2.4 (1.3-3.1)	3.9 (2.2-3.9)	.117
WBC	13.0 (9.3-18.2)	14.3 (10.7-22.1)	16.3 (12.4-42.1)	.340
Neutrophil	11.1 (6.5-16.1)	12.8 (8.7-20.3)	13.5 (9.5-38.0)	.302
Lymphocyte	1.0 (0.6-1.8)	0.9 (0.6-1.3)	1.3 (0.8-1.9)	.601
Platelet	218 (152.5-323.0)	220.0 (114.7-553.0)	284.0 (179.0-366.0)	.691
NLR	11.3 (4.9-27.3)	14.8 (10.0-19.7)	11.4 (5.9-28.1)	.596
PLR	185.6 (124.7-331.9)	112.4 (96.8-494.1)	187.8 (140.5-245.2)	.737
ALT	23.0 (12.0-58.0)	40.0 (10.2-121.0)	25.0 (9.0-38.7)	.701
AST	32.5 (19.2-56.7)	52 (22.5-234.5)	29.0 (21.0-73.7)	.459
LDH	265.0 (232.0-385.0)	568.5 (211.5-743.0)	250.0 (215.0-540.0)	.372
CRP	128.3 (58.7-205.0)	209.2 (103.4-259.5)	184.4 (133.5-265.8)	.179
Procalcitonin	2.2 (1.0-14.2)	27.1 (0.9-57.3)	1.7 (0.6-7.2)	.819

Abbreviations: Ex, exitus; WBC, white blood cell; NLR, neutrophil lymphocyte ratio; PLR, platelet lymphocyte ratio; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein.

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