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Correlation of lactate levels with sequential organ failure assessment (SOFA) score in sepsis patients in H. Adam Malik Hospital Medan



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ABSTRACT

Introduction: Lactate is an intermediate metabolic that is non-toxic and were produced by all cells. In sepsis patients, increased lactate occurs due to tissue hypoperfusion and represent a sign of tissue hypoxia. A clinical scoring system such as Sequential Organ Failure Assessment (SOFA), was commonly utilized to assess the severity of sepsis periodically based on several clinically significant organ dysfunction. The purpose of this study was to investigate the correlation of lactate levels with SOFA scores on sepsis patients treated in ICU.

Method: This is a prospective cohort study, involving 57 patients with sepsis who met the inclusion and exclusion criteria. The blood lactate levels were measured, and the SOFA scores were calculated, which then analyzed with Spearman correlation test.

Results: There was a weak but significant correlation between lactate levels and 24-hour SOFA Score ($r = 0.303$, $p = 0.022$). An intermediate correlation was obtained with 48 hours SOFA Score ($r = 0.449$, $p = 0.000$). Organ dysfunction that plays a significant role in increased lactate in this study were the central nervous system, respiratory system, liver, and kidneys.

Conclusion: There was an association between lactate levels and SOFA scores at 24th and 48th hour. SOFA Score can be considered as proper parameters to evaluate the deterioration of septic patients treated in the ICU.

Keywords: Lactate, Organ Dysfunction, Sepsis, SOFA Score

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INTRODUCTION

Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection.^{1,2} Global incidence between 1995 - 2015 was 437 per 100 thousand peoples per year for sepsis and severe sepsis. Sepsis contributes to one of the two to three mortality in hospital cohort studies.³

Sepsis causes death in more than 200,000 people per year in the United States. The incidence of severe sepsis and septic shock has increased in the last 20 years.⁴ Data from Indonesia is scarce, but one study conducted in a hospital in Bandung, 192 patients were obtained for a period of a year.⁵

To assess the severity of the disease based on serial organ dysfunction, a clinical score was routinely used. One that widely used in sepsis was Sequential Organ Failure Assessment (SOFA). Compared to other scores, SOFA scores allow clinicians to monitor the entire disease process.⁶ This score was derived from the values of clinical and laboratory parameters. Albeit, there were obstacles in the process of implementing this scoring system, among those was the number of laboratory parameters needed as it might increase the health cost.³

In sepsis patients there can be an increase in lactate due to tissue hypoperfusion, and lactate can represent a sign of tissue hypoxia. Lactate is an intermediate substrate that is actually non-toxic and was produced by all cells. Blood lactate has long been known as an indicator of disease severity and as a predictor of disease prognosis. Lactate can also be used to monitor the progress in the management of circulatory shock and as a prognosis variable in a variety of acute and critical conditions.⁷

The study conducted by Khater et al. found a significant correlation between lactate levels and SOFA scores ($r = 0.403$ with a value of $P = 0.010$).⁸ The similar result reported by Irwan, et al. shown by significant Spearman correlation test of $r = 0.767$ ($p < 0.001$).⁹ Based on those result, the purpose of this study was to confirm the relationship of lactate levels with SOFA scores in septic patients. The intention was to support the use of SOFA Score as alternative parameter which more accessible, low cost and simple enough to utilized in limited resources facilities with adequate accuracy.

METHOD

The research was conducted at Department of Clinical Pathology FK USU / RSUP H. Adam Malik Medan in collaboration with the Department of Anesthesiology and Intensive Therapy, FK-USU / RSUP H. Adam Malik Medan. This study began in May 2018 till July 2018. The research subjects were male and female patients who were diagnosed with sepsis and were admitted to RSUP H. Adam Malik Medan. A total of 57 sepsis patients (29 males and 28 females) who fulfill the inclusion criteria (ages 18-65 years) and exclusion criteria (patients with chronic liver failure, chronic renal failure, and patients who had received bicarbonate therapy). Each patient has its blood lactate measured and SOFA scores calculation. Both SOFA Score and Blood Lactate was examined three times, at arrival (H-0), at 24th hour (H-24) and at 48th hour (H-48). SOFA score consist of an assessment of 6 organ systems, each of which has a value between 0 - 4 based on the degree of dysfunctions. Determining the value of each organ system is based on one or more variables. Blood lactate examination conducted according to the principle of colorimetric examination by Accutrend Plus Cobas tool.

This research was conducted after obtaining approval from the Health Research Committee, Faculty of Medicine, University of North Sumatra. The results of the study were analyzed statistically with Computer software. Characteristics of

the subjects in the study were presented in table format. The relationship between lactic acid levels and SOFA scores was analyzed using the Spearman correlation test.

RESULT

From 57 samples participating in this study, almost equal male (50.9%) and female (49.1%) were recruited. The results of the statistical analysis found the mean (SD) age of the study sample was 51.1 years (14.2 years). The median of procalcitonin is 10.0 with a min-max value of 3.08-100. The underlying disease was dominantly non-surgical 47 people (82.5 %), while surgical only ten samples (17.5%).

The results of the statistical analysis found that the median SOFA score at H-0 of the study sample was 5.0, with a min-max 2.0 - 11.0 value. The median SOFA score at H-24 of the study sample was 4.0, with a min-max value of 0.0 - 12.0. The median SOFA score at H-48 of the study sample was 3.0, with a min-max value of 0.0 - 12.0 (table 2).

The results of the statistical analysis found that the median lactate level at H-0 in the study sample was 2.5 mmol / L, with a min-max value of 2-5.6 mmol / L. The median lactate levels H-24 of the study sample was 2.3 mmol / L, with a min-max value of 0.9 - 10.5 mmol / L. The median lactate levels H-48 of the study sample was 2.1 mmol / L, with a min-max value of 0.7-20.0 mmol / L (table 3).

Table 1 Characteristics of Subjects (n=57)

Characteristics	N (%)	Mean \pm SD* or Median (min - max)**
Gender, (%)		
Male	29 (50.9)	
Female	28 (49.1)	
Age (year)		51.1 \pm 14.2
Underlying disease (%)		
Surgical	10 (17.5)	
Non-surgical	47 (82.5)	
Procalcitonin		10 (3.08-100)

Note: Data variables that are normally distributed are presented in mean and standard deviation (SD)*, while variable data that are not normally distributed are presented in the median value (min-max)**

Table 2 Characteristics of Initial Measurement of the SOFA Score (n=57)

Characteristic	Median	Min.	Max.
SOFA Score H-0	5.0	2.0	11.0
SOFA Score H-24	4.0	0.00	12.0
SOFA Score H-48	3.0	0.00	12.0

Note: Data are presented as mean \pm SD and Median (min-max)

Table 3 Characteristics of Measurement of the lactate (n=57)

Characteristic	Median	Min.	Max.
lactate H-0	2.5	2	5.6
lactate H-24	2.3	0.9	10.5
lactate H-48	2.1	0.7	20.0

Note: Data are presented as mean ± SD and Median (min-max)

Table 4 Correlation between lactate levels with SOFA Score

Variable	r	P
lactate -SOFA score H-0	0.010	0.940
lactate -SOFA score H-12	0.303	0.022
lactate -SOFA score H-24	0.449	<0.0001

Note : Correlation between lactate levels with SOFA scores was analyzed using the Spearman correlation test. The significance of the correlation is at the level of <0.05. The strength of correlation 0.0- <0.2 is very weak; 0.2- <0.4 is weak; 0.4- <0.6 medium; 0.6- <0.8 strong; 0.8-1.0 is very strong

Table 5 Correlation between lactate levels in Each SOFA Score Variable

Variable	r	P
Lactate -PaO2/FiO2		
H-24	-0.287	0.030*
H-48	-0.234	0.049*
Lactate -GCS		
H-24	-0.321	0.015*
H-48	-0.327	0.013*
Lactate - Total Bilirubin		
H-24	0.255	0.056
H-48	0.518	<0.0001*
Lactate -Creatinine		
H-24	0.128	0.341
H-48	0.345	0.008*
Lactate -Platelets		
H-24	-0.013	0.925
H-48	-0.164	0.223
Lactate-MAP/Vasopressor		
H-24	-0.066	0.624
H-48	-0.229	0.086

Note : Correlation of lactate levels with SOFA scores was analyzed using the Spearman correlation test. The significance of the correlation is at the level of <0.05. The strength of correlation 0.0-1.9 (very weak); 0.2-3.9 (weak); 0.4-5.9 (medium); 0.6-7.9 (strong); 0.8-1.0 (very strong).

The results of statistical analysis showed that there was no significant correlation between lactate level with SOFA scores at H-0 with values $r = 0.010$ and $P = 0.940$. The results of statistical analysis showed that there was a significant positive correlation between lactate level H-24 and SOFA score H-24 with a value of $r = 0.303$ and $P = 0.022$. The results of the statistical analysis showed that there was a significant positive correlation with lactate level H-48 with SOFA

score H-48 with $r = 0.449$ and $P = <0.0001$ (table 4).

DISCUSSION

In this study, it was seen that the number of male sepsis patients was almost the same as female patients, in contrast to study in Australia showing the proportion of male patients as much as 59.6%. Likewise European studies which found that the

proportion of male patients was two times more than the female patient.¹⁰ Age of patients varied with the youngest 18 years old and the oldest 65 years old with a mean of 51.1 ± 14.2 years. The age mean and the range was younger than research data in the United States in 1995-2000 which showed an average of 60.8 ± 13.7 years.¹¹ This could be due to the fact that in Indonesia it is still dominated by infectious diseases.¹²

The reduction of SOFA score in the first 48 hours is obtained after the patient enters the ICU (table 2), from the initial score of 5.0 to 3.0. According to Ferreira et al., that initial SOFA scores, highest and average sofa scores are related to mortality rates and can be used to assess the degree of organ dysfunction when first entering the ICU. Sofa score ≥ 11 has a mortality rate of $> 90\%$ and a reduction in this score in 48 hours is associated with a 6% decrease in mortality rate and if this score does not change or tends to increase then the mortality rate increases by 37% in the initial score of 2-7 and 60% if the initial score is 8-11.¹³

The tendency to decrease the level of arterial lactate seen from the beginning of hospital admission to 48 hours of treatment. Changes in lactate value (kinetic lactate) from 0 to 48 hours (table 3) illustrate changes in anaerobic metabolic conditions which are mainly affected by changes in disease conditions and interventions carried out on critically-ill patients.¹² This supports the use of blood lactate concentration as a parameter to assess tissue oxygenation of patients treated in the ICU.⁷

Lactate levels and SOFA scores in the first hour were examined at the first time when the patient entered the ICU (table 4), and it showed no significant correlation between the two. Sepsis will cause changes in the metabolic and hormonal systems in order to maintain body homeostasis. Intensive and prolonged stress responses will be associated with increased morbidity and mortality. In patients in critical condition, failures of compensatory mechanism, initiates imbalances which threaten body homeostasis. The initial metabolic response is characterized by tissue hypoperfusion and a decrease in overall metabolic activity and lasts 12-24 hours, and the peak is around 3-5 days.¹⁴

Investigations of lactate clearance at 6th, 12th and 24th hours in septic patients showed only 24th-hour lactate clearance associated with mortality.¹⁵ Bakker et al., reported that lactate clearance at the 24th hour and the length of lactic acidosis was a predictor significant for hospital mortality.¹⁶

The Spearman correlation test was also conducted between lactate levels on the variable which composed SOFA score. The analysis

included PaO₂ / FiO₂, GCS, total bilirubin, creatinine, platelets and MAP / Vasopressor at 24th and 48th hours. Based on the analysis conducted, it was found that organ dysfunction which has a significant role in increasing lactic acid in this study is the central nervous system, respiration, liver, and kidney. The same was found in the study conducted by Hambali, where the organ dysfunction was most often found.¹²

In this study, there was no association between lactate and platelet and cardiovascular variables. In contrast to the research conducted by Irwan, significant correlation was found between coagulation dysfunction and lactate levels ($r = 0.469$, $P = <0.0001$) and cardiovascular dysfunction with lactate levels ($r = 0.618$, $P = <0.0001$).⁹ These results indicate that in a state of hyperlactatemia, increased lactate formation in critical patients does not only occur under hypoxic conditions but can also occur as a result of increased aerobic glycolysis (cell hypermetabolism) with sufficient oxygen supply conditions.¹⁶

CONCLUSIONS

There is a significant positive correlation between lactate levels and SOFA score at 24th and 48th Hour. Additionally, PaO₂ / FiO₂, GCS, total bilirubin and creatinine, components of SOFA scores were related to lactate levels. This results indicate that SOFA Score at 24th and 48th hour can be considered as proper parameters to evaluate the deterioration of septic patients treated in the ICU. It is simpler, more accessible and cheaper.

ETHICAL CLEARANCE

Ethical approval had been conducted by Ethics of Committee at University of Sumatera Utara.

CONFLICT OF INTEREST

The authors declare there is no competing interest regarding manuscript.

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AUTHOR CONTRIBUTION

All authors are responsible as contributor regarding the content of manuscript.

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