



THE LACTATE/ALBUMIN RATIO AS A PREDICTOR OF MORTALITY SEPSIS PATIENTS IN ICU. H. ADAM MALIK HOSPITAL MEDAN AND CONNECTED TO SOFA SCORES

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KEYWORDS :

I. Introduction

Sepsis is a systemic inflammatory response syndrome with a proven or suspected microbial etiology. The clinical evidence is abnormal body temperature ($> 380\text{ C}$ or $< 360\text{ C}$), tachycardia; metabolic acidosis; usually accompanied by respiratory alkalosis and tachypneu; and increase or decrease in the number of white blood cells. Sepsis can also be caused by a viral or fungal infection.¹⁵

Sepsis is still the leading cause of death in critical cases in various parts of the world. The high incidence and problems of infection which are usually associated with developing country conditions or places with less hygiene, are not entirely true. Data from the Center for Disease Control (CDC) shows that the incidence of sepsis increases $\pm 8.7\%$ every year, from 164,000 cases (83 per 100,000 populations) in 1979 to 660,000 cases (240 cases per 100,000 population) in 2000. Sepsis is cause of death number 11 from all causes of death. In the United States as well as a developed country, annual deaths from sepsis reach 70,000 people. About 500,000 new cases experience sepsis where the death reaches 35%. This mortality rate tends to rise and now ranks 10th in the cause of death in the United States.^{8,12,16,17}

Multi organ dysfunction syndrome is common in intensive care units. The occurrence of multi-organ dysfunction syndrome increases patient mortality. Tissue hypoperfusion is an important factor in the occurrence of organ dysfunction. In tissue hypoperfusion occurs distribution of blood flow to the organ or microvascular or the inability of cells to use oxygen (hypoxic cytotoxic). Cytotoxic hypoxia results in anaerobic metabolism in the cytosol which will increase lactate formation. Increased blood lactate levels indirectly indicate overall severity of organ dysfunction associated with increased mortality risk.¹⁸

Lactate is considered a byproduct of the glycolysis process under hypoxic conditions. Hyperlactatemia in sepsis occurs due to tissue hypoperfusion, and lactate represents a sign of tissue hypoxia. This occurs because of microcirculation dysfunction that has occurred since the beginning of sepsis and is the initial critical stage of the condition of tissue hypoxia and organ failure.^{1,10,20}

High blood lactate levels at the start of the examination and levels that remain high, are associated with poor outcomes. Duke and colleagues conducted a prospective study of 31 patients with severe sepsis in the ICU, he found that blood lactate was the earliest predictor of mortality known at the earliest measurement 12 hours after entering intensive care. Blood lactate levels $> 3\text{ mmol / L}$ at 12 hours after entering PICU had a positive predictive value for death of 56%.^{2,3}

The incidence of hypoalbuminemia can occur in 60-70% of patients with sepsis. Hypoalbuminemia is said if the plasma albumin level is $< 3.5\text{ gr / dL}$. Hypoalbuminemia can increase the risk of morbidity and mortality. In a meta-analysis study found that every decrease in blood albumin was 1.0 gr / dL , the mortality rate increased by 137% and morbidity 89%.

In sepsis patients there is a decrease in albumin synthesis, a shift in distribution from the intravascular compartment to the interstitial, and the release of hormones that increase the deconstruction of albumin metabolism associated with the inflammatory reaction. Low blood albumin levels in sepsis describe endothelial leakage, rather than describing malnutrition.^{5,13}

In sepsis patients there is a metabolic stress response that affects albumin distribution in the intravascular and interstitial compartments, and changes the rate of protein synthesis and degradation. Sepsis is an infection condition accompanied by a systemic response where there is an increase in the release of inflammatory mediators such as Interleukin-1 (IL-1), Interleukin-6 (IL-6) and tumor necrosis factor (TNF) and increased production of counter regulatory hormones such as catecholamine, cortisol, glucagon, growth hormones, which have an effect on the metabolic status and nutrition of patients.

Based on the concept above, it is necessary for a laboratory marker or physiological organ to be needed to describe the presence of organ dysfunction that is in line with the inflammatory concept of sepsis. This is needed in defining more specifically the occurrence of multi-organ dysfunction syndrome that is useful in the classification or scoring of organ dysfunction scoring system such as overall SOFA score is an objective measurement specifically in measuring multi-organ dysfunction syndrome and aims to describe the severity of the disease or prognosis of patients in intensive care.¹³

Then the Lactate / albumin ratio can be used as a marker of predictors of mortality in patients with sepsis. And high mortality and poor prognosis were seen in patients with Lactate / albumin ratios > 0.15 , this result was obtained based on the Lichtenauer et al. Study, data collected retrospectively from 348 patients from January 2004 - December 2009 septic patients treated in ICU. Assessment of organ dysfunction using a SOFA score and quantitative measurement of the Lactate / albumin ratio.¹³

II. Research Purposes

This study aims to determine the Lactate / Albumin ratio in sepsis patients, so that it can be used as a marker marker

predictor of mortality in sepsis patients that is more accessible at a cheaper and more specific cost for sepsis that can be used in simple facilities without reducing accuracy.

III. Research Methods

The research was carried out in the Faculty of Medicine, Universitas Sumatera Utara Pathology Department / H. Adam Malik General Hospital in Medan in collaboration with the Department of Anesthesiology & Intensive Therapy at the Faculty of Medicine, Universitas Sumatera Utara / H. Adam Malik General Hospital in Medan. This study was an observational study with a cohort data collection method - prospective. The study was conducted in August 2018 - September 2018. The research subjects were men and women age > 17 years and <65 years and sepsis patients according to the Surviving Sepsis Campaign: The International Guidelines for Management of Severe Sepsis and Septic Shock: 2016 were treated in the Medan Adam Malik Hospital ICU. The research subjects were 61 patients, with 4 patients dropping out. Routine blood tests using K2EDTA blood samples which were examined under 5 hours using the Sysmex XN-1000 automatic cell counter analyzer, this tool uses a combination of electric impedance and flow cytometry. Examination of arterial lactate using the Accutrend Plus Cobas device with the principle of colotimetry examination. Albumin examination in serum (quantitation) was examined with bromocresol green method, using ARCHITECT PLUS C1 4100 with the principle of specometry.

IV. Statistic Analysis

Data analysis was performed using SPSS software (Statistical Package for Social Sciences, Chicago, IL, USA) for Windows. Characteristics of the subjects in the study are presented in tabulation form and described. Correlation of lactate / albumin levels was used Pearson correlation test if the data were normally distributed. If the data is not normally distributed, Spearman rank test is used. All statistical tests with a value of p <0.05 were considered significant.

V. Results and Discussion

This study used collected samples according to the inclusion criteria in this study as many as 57 patients who were admitted to the H. Adam Malik Hospital ICU Medan. 29 people from all samples were male (50.9%) and the remaining 28 people (49.1%) were women. In contrast to research in Australia, the proportion of male patients was 59.6%. Likewise European studies found that the proportion of male patients was 2 times more than the female patient group.¹⁴ Overall participants had an average age of 51.31 years with a standard deviation of 13.94 years. The youngest age is 18 years and the oldest is 65 years old. This can be caused because in Indonesia is still dominated by infectious diseases. The level of control of lower comorbidities is another factor that is believed to cause the average age of patients with severe sepsis in this study to be lower compared to existing studies abroad (Table 1).⁷

Table 1. Characteristics of Patients (n=57)

Variable	n (%)
Gender	29 (50,9 %)
• Man	28 (49,1 %)
• Women	
Age (Mean±SD / Min / Max)	51,31 ± 13,94 / 18 / 65

Remarks: Data are presented as mean ± SD and Median (min / max) 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 Measurements

Variable	Median	Min – Max
Laktate Day 1	2,50	2,0 – 5,60

Laktate Day 3	2,10	0,70 – 10
Albumin Day 1	2,7	1,30 – 3,80
Albumin Day 3	2,5	1,60 – 3,80
SOFA Score Day 1	5	1,00 – 11,00
SOFA Score Day 3	3	0,0 – 12,00
Ratio Laktate / Alb Day 1	0,89	0,55 – 2,52
Ratio Laktate / Alb Day 3	0,84	0,21 – 3,86

In this study there was a tendency to decrease arterial lactate levels from the start of hospital admission to 48 hours of treatment. Changes in the value of lactic acid (kinetic lactate) from the 0th to 48th hours illustrate changes in anaerobic metabolic conditions which are mainly affected by changes in disease conditions and interventions carried out on critically ill patients.⁷

Day 1 albumin measurement with a range of 1.30 g / dl - 3.80 g / dl with a median of 2.7. While the level of albumin day 3 with a range of 1.60 g / dl - 3.80 g / dl with a median of 2.5. There was no difference with the Farhad et al 2016 study, where there was a tendency for the average albumin concentration to decrease from the beginning to the third day's observation. Albumin is an acute phase protein, thus the level of hypoalbuminemia in sepsis patients correlates with the intensity of the inflammatory response triggered by infection.

The measurement of the SOFA score obtained varies greatly with a range of 1-11 on the first day with a median of 5. The third day SOFA score with a range of 0 - 12 with a median 3. There is no difference with the Harnowo Wilujeng study showing the results of the average SOFA score observation the beginning of the first day (24th hour), and the third (72nd hour) shows a decrease.²¹ 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 decrease in this score in 48 hours is associated with a decrease in mortality rate of 6% and if this score does not change or tends to increase then the mortality rate increases 37% in the initial score of 2-7 and 60% if the initial score is ^{8-11,4}

The measurement of day 1 Lactate / Albumin ratio varies greatly with a range of 0.55 - 2.52 with a median of 0.89, while the Lactate / Albumin ratio of day 3 with a range of 0.21 - 3.86 with 0.84. There is a tendency for the lactate / albumin ratio to decrease from the first day to the third day due to improved perfusion and reduced tissue hypoxia so that anaerobic glycolysis also decreases with the final result of reduction in lactate production. And also a decrease in the risk of albumin destruction caused by the inflammatory response. This is in line with the process of glycolysis under hypoxic conditions. Hyperlactatemia in sepsis occurs due to tissue hypoperfusion. At the same time there will be an increase in counter regulation hormones which result in albumin destruction to hypoalbuminemia in sepsis patients correlated with the intensity of the inflammatory response triggered by infection.

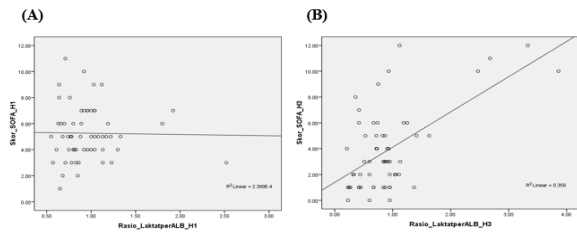
Table 3. Relationship to Lactate Ratio / Day Albumin with SOFA Score Day 1, and Relationship to Lactate Ratio / Albumin Day 3 With SOFA Score Day 3

Variable	R	P value
Ratio Laktat / Albumin Day 1		
SOFA Score Day 1	0,054	0,690
Ratio Laktat / Albumin Day 3		
SOFA Score Day 3	0,361	0,006

Description: The relationship of the lactate / albumin ratio in each SOFA score variable was analyzed using the Spearman

correlation test statistical test. The significance of the correlation is at the level of <0.05 . The strength of the correlation 0.01 - 0.09 is less significant; 0.10 - 0.29 weak; 0.30 - 0.49 medium; 0.50 - 0.69 is strong; 0.7 - 0.89 is very strong; > 0.90 is near perfect, (-) there is an inverse relationship between the two variables measured.

Figure 1. (A) Relationship of Lactate Ratio / Day Albumin With SOFA Score Day 1, (B) Relationship to Lactate Ratio / Albumin Day 3 With SOFA Score Day 3



The Spearman Correlation Test statistical test showed that the Lactate / Albumin ratio of day 1 did not have a significant relationship with the day 1 SOFA score with ($r = 0.054$ and $p = 0.690$). But based on the Spearman Correlation Test statistical test shows the Lactate / Albumin ratio of day 3 there is a significant relationship with the day 3 SOFA score with ($r = 0.361$) and ($p = 0.006$).

Based on the research of Lichtenauer et al., Using the Lactate / albumin ratio > 0.15 , the same cut-off was used in this study and the same results were obtained so that the lactate / albumin ratio could be used as a predictor of mortality in sepsis patients.

VI. Conclusions and recommendations

In this study there is a significant positive relationship between day lactate / albumin ratio 3 and day 3 SOFA score in sepsis patients, so that the Lactate / Albumin ratio can be used as a predictor of mortality in sepsis patients associated with SOFA scores. But there was no significant relationship between day lactate / albumin ratio level and day 1 SOFA score in sepsis patients. Based on the results of this study it can be suggested that the serial lactate / albumin ratio associated with the SOFA score can be used as a marker for predictors of mortality in septic patients admitted to the ICU.

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