



## Comparison between plasma lactate and lactate clearance with the impact of acute phase complication in burn injury patient

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### ABSTRACT

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Severe burn can cause rapid loss of intravascular volume with resultant a decrease in peripheral blood flow which reduces tissue oxygen transport and in turn, increases plasma lactate. Plasma lactate and lactate clearance are useful parameters to compare complicated and uncomplicated burn patients in the acute phase. The study aimed to evaluate the initial and 24-h plasma lactate levels as well as lactate clearance as useful parameters to assess acute phase complications of burn patients. This was a cross-sectional study involving 35 burn patients who admitted at Abdul Wahab Sjahranie District Hospital, Samarinda during the period of September 2018 to September 2019. The study was immediately begun after admission of the patients. Plasma lactate levels were measured at admission and 24-h after the first measurement. The acute phase complication was assessed 72 h after burns from the laboratory parameter. Fisher's exact test and t test using SPSS software version 24 were applied for statistical analysis. The 24-h plasma lactate level ( $p = 0.001$ ) and plasma lactate clearance ( $p = 0.002$ ) were significantly correlated with the occurrence of acute phase complications of burns. However, the initial plasma lactate level was not significantly correlated ( $p = 0.609$ ). In conclusion, there is a significantly correlation between 24-h plasma lactate level and plasma lactate clearance are with the occurrence of acute phase complications of burns.

### ABSTRAK

Luka bakar yang parah dapat menyebabkan hilangnya cairan intravaskuler dengan cepat yang berakibat terjadinya penurunan aliran darah perifer dan kurangnya transport oksigen jaringan yang pada gilirannya, meningkatkan laktat plasma. Kadar laktat plasma dan klirens laktat merupakan parameter yang bermanfaat untuk membedakan pasien luka bakar dengan komplikasi dan tidak dengan komplikasi pada fase akut. Penelitian ini bertujuan untuk mengkaji kadar laktat plasma awal dan 24-jam serta klirens laktat sebagai parameter yang bermanfaat untuk mengukur komplikasi fase akut pasien luka bakar. Penelitian dengan rancangan potong lintang ini melibatkan 35 pasien luka bakar yang masuk di RSUD Abdul Wahab Sjahranie, Samarinda selama periode September 2018 sampai September 2019. Penelitian segera dimulai saat pasien masuk untuk dirawat di rumah sakit. Kadar laktat plasma diukur pada saat masuk rumah sakit dan 24-jam setelah pengukuran pertama. Komplikasi fase akut ditetapkan 72-jam setelah kejadian luka bakar berdasarkan parameter laboratorium. Uji eksak Fisher dan uji t menggunakan perangkat lunak SPSS versi 24 dilakukan untuk analisis statistik. Kadar plasma laktat 24-jam ( $p = 0.001$ ) dan klirens plasma laktat secara bermakna berhubungan dengan kejadian komplikasi fase akut pada luka bakar. Namun demikian, kadar plasma laktat awal tidak mempunyai hubungan yang bermakna ( $p = 0.609$ ). Dapat disimpulkan, terdapat hubungan bermakna antara kadar laktat plasma 24-jam dan klirens laktat plasma dengan kejadian komplikasi akut pada luka bakar.

### Keywords:

initial plasma lactate;  
24-h plasma lactate;  
plasma lactate clearance;  
acute phase complication;  
burn;

## **INTRODUCTION**

Burn is tissue damage caused by contact with a heat source such as fire, hot liquid, chemicals, electricity, and radiation.<sup>1</sup> Burns is still a trauma with high morbidity and mortality.<sup>2</sup> Severe burn or burn that over 20% in adults and 10% in children develop a severe capillary leak that results in rapid loss of intravascular volume called burn shock.<sup>3,4</sup> Decreased total plasma volume caused by hemodynamic change resulting in decreased peripheral blood flow.<sup>5</sup> This hypovolemic condition will cause reduced tissue oxygen transport. As a result, oxygen delivery to vital organ is unable to meet oxygen demand.<sup>6,7</sup> Cells switch from aerobic metabolism to anaerobic metabolism, resulting in increased plasma lactate levels.

Lactate is produced by most tissues in the human body, with the highest level of production found in muscle. Under normal conditions, lactate is rapidly cleared by the liver with a small amount of additional clearance by the kidneys. In anaerobic conditions, pyruvate is produced via glycolysis and then enters the Krebs cycle, largely bypassing the production of lactate. Under anaerobic conditions, lactate is an end product of glycolysis and feeds into the Cori cycle as a substrate for gluconeogenesis. Prolonged anaerobic conditions will cause cells to become damaged which eventually causes multiorgan damage.<sup>8,9</sup>

If the hypovolemic condition is not corrected, the cells will suffer a prolonged hypoxic state characterized by an increase in plasma lactate, which will eventually lead to multiorgan disorder. Acute phase complication occurs 48-72h after exposure to burns, and are the earliest complication that can be assessed if the resuscitation management of burns is inadequate.<sup>8</sup> Therefore, optimal guidelines for successful resuscitation are still being studied. Ideal markers of adequate resuscitation are by monitoring

tissue hypoxia, that can predict patient with acute phase complication. Normal lactate values are <2mmol/L, previous studies have shown a plasma lactate cutoff of 2mmol/L. where plasma lactate values  $\geq 2$  mmol/L is associated with complications and plasma lactate clearance 10% is associated with a reduction in the rate of complications.<sup>9,10</sup>

Initial plasma lactate, 24-h plasma lactate, and plasma lactate clearance are expected to be markers of cell hypoxia and shock. The study aimed to evaluate if initial plasma lactate, 24-h plasma lactate, and lactate clearance is a useful parameter to assess acute phase complications of burned patients.

## **MATERIALS AND METHODS**

### **Subjects**

This was a cross-sectional study to evaluate the correlation between initial plasma lactate, 24-h plasma lactate, and plasma lactate clearance with the occurrence of acute phase complications of patients with burn injury. The population in this study were patients with burn injury that admitted at the Department of Surgery, Abdul Wahab Sjahranie District Hospital, Samarinda during the period of September 2018 to September 2019 who met the inclusion and exclusion criteria. The inclusion criteria used were patients diagnosed with a severe burn or burn more than 20% in adult and 10% in children that treated at our burn unit. Protocol of the study has been approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Mulawarman / Abdul Wahab Sjahranie District Hospital, Samarinda (No. No 120/KEPK-AWS/VII/2019).

### **Protocol of the study**

Previously, in the patient recruitment, the aim and method of

study as well as the risk of involving in the study were explained to patients. The patients were then given opportunity to ask question concerning the study, before they were willing to be involved in the study by sign an inform consent. Thirty-five patients admitted to our the Burn Unit, Abdul Wahab Sjahranie District Hospital, Samarinda due to burns within the past 1 years, were enrolled in this study. Only burns that over 20% in adults and over 10% in children within one hours after burns were included in the study. Immediately after admission, 1 mL arterial blood sample of each patient was drawn into a heparin-coated syringe for initial plasma lactate measurement. Plasma lactate level was then analyzed using the Blood Gas and Lactate Analyzer OPTI CCA-TS (OPTI Medical Systems, Roswell, USA). Followed after 24-h after the initial plasma lactate measurement, the 24-h plasma lactate level was measured. Plasma lactate clearance was then calculated based on the difference between the initial and 24-h plasma lactates.

On admission, patients in the surgical unit, resuscitation began with Ringer's solution according to Parkland formula. Based on the burn size and patient's weight, the amount of resuscitation fluid was calculated with the target urinary output of 1mL/kg body weight/h.<sup>11</sup> The acute phase complication was assessed after 72-h of burns based on the laboratory parameter such as PaO<sub>2</sub>/FiO<sub>2</sub> ratio, elevated liver enzymes, increased level of urea, and creatinine.<sup>12,13</sup>

For the evaluation of plasma lactate clearance, a 10% cut off was used to

compare between complicated and uncomplicated burns. Based on the initial and 24-h plasma lactate levels, patients were divided into two groups based on cut off 2 mmol/L. Subjects was considered as normal plasma lactate if the level <2 mmol/L and subjects was considered with elevated plasma lactate if the level ≥2 mmol/L.

### Statistical analysis

Data were presented as mean ± standard deviation (SD) or frequency or minimum-maximum and then analyzed using SPSS version 24 program. The Fisher's exact test was applied to evaluate the correlation between the initial plasma lactate, 24-h plasma lactate, and plasma lactate clearance with the occurrence of the acute phase complication. The t test was applied to evaluate the difference between groups. p value less than 0.05 was considered significant.

## RESULTS

A total 35 patients with burn injury aged from 10 to 61 years involved in this study. The burn injury suffered more male (62.9%) than female (37.1%). The characteristics of patients included cause of burn, initial and 24-h plasma lactate levels, plasma lactate clearance, total complications, breathing complication and circulation complications are presented in TABLE 1. The mean and range of age, burn size, initial and 24-h plasma lactate levels as well as the plasma lactate clearance are presented in TABEL 2.

**TABLE 1. Characteristics of patients**

Variable	n (%)
<b>Sex</b>	
• Men	22 (62.9)
• Women	13 (37.1)
<b>Cause</b>	
• Flame	15 (42.9)
• Scald	20 (57.1)
<b>Initial plasma lactate</b>	
• < 2 mmol/L	9 (25.7)
• ≥ 2 mmol/L	26 (74.3)
<b>24 h plasma lactate</b>	
• < 2 mmol/L	18 (51.4)
• ≥ 2 mmol/L	17 (48.6)
<b>Plasma lactate clearance</b>	
• < 10 %	13 (37.1)
• ≥ 10 %	22 (62.9)
<b>Total complication</b>	
• Complication	10 (28.6)
• No complication	25 (71.4)
<b>Breathing complication</b>	
• Complication	2 (5.7)
• No complication	33 (94.3)
<b>Circulation complication</b>	
• Complication	9 (25.7)
• No complication	26 (74.3)

**TABLE 2. Age, burn size, initial plasma lactate, 24 h plasma lactate levels and plasma lactate clearance**

Variable	Mean ± SD (min-max)
Age (years)	29.86 ± 16.539 (10 - 61)
Burn size (cm)	25.50 ± 19.072 (11 - 93)
Initial plasma lactate (mmol/L)	2.94 ± 1.48 (0.8 - 6.7)
24 h plasma lactate (mmol/L)	2.36 ± 1.12 (0.7 - 5.2)
Plasma lactate clearance (mmol/L)	22.96 ± 21.09 (0 - 67.41)

The 24-h plasma lactate levels ( $p=0.001$ ; 95%CI: 0.624-2.069) and plasma lactate clearance ( $p=0.002$ ; 95%CI: 8.806-37.07) were significantly correlated with the occurrence of acute phase

complications (TABLE 3). However, there was no significantly correlation between the initial plasma lactate levels and the occurrence of acute phase complications ( $p=0.609$ ).

TABLE 3. The correlation between initial plasma lactate levels, 24 h plasma lactate levels, plasma lactate clearance, and complications

Variable	Complication	Total	Mean $\pm$ SD (mmol/L)	p	95 % CI
Initial plasma lactate	Yes	10	3.1510 $\pm$ 2.09719	0.609	0.854-1.436
	No	25	2.8600 $\pm$ 1.21094		
24 plasma lactate	Yes	10	3.3240 $\pm$ 1.17781	0.001	0.624-2.069
	No	25	1.9772 $\pm$ 0.84760		
Plasma lactate clearance	Yes	10	4.3400 $\pm$ 3.48272	0.002	8.806-37.07
	No	25	29.5152 $\pm$ 20.65037		

\*independent t test (p < 0.05)

Patients with an initial and 24-h plasma lactate levels were divided based on cutoff 2 mmol/L, while plasma lactate clearance was divided based on cutoff 10%. Patients with 24-h plasma lactate levels  $\geq$  2 mmol/L had 19 times greater chance of complications compared to patients who had plasma lactate level <

2 mmol/L (p= 0.003; OR=19.125; 95%CI: 2.056 – 177.921). In addition, plasma lactate clearance >10% significantly reduced the risk of acute phase complications (p= 0.002; OR=0.630; 95%CI: 0.010 – 0.691) as presented in TABLE 4.

TABLE 4. The comparison between initial plasma lactate levels, 24 h plasma lactate levels, plasma lactate clearance, and complications

Variable	Complication		p	Odds Ratio (OR)	95% CI
	Yes n (%)	No n (%)			
Initial plasma lactate					
• < 2 mmol/L	3 (8.6)	6 (17.1)	0.694*	0.737	0.144 – 3.778
• $\geq$ 2 mmol/L	7 (20)	19 (54.3)			
24 h plasma lactate					
• < 2 mmol/L	1 (2.9)	17 (48.6)	0.003*	19.125	2.056 – 177.921
• $\geq$ 2 mmol/L	9 (25.7)	8 (22.9)			
Plasma lactate clearance					
• < 10 %	8 (22.9)	5 (14.3)	0.002*	0.630	0.010 – 0.691
• $\geq$ 10 %	2 (5.7)	20 (57.1)			

\*Fisher's exact test (p < 0.05)

## DISCUSSION

Plasma lactate levels and plasma lactate clearance are associated with tissue hypoperfusion states leading to cellular hypoxia, ultimately leading to multiorgan damage. This study observed that there is a significant relationship between 24-h plasma lactate levels

and plasma lactate clearance on the incidence of acute phase complications of burns. The decrease of 24-h plasma lactate levels and the increase of plasma lactate clearance associated with the decrease of the incidence of acute phase complications in burn patients. It is indicated that the improvement of both parameters i.e. 24-h plasma lactate

levels and plasma lactate clearance lead improve the hypoperfusion state causing hypoxic cells.

Hypovolemic conditions on severe burns will cause a rapid loss of intravascular fluid and in turn will decrease peripheral blood flow called burn shock causing anaerobic cell metabolism. Lactate is formed from anaerobic cell metabolism due to insufficient oxygen supply. The prolonged hypovolemic condition will cause an increase in plasma lactate levels.<sup>14,15</sup>

Prolonged hypovolemic conditions will eventually lead to multiorgan disorders, where the earliest or acute complications occur within 48-72 h after burns such as respiratory disorders and circulatory disorders characterized by a decrease in the PaO<sub>2</sub>/FiO<sub>2</sub> ratio, an increase in liver and kidney enzymes.<sup>16</sup>

Some clinical parameters, such as blood pressure and urine output, are often used to describe tissue perfusion. However, they are not enough to assess overall improvement in tissue perfusion and resuscitation success.<sup>17</sup> Multiorgan damage occurs due to prolonged hypoperfusion conditions. Therefore, easy, accurate, reproducible, and rapid use parameters that are widely available to evaluate hypoperfusion conditions are needed. Plasma lactate levels and plasma lactate clearance could be considered as potential markers of hypoperfusion conditions and successful resuscitation.

Mokline *et al.*<sup>18</sup> reported that plasma lactate levels is higher in patients with total body surface area (TBSA)  $\geq$  20% rather than TBSA  $\leq$  20%. This suggests that the degree of burns is closely related to the state of cellular hypoxia which causes an increase in plasma lactate. Higher plasma lactate levels can be used to identify patients at high risk of developing organ dysfunction and mortality following major burns.<sup>18</sup> When presenting with a severe elevation

and persistence of serum lactate, the clinician would be advised to maximize patient monitoring, patient care and fluid resuscitation.

In this study, 24-h plasma lactate and plasma lactate clearance could be considered as good markers of hypoperfusion and burns resuscitation. The improvement of 24-h plasma lactate correlated strongly with a good outcome. Good results were obtained when the value of 24-h plasma lactate levels returned to normal ( $<2$  mmol/L), where the complication rate was only 2.9 %. Conversely, when the value of 24-h plasma lactate that did not return to normal values ( $\geq 2$ mmol/L), the complication rate was 25.7% (TABLE 4). This result is in accordance with previous study showing that the plasma lactate levels  $>2$  mmol/L can increase the occurrence of complications.<sup>18</sup>

Lactate clearance is associated with a reduction in complications.<sup>19-20</sup> Failure of the body to excrete the lactate will worsen the prognosis of a disease. Reduction in lactate clearance  $\geq 10\%$  is associated with a reduction in the incidence of burn complications. In this study, it was found that lactate clearance  $>10\%$  is significantly associated with a reduction in the incidence of burn complications (TABLE 4).

## CONCLUSION

The 24-h plasma lactate levels and plasma lactate clearance have a significantly relationship with the occurrence of acute phase complications in burns patients. These two parameters are expected to be used to assess the improvement of hypoperfusion conditions due to burns injury so that cells do not fall into a hypoxic state that can cause multiorgan disorder. Furthermore, these two parameters can also be used to determine target resuscitation in burn patients.

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