

Correlation Analysis of Lactic Acid Level as A Predictor of Severity of Patients with Acute Appendicitis

Reno Rudiman, Tommy Ruchimat, Cytra Givanni Rossy

Department of Surgery, Faculty of Medicine Universitas Padjadjaran/
Dr. Hasan Sadikin General Hospital Bandung, Indonesia

Abstract

Perforated appendicitis is a leading cause of morbidity and mortality in all appendicitis cases, both for adults and children. Delay in preoperative diagnosis is the main reason for perforation. In previous studies, it was revealed that diagnostic modalities such as radiological examination and the current scoring system have not been able to predict the onset of perforated appendicitis. Serological biomarkers of lactic acid are associated with intestinal obstruction and ischemia. The increase in the serological value of lactic acid in perforated appendicitis compared to acute one was shown to increase significantly by 0.25 mmol/L ($p < 0.05$) according to a previous study. This study aimed to determine the correlation between lactic acid level and the severity of appendicitis in patients visiting Dr. Hasan Sadikin General Hospital. This was a cross-sectional prospective analytic observational study on adult patients diagnosed with appendicitis who were admitted to the emergency room of Dr. Hasan Sadikin General Hospital from January 1, 2021 to June 1, 2021. Data analysis was performed using bivariate analysis and correlation tests of difference. This study involved 54 subjects with a mean lactic acid level of 2,5093 mmol/L (0.9 mmol/L - 11.8 mmol/L). In the complicated appendicitis group, 20 subjects (37%) was found to experience an increase in lactic acid (OR 1.07; 95% CI: -0.03-0.22; $p = 0.14$). The correlation analysis showed the direction of negative correlation. Thus, it is concluded that there is no significant correlation between lactic acid level and the severity of appendicitis in patients with appendicitis.

Keywords: Correlation, lactic acid, perforated appendicitis

Introduction

Acute appendicitis is a frequent case that is often found in the field of digestive surgery. Research revealed the incidence of perforated appendicitis in adults ranges from 4–19%. The risk of perforation is very high in the first 24 hours and increases to 6% in the next 36 hours from the beginning of symptoms. Based on this research, surgery is recommended in the first 36 hours of symptoms to prevent complications from appendicitis. Delay in diagnosis is the main cause of these complications. An accurate examination that can predict the risk of perforated appendicitis is currently still not found.^{1,2}

A complete history taking and good physical examination in cases of appendicitis are believed to have the same accuracy as other investigation

modalities in establishing the diagnosis. However, in different cases of complicated appendicitis that cannot be distinguished with certainty from non-complicated appendicitis at the time of the initial examination at the hospital, causing a delay in diagnosis. This problem increases morbidity and mortality due to the risk of perforated appendicitis.³

Several previous studies tried to establish the diagnosis of appendicitis with radiological examinations: CT scan, USG, and scoring systems such as the Alvarado score, pediatric appendicitis score (PAS), and appendicitis inflammatory response (AIR). These supporting modalities have proven to be very useful in predicting acute appendicitis in patients with complaints of right lower abdominal pain but are still unable to predict the risk of perforated appendicitis.^{4,5,6}

Serological biomarker of lactic acid value is associated with the presence of intestinal obstruction and ischemia based on the pathophysiology of appendicitis so that it can facilitate early detection of the risk of perforated appendicitis. Previous studies in patients with perforated appendicitis found higher plasma

Corresponding Author:

Reno Rudiman
Department of Surgery, Faculty of Medicine, Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital Bandung, Indonesia
Email: renorudiman@yahoo.com

levels of lactic acid than in patients with acute nonperforated appendicitis (96% sensitivity; 87% specificity).⁷ Research in Indonesia on lactic acid biomarkers as a risk predictor of perforated appendicitis is rare and currently has not been done in Bandung. The researcher intends to find out the correlation between lactic acid values as a predictor of perforated appendicitis in adult patients who had been previously diagnosed with acute appendicitis in Dr. Hasan Sadikin General Hospital Bandung, Indonesia. This research is expected to be able to provide benefits for clinicians to conduct an early intervention in cases of appendicitis at risk of perforation with appropriate and efficient investigations.

Methods

The study was conducted on subjects who met the inclusion criteria, adult patients (>18 years), diagnosed with appendicitis which was established through history taking, physical examination, Alvarado and Tzanakis scoring, underwent emergency surgery, and did not meet the exclusion criteria. The research was conducted at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia in the period from January 1st, 2021 to June 1st, 2021. The research was carried out after obtaining Ethical Approval No: LB.02.01//X.6.5/343/2021 from the Health Research Ethic Committee of Dr. Hasan Sadikin General Hospital Bandung.

This study is a prospective analytic observational study with a cross-sectional design. The independent variable is the value of blood lactic acid and the dependent variable is perforated appendicitis. The sample size is determined by the two-proportion hypothesis formula with each proportion totaling a minimum of 66 samples. The sampling method is consecutive sampling.

Data processing through the steps of editing, coding, data entry, and cleaning. Analysis of the characteristics data was analyzed descriptively. The bivariate analysis uses simple logistic regression bivariate analysis. The risk probability in the bivariate analysis is shown as crude odds ratio (OR) with a 95% confidence interval (CI). The p-value is considered significant if $p < 0.05$. The OR value is considered a risk factor if the $OR \geq 1.00$. The analysis between numerical variables and categorical variables uses the independent T-test if the data is normally distributed and the Mann-Whitney test if the data is not normally

distributed. The normality test of the data used the Kolmogorov-Smirnov test. The candidate variables that will be included in the multivariate analysis are variables that have a P-value < 0.25 . The multivariate analysis uses multiple logistic regression with a determinant model. Statistical analysis was processed with SPSS version 21.0 for Windows.

Results

This study involved 54 subjects in two groups, consisting of the acute appendicitis group (the study group) and the complicated appendicitis group (the control group) by monitoring the increase in lactic acid in these patient groups (Table 1). Regarding the characteristics of the subjects, It was found that the subjects suffering from appendicitis were more women than men with a ratio of 1.25:1 with a mean value of age was 40.16 years old (18–81). In the characteristic description based on the severity of the disease, it was found that 94.4% perforated appendicitis and 5.6% acute appendicitis (Table 1). Based on the increase in lactic acid, it was found that 37% (20 subjects) had an average value of lactic acid at 2.5093 mmol/L (0.9–11.8).

Based on the Simple Regression Logistic test, there was an increase in lactic acid levels in subjects with acute appendicitis and perforated appendicitis with $p\text{-value} > 0.05$ ($p = 0.14$; $OR: 1.07$; $95\%CI: -0.03-0.22$) so that there was no significant difference between lactic acid levels in patients with acute appendicitis and

Table 1 Characteristics of The Subjects

Variables	n=54
Age	
Mean±Std	40.16±15.5
Range (min-max)	18.00-71.00
Sex	
Male	24 (44.4%)
Female	30 (53.6%)
Severity	
Complicated appendicitis	51 (94.4%)
Acute appendicitis	3 (5.6%)
Level of lactic acid	
Increase	20 (37%)
Normal	34 (63%)

Table 2 Simple Regression Analysis for Variables of Perforated Appendicitis Predictors

Variables	Perforated Appendicitis		Acute Appendicitis		OR	CI 95%		P-Value
	n	%	n	%		Min	max	
Sex								
Male	24	47	0	0				
Female	27	53	3	100	-0.11	-0.23	0.02	0.09
Onset of symptoms								
<24 hours	0	0	3	100	9.86	1.99	3.01	0.00
>24 hours	51	100	0	0				
Lactic acid								
Increase	20	39	0	0	1.07	-0.03	0.22	0.14
Normal	31	61	3	100				

perforation. The results were the same for the gender variable with p-value >0.05 (p=0.09; OR: -0.11; 95%CI: -0.23 -0.02). Appendix obstruction based on symptom onset with a time limit of 24 hours showed a significance value of p<0.05 (p=0.00; OR: 9.86; 95% CI: 1.99 -3.01) so it can be concluded that there was a significant difference between lactic acid levels in patients with obstruction less than 24 hours and more than 24 hours (Table 2). In the correlation analysis of the value of lactic acid and the severity of appendicitis, the Pearson Correlation value was 0.186, which means the correlation is very weak (Table 3).

Discussion

In this study, univariate and bivariate analysis was carried out on the characteristics of the research subjects. In this study, there was no significant difference between gender in acute and perforated appendicitis patients. This is following the results of a study in Turkey involving 576 appendicitis patients which showed that the group of perforated appendicitis

was dominated by the male sex, but there was no significant difference between men and women in the statistical test of both groups.⁷

In the bivariate analysis between increased levels of lactic acid in patients with acute appendicitis and perforation, the p-value> 0.05 (p=0.14; OR:1.07; 95%CI: -0.03-0.22) It means that there were no significant results between the increase in the value of lactic acid with the severity of appendicitis. These results were strengthened by the correlation analysis of lactic acid values and the severity of appendicitis, the Pearson Correlation value was 0.186, which means the correlation was very weak. This was probably because patients with high lactic acid levels and unstable hemodynamics parameters who were admitted to an emergency department in Dr. Hasan Sadikin General Hospital had already received intensive fluid intravenous therapy earlier based on sepsis bundle protocols and were proved by intraoperative findings where the complications of appendicitis do not occur. This assumption is following studies conducted by previous studies that patients who received intravenous fluid therapy more than 30 minutes since the diagnosis of sepsis was made had a higher mean lactic acid level (3 mmol/L) than patients who received intravenous fluids 30 minutes after the diagnosis of sepsis was made (2.6 mmol/L). The result was that patients who received intravenous fluids before 30 minutes had a 12% shorter length of stay compared to patients who received intravenous fluids after 30 minutes (HR 1.14; 95% CI, 1.02-1.27).^{4,8,9}

This study has several limitations that might have an influence on the results of this study which showed a negative correlation between lactic acid levels and the incidence of perforated appendicitis. This study had a sample size that

Table 3 Pearson Correlation Between Lactic Acid and Severity of Appendicitis

	KAL_X	KUB_Y
Pearson Correlation	1	.186
KAL_X Sig. (2-tailed)		.178
N	54	54
Pearson Correlation	.186	1
KUB_Y Sig. (2-tailed)	.178	
N	54	54

was less than the minimum number of samples because the study was conducted in a type A general hospital (main referral hospital) where cases of acute appendicitis were rare. The research was only conducted in one hospital, so the amount of research data was still limited. Most of the patient's lactic acid data were not taken every day so the researcher must adjust the clinical data with the lactic acid data on the day when the patients were admitted to the hospital.

This study concluded that there was no significant correlation between lactic acid levels and the severity of appendicitis in Dr. Hasan Sadikin General Hospital Bandung. This study could be used as a clinician's/surgeon's consideration to choose the laboratory parameters for supporting the diagnosis of the severity of appendicitis. Surgeons are expected not to rely solely on the lactic acid parameter because it could be proven that it did not correlate with the severity of appendicitis based on this study. Further research is needed by involving a larger number of subjects in a multicenter and using multivariable parameters which will be tested for statistical quality as a predictor of severity in appendicitis patients.

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