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The Relationship between Blood Gas Analysis Profile and the Outcome of Severe COVID-19 Patients

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ABSTRACT

Coronaviruses commonly infect the respiratory tract, leading to severe pneumonia. Respiratory problems cause numerous acid-base disorders in 2019 Coronavirus Disease (COVID-19) patients. Several studies have explored laboratory biomarkers used in the management and prognosis of COVID-19 patients during this pandemic; however, only a few focused on blood gas analysis. Determine the blood gas analysis pattern and its association with the outcome of severe COVID-19 patients treated in the Intensive Care Unit (ICU). This retrospective cohort study used secondary data from patients with severe COVID-19 treated in the ICU of Hasanuddin University Hospital between January and December 2021. There was a higher number of male (58.8%) compared to female patients (41.5%), with a mean age of 62 years. Respiratory alkalosis was the most prevalent blood gas disorder (24.4%). Metabolic alkalosis was a blood gas disorder with the highest number of recovery/improvement outcomes (8 patients). There was no significant relationship between blood gas analysis results and the outcome of severe COVID-19. In addition, no specific pattern was found in the results of blood gas analysis. Respiratory alkalosis was the most frequent blood gas disorder detected in these patients.

Keywords: COVID-19, SARS-Cov-2, rt-PCR, intensive care unit, blood gas analysis

INTRODUCTION

Coronavirus Disease 2019 (COVID-19) has been declared by the World Health Organization (WHO) as an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). On December 31, 2019, an outbreak of the respiratory disease was later proven to be caused by a new Coronavirus, officially named Coronavirus Disease 2019 (COVID-19), and was first announced in Wuhan, a city in Hubei province and quickly spread to other areas. Data on the development of COVID-19 based on data from WHO and the Ministry of Health showed that the total number of confirmed cases of COVID-19 worldwide until November 2021 was 258,164,425 cases with 5,166,192 deaths. As of November 2021, there were 4,254,443 positive confirmed cases of COVID-19; 143,766 deaths and 4,102,700 recovered patients in Indonesia.[1,2]

Coronavirus tends to infect the respiratory tract, which develops into severe pneumonia. Most cases of COVID-19 result in mild, moderate to severe symptoms causing respiratory failure, septic shock, and organ dysfunction. Angiotensin Converting Enzyme 2 (ACE-2) is a cell surface receptor found in several organs such as the lungs, heart, arteries, kidneys, and intestines. Because ACE-2 is the entry point for SARS-CoV-2, it causes the renin-angiotensin system to affect COVID-19. SARS-CoV-2 entry into cells causes excessive activity of the renin-angiotensin-aldosterone system, which is mediated by an increase in angiotensin [2]. High serum aldosterone levels can cause metabolic alkalosis through the loss of hydrogen ions from the renal tubular cells. A large number of acid-base disorders originate from breathing in people with COVID-19. As COVID-19 gets worse, many patients require treatment in an intensive care unit, which requires blood gas analysis.[3,4] Lakhani *et al.* reported that 20% of COVID-19 patients treated in the ICU experience respiratory alkalosis and metabolic acidosis, 18.75% experience respiratory alkalosis and metabolic alkalosis, and 15.63% experienced respiratory acidosis and metabolic acidosis died. Mondal *et al.* reported that 58.3% of COVID-19 patients experienced respiratory alkalosis (55.4%) and metabolic alkalosis (45.9%), whereas no death was reported from 6.0% of patients who experienced acidosis. Alfano *et al.* reported that COVID-19 patients experienced 33.6% metabolic alkalosis, and

30.6% respiratory alkalosis, and 6 of them died with metabolic acidosis. Bezuidenhout *et al*. reported that 64.3% of COVID-19 patients who were treated in the ICU experienced alkalemia, of which 74.2% lived and 52.0% died. Contrastingly, of 12.7% of patients who experienced acidemia, 6.5% lived and 20.0% died.[3-5,6]

Various laboratory tests have been identified as risk predictors that can assist in staging the disease, monitoring, treatment, and prognosis of patients with COVID-19. Most of the research on COVID-19 patients was focused on biochemical and hematological laboratory parameters, whereas the data on Blood Gas Analysis (BGA) remained limited. Therefore, this study aimed to determine the profile of blood gas analysis in patients with severe COVID-19 who were treated in the ICU to help clinicians treat patients with COVID-19.[5]

METHODS

This study was a retrospective cohort research by collecting secondary data from patients with severe degrees of COVID-19 who were treated at the ICU of Hasanuddin University Hospital from January to December 2021. The study population was all patients with confirmed COVID-19 based on Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) test results. The research subject was all patients with severe COVID-19 who were treated at the ICU of Hasanuddin University Hospital Makassar from January to December 2021. Inclusion criteria were patients aged 18 years and above, patients with confirmed COVID-19 based on the results of the Reverse-Transcriptase Polymerase Chain Reaction (RT-PCR) test results in the ICU of Hasanuddin University Hospital Makassar, and patients whose BGA results. Patients whose incomplete medical record data were excluded.

Data were statistically analyzed using SPSS version 25. Descriptive statistical calculations with frequency distribution were fused for statistical analysis. Fisher's Exact statistical test was used to determine the relationship between BGA and the Outcome of Severe Covid-19 patients. The p-value <0.05 was reported as significant. Ethical eligibility approval was obtained from the Health Research Ethics Commission (KEPK) Faculty of Medicine, Hasanuddin University (No: 24/UN4.6.4.5.31/PP36/2022), and Hasanuddin University Hospital.

RESULTS AND DISCUSSIONS

The analysis was carried out on 41 patients with severe COVID-19. The mean age in this study was 61±15 years. The distribution of subjects according to gender, BGA, and outcomes is shown in Table 1.

Based on Table 1, it was found that there were a higher number of male (58.5%) than female patients (41.5%). Disease outcomes found in this study were recovery (36.6%), improvement (34.1%), and 12 (29.3%) deaths. The most frequent BGA results were respiratory alkalosis in 10 patients (24.4%) and

Table 1. Characteristics of research subjects (n=41)

Variable	n	%
Gender		
Male	24	58.5
Female	17	41.5
Age (mean±SD)	61±15	
BGA results		
Metabolic acidosis	1	2.4
Partially compensated metabolic acidosis	4	9.8
Metabolic alkalosis	9	22.0
Partially compensated metabolic alkalosis	1	2.4
Respiratory acidosis	5	12.2
Fully compensated respiratory acidosis	1	2.4
Partially compensated respiratory acidosis	4	9.8
Respiratory alkalosis	10	24.4
Fully compensated respiratory alkalosis	1	2.4
Partially compensated respiratory	3	7.3
Metabolic and respiratory acidosis	1	2.4
Outcome		
Recovery	15	36.6
Improvement	14	34.1
Death	12	29.3

Table 2. Relationship between BGA results and disease outcome

BGA	Outcome		Total	p*
	Recovery/Improvement	Death		
Respiratory alkalosis	6	4	10	0.441
Metabolic alkalosis	8	1	9	0.240
Respiratory acidosis	3	2	5	0.620
Partially compensated metabolic acidosis	2	2	4	0.567
Partially compensated respiratory acidosis	3	1	4	1.000
Partially compensated respiratory alkalosis	2	1	3	1.000
Metabolic acidosis	0	1	1	0.293
Fully compensated metabolic alkalosis	1	0	1	1.000
Partially compensated metabolic alkalosis	1	0	1	1.000
Fully compensated respiratory acidosis	1	0	1	1.000
Fully compensated respiratory alkalosis	1	0	1	1.000
Metabolic and respiratory acidosis	1	0	1	1.000
Total	29	12	41	

*Fisher Exact test = $p<0.05$

metabolic alkalosis in 9 patients (22.0%). In addition, respiratory acidosis was found in 5 patients (12.2%), partially compensated metabolic acidosis was found in 4 patients (9.8%) and partially compensated respiratory alkalosis was found in 4 patients (9.8%).

Table 2 shows that metabolic alkalosis was found in 8 patients who recovered/improved (the highest outcome in this study), whereas respiratory alkalosis was found in 4 patients who died. Statistical tests showed that there was no significant relationship between the results of the BGA and the outcome of COVID-19 with a p-value >0.05.

A total of 41 patients participated in this study as research subjects. Table 1 shows a higher number of male (58.8%) compared to female patients (41.5%) with an average age of 62 years. This was in line with a study by Mondal *et al.*, which found a higher number of male COVID-19 patients than females. A similar study by Jin *et al.* also showed that there was a higher percentage of male than female COVID-19 patients with an average age > 65 years. In previously reported cases, patients who were older than 65 years were highly at risk of COVID-19 infection, which can develop into severe cases. In addition, males who are infected with COVID-19 are more at risk of worse clinical manifestation due to higher ACE-2 (a receptor through, which SARS Cov-2 enters) levels in males than females, especially in patients who suffer from diabetes or heart disease.[7,8]

The most common BGA test result in this study was respiratory alkalosis (24.4%). A study by Wu *et al.* reported that COVID-19 patients with respiratory alkalosis had a high risk of disease severity, although the reasons remain unknown. Generally, hypoxia results in hyperventilation as an attempt to correct hypoxia at the expense of CO_2 loss in pulmonary disease. Although some patients do not show significant hypoxemia in the early stages if respiratory alkalosis occurs, they may already experience compensatory hyperventilation and worsen; therefore, COVID-19 patients with respiratory alkalosis need to be given adequate monitoring although they have not shown hypoxemia.[9,10] Chen *et al.* al in a study of 799 people with COVID-19 found that arterial CO_2 levels were significantly lower in patients who died compared to patients who survived.[11,12]

Table 2 shows that the highest number of outcomes reported in this study were recovery/improvement, which was found in 8 patients with metabolic alkalosis. This was due to prompt and appropriate treatment by the clinician to correct acid-base disorders in these patients. However, in contrast to our study, a study by Jiang reported that out of 16 patients with COVID-19 who were treated in the ICU, 100% of subjects experienced metabolic alkalosis, which caused 95.5% death.[13] A study by Rood *et al.* reported that COVID-19 patients who experienced metabolic alkalosis were caused by the effects of excessive mineralocorticoids or hypokalemia excreted via the kidneys or gastrointestinal. The antagonistic effect of the renin-angiotensin system via ACE-2 is the binding of SARS Cov-2 and degradation of ACE-2, thus potentially reducing the counter-regulatory effect. Increased activity of the renin-angiotensin system with increased effects of angiotensin II and aldosterone can lead to increased sodium reabsorption in the distal nephron and increased potassium excretion in the urine.[14] Bezuidenhout *et al.* reported that metabolic alkalosis in patients with COVID-19 is due to excessive mineral corticoid

activity (both endogenous and exogenous). The renin-angiotensin system is involved in the regulation of blood pressure, fluid balance, electrolyte concentration, and acid-base status in the body. The renin-angiotensin system can cause vasoconstriction, cell proliferation, oxidative stress, and aldosterone release, causing metabolic alkalosis.[5,6] A similar study by Lakhani *et al.* reported that 11 (23%) COVID-19 patients with metabolic alkalosis survived and a similar pattern of BGA was observed in those who died. Therefore, it was concluded that the BGA pattern could not be used as a prognostic indicator of the need for mechanical ventilation.[8]

Table 2 shows that there was no significant relationship between BGA results and the outcome of COVID-19 patients. Because there was no specific BGA pattern for each outcome, this study found that the most common BGA result was metabolic alkalosis in the recovered/improved group. In addition, this study was retrospective by collecting data only from medical records and did not analyze the presence of comorbidities in patients with severe degrees of COVID-19 who were treated in the ICU. A small number of samples disabled a further analysis of specific patterns of BGA.

CONCLUSIONS AND SUGGESTIONS

There was no specific pattern of BGA in COVID-19 patients who were treated in the ICU. However, the most common result of BGA was respiratory alkalosis and there was no significant relationship between BGA and the outcome of COVID-19 patients.

Further research is recommended with a larger sample to see the profile of BGA in COVID-19 patients by considering the risk factors.

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