ORIGINAL ARTICLE

The Effect of CO2, plasma protein, and hemoglobin changes on increasing blood acidity of patients with respiratory acidosis in the ICU room of Dr. Slamet Martdirjo – Pamekasan

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ABSTRACT

Introduction*: Respiratory acidosis or primary hypercapnia can cause respiratory distress because the lungs are not optimal in removing carbon dioxide (CO2). Buffer systems such as proteins and haemoglobin alter and regulate acid-base balance.* ***Objectives****: This study wants to evaluate these three factors' interaction in influencing respiratory acidosis.* ***Methods****: This study was a cross-sectional observational analytic. The population is 226 patients, and a sample of 30 respondents is taken based on a non-probability purposive sampling technique. The research data were analysed using multiple linear regression statistical tests. The partial test uses the T-test, while for the simultaneous use, the F test with a significant value of p < (0.05) with the highest Odds Ratio value of 2.34.* ***Results:*** *Statistical test results showed PaCO2 had a significant effect with a p-value < 0.05. In contrast, the Hb factor did not show a significant effect, with a p-value = of 0.057. Meanwhile, albumin did not show a significant effect with p = -0.130 in increasing the occurrence of respiratory acidosis. Simultaneous test with the F test showed a significant effect on the value of p = 0.041, and the coefficient of determination showed that all three factors were 26.7% influential in the incidence of respiratory acidosis.* ***Conclusion****: CO2 partial pressure is dominant in influencing respiratory acidosis, while albumin and haemoglobin as a buffer system cause the compensatory effect to decrease due to physiological and pathological factors.*

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1. Introduction

Respiratory acidosis is one of the clinical-pathological conditions that can cause respiratory distress to the patient's death. Respiratory acidosis, or primary hypercapnia, is caused by the lungs' inability to remove carbon dioxide (CO2) (Johnson, 2017). As a result, respiratory acidosis is divided into an increase in the partial pressure of carbon dioxide (PaCO2) and the concentration of hydrogen ions (H+) (Kamel & Halperin, 2017), which can be acute or chronic (Johnson, 2017). Asidosis respiratorik ditandai denga PaCO2 > 40 mmHg dan HCO3- >24 mmol.l-1 dengan pH < 7.35 (Allyn et al., 2016). Various pathological conditions, such as pneumonia or conditions during general anesthesia, can initiate respiratory acidosis (Schoster & Mitchell, 2019). The system buffers have a rapid response as a line of defense in acid-base imbalances; this system resists changes in blood pH but cannot restore acid or excess base by itself (Zbacnik et al., 2017). Therefore, this study highlights the importance of looking at the interaction of the three factors influencing respiratory acidosis.

The preliminary study at dr. Slamet Martodirdjo Hospital in Pamekasan East Java found that in 2019-2020, the number of patients with respiratory acidosis in the ICU was 266, and 34%

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died. These results are related to several studies on respiratory acidosis, which were estimated to have a relatively high mortality rate of around 40-60%. The decrease in condition occurs due to stress, anxiety, anxiety, and spiritual distress when the individual is admitted to the intensive care unit (Hafifah & Diani, 2020). The leading cause of respiratory acidosis due to hypercapnia, which is not resolved, can lead to complications in coronary artery disease, heart failure, cardiac arrhythmias, or pulmonary hypertension with right ventricular dysfunction (Johnson, 2017). It was because hypercapnia is associated with high circulating catecholamines, exacerbated in patients with head injury or cerebrovascular disease (Kamel & Halperin, 2017). Physiologically, the increase in CO2 and non-volatile factors such as plasma protein and hemoglobin levels affect the blood's acidity. It worsens if pathological conditions such as hypoalbuminemia or anemia chronically impact the course of the disease. If the PaCO2 is greater than 80 mm Hg or the condition is progressive respiratory acidosis and the development of life-threatening hypoxemia (Hopper, 2017). These conditions were possible, especially during the COVID-19 pandemic, where acute respiratory distress syndrome (ARDS) can be exacerbated by respiratory acidosis. It can be assessed with a paCO2 >107mmHg, and arterial pH remains between 7.3-7.4 because the serum bicarbonate (HCO3-) concentration is up to 70mEq/L (Andreis et al., 2021).

Respiratory acidosis requires rapid identification and expert management. In-depth assessment to diagnose and manage respiratory acidosis by experts must be fast and appropriate (Allyn et al., 2016). Observe decreased myocardial contraction, tachyarrhythmias, vascular system resistance, cardiac output, disorientation, narcosis, and coma (Johnson, 2017). Pharmacological therapy must also be appropriate according to the Evaluation and Initial Management of Acute Hypercapnic Respiratory Failure algorithm (Landsberg, 2018). The care provided by nurses must also be professional and qualified so that they can meet basic human needs (Ariani & Aini, 2018). In addition, family support must also be increased to reduce anxiety and accelerate patient recovery (Hafifah & Diani, 2020). This study aimed to determine the involvement of carbon dioxide, plasma protein, and hemoglobin with the incidence of respiratory acidosis.

2. Methods

The research design used is correlation analytical research with a cross-sectional approach. This plan seeks to reveal causal relationships between variables. Variables independent are PaCO2, plasma protein, and hemoglobin, which dependent variable is acidosis respiratory.

This study's population was patients with respiratory acidosis in the ICU RSUD Dr. H. Slamet Martodirjo, Pamekasan, with 226 patients. A sample of 30 respondents was taken based on a non-probability purposive sampling technique. The research data were analyzed using multiple linear regression statistical tests operating with the SPSS 17 software. The T-test has used the test to determine the partial effect of each independent variable on the dependent variable. Meanwhile, to test the simultaneous effect of 3 variables on the dependent variable using the F test with a significant value of $p < (0.05)$. The method of data collection is by taking data from the medical record sheet of patients who meet the inclusion criteria and having laboratory data on arterial blood gases, blood albumin levels, and hemoglobin.

This research was declared ethically appropriate according to the World Health Organization (WHO) (2011) seven standards: 1) social values. 2) scientific value, 3) equal distribution of burdens and benefits, 4) risk, 5) exploitation reference, 6) confidentiality, and 7) approval after receiving an explanation that refers to 2016 CIOMS guidelines. This ethical certificate was declared by the Health Ethics commission of Dr. RSUD. H. Slamet Martodirjo Pamekasan with No: 070/54/432.603/KEPK/2021.

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3. Results and Discussion

3.1 Respondents' Characteristics

Table 1 describes the respondents' characteristics. The majority of respondents were at age over 60 years (37%), men (53%), had abnormal PaCO2 (77%), had abnormal albumin levels (hypoalbuminemia) (60%), had normal hemoglobin (57%), and same proportion of status mild and severe acidosis (50% respectively).

Table 1. Distribution frequency and percentage of respondents' characteristics

Factors	frequency (n: 30)	Percentage (%)
Ten years age groups:		
10-19 years old	2	7%
20-29 years old	3	10 %
30-39 years old	1	3%
40-49 years old	4	13%
50-59 years old	9	30%
> 60 years old	11	37 %
Gender:		
Men	16	53 %
Woman	14	47 %
PaCO2		
Normal <40mmHg	7	23 %
Abnormal >40 mmHg	23	77 %
Albumin		
Normal >3,5 mg/dl	12	40 %
Abnormal <3,5 mg/dl	18	60 %
Hb(hemoglobin)		
Normal > 11 mg/dl	17	57 %
Abnormal < 11 mg/dl	13	43 %
Blood pH		
Mild acidosis	15	50%
Severe acidosis	15	50%

The T-test results in a linear regression indicated that only PaCO2 significantly increases respiratory acidosis (p-value <0.05) (Table 2). The table also indicates that PaCO2 has the most extensive influence on changes in blood acidity, with the highest beta coefficient value of 0.393, followed by hemoglobin (0.335), which is greater than plasma protein or albumin (-0.22). In addition, the risk of exposure to CO2 has the highest Odds Ratio in increasing blood acidity, with a value of 2.34. It means that the increase in CO2 and PaCO2 levels has the most significant risk of causing respiratory acidosis compared to the other two variables.

Table 2. Multivariate Analysis of the Effect of an increase in PaCO2, plasma protein, and Hb on the increase in blood acidity in the Intensive Care Unit (ICU) RSUD dr.H.Slamet Martodirdjo Pamekasan in 2021

Variable	B	*P*-Value	Exp β	OR 95% Cl
PaCO2	0,465	0,027*	0,393	2,34
Hb(hemoglobin)	0,338	0,057	0,335	1,994
Albumin	-0,22	0,898	-0,22	-0,130

*Note: *p-value were significant at 0.05 level*

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Table 3 demonstrates the Multiple Linear Regression Correlation Analysis using the F test. The statistical test results show a strong relationship between the three variables influencing blood acidity levels with a correlation coefficient (R) of 0.517. The coefficient of determination or R-squared (R) obtained a value of 0.267, which means that in this study, 26.7% of the condition of increasing blood acidity can be influenced by three variables, including PaCO2, Hemoglobin, and Albumin. It notes that the remaining 73.3% is influenced by other variables that have not been studied in this study. The results of the simultaneous influence test using the F test obtained a significant value of 0.041 < 0.05, so H1 is accepted. It means that an increase in arterial Pa CO2, Hb levels, and plasma protein significantly indicates a combined effect on the variable of increasing blood acidity.

Table 3. Multivariate Analysis of the Effect of an increase in PaCO2, plasma protein, and Hb on the increase in blood acidity

Variable	Correlation coefficient (R)	Coefficient of determination (R-Square)	Value Significance	Conclusion
Pa Co2 Hb(hemoglobin) Albumin	0,517	0,267	0,041	Significant

3.2 Discussion

Acidosis is an acid-base balance disorder that is described by a decrease in the pH value of the blood (acidemia) and can result in multi-system disorders. The increased partial pressure of carbon dioxide (PaCO2) is the dominant factor in the occurrence of respiratory acidosis. An increase in PaCO2 has been shown to contribute to acid-base changes involving the respiratory system and kidneys (Mallat, 2016; Andreis et al., 2021), thereby lowering blood pH (González et al., 2018) and brain intracellular pH up to 6.65 (Holtzmann et al., 2016). This study showed a significant relationship between PaCO2 and respiratory acidosis with a p-value of 0.027. Statistical tests also show that PaCO2 has the most significant risk of causing respiratory acidosis, with the highest odds ratio of 2.34. An increase in PaCO2 that exceeds 45 mmHg is a decisive factor that can cause respiratory acidosis with a pH < 7.35 (Landsberg, 2018), which can be acute or chronic (Adrogué & Madias, 2020). It happens because exposure to CO2 with H2O will produce carbonic acid (H2CO3), which dissociates into hydrogen ions (H+) and bicarbonate (HCO3-)(Langer et al., 2019). The respiratory system works by regulating plasma PaCO2, which regulates the formation of carbonic acid (H2CO3), and together with the kidneys, it works by adjusting bicarbonate (HCO3-) levels so that the pH is within homeostatic values (Zbacnik et al., 2017). Bicarbonate is one of the most important buffer systems in the carbonic anhydrase-mediated acid-base balance (Clayton-Smith & Sharma, 2021; Tanios et al., 2018). Mild changes in CO2 levels affect pulmonary vasoconstriction perfusion and modulation of inflammation (Petran et al., 2021), which can lead to hypoxemia and even respiratory failure (Adrogué & Madias, 2020; Johnson, 2017).

PaCO2 is the dominant but not the only factor that determines the pH balance of the blood. Interactions of various fluids, intense ions, total concentration, weak acids, volatile and non-volatile acids (Hickish & Farmery, 2021), and interactions between proteins are involved in blood pH homeostasis (Pavani et al., 2021). Endogenous systems such as bicarbonate, intracellular and extracellular proteins, hemoglobin, and phosphate are also active in maintaining pH balance as a buffer system (Clayton-Smith & Sharma, 2021; Hickish & Farmery, 2021). The results showed that the buffering system played by plasma protein and hemoglobin did not significantly affect respiratory acidosis with p values of 0.057 and 0.898, respectively. According to researchers, many factors are involved, including the degree of respiratory acidosis and the etiology of the disease. The etiology of respiratory acidosis is defects in the respiratory drive, neuromuscular

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defects, and derangement of pulmonary parenchyma (Langer et al., 2019). Respiratory acidosis with a pH < 7.25 is at risk of causing pathological conditions related to the cardiovascular and respiratory systems (Landsberg, 2018) and kidney failure. Severe respiratory acidosis with a PaCO2 value > 60 mmHg is at risk for respiratory distress (Hopper, 2017). The condition of heart failure causes shortness of breath, fatigue, and fluid retention (Prihatiningsih & Widaryati, 2021). Meanwhile, kidney failure results in the inability to express metabolic waste and regulate fluid balance (Kurniawaty et al., 2020). These factors reduce the physiological compensatory effects of hemoglobin and albumin in acid-base regulation. Respiratory acidosis with a pH value below normal will fatigue the buffer system (Holtzmann et al., 2016). Researchers argue that physiologically the buffering system by protein cannot restore the acid-base balance of the blood.

Plasma proteins such as albumin as a monomer, globular, and multi-carrier are the most abundant in the body (Al-Harthi et al., 2019). Our findings indicate no effect on respiratory acidosis with a p-value of 0.898 and the risk of exposure with an Odds ratio (OR) value of -0.130. It is related to the function of albumin in producing amino acids and the adaptive response to acid-base balance. Pathological conditions such as poor nutrition and metabolic disorders must be studied to prevent hypoalbuminemia. Hypoalbuminemia can obscure unmeasured anion-like acidosis using conventional blood pH measuring devices (Figge et al., 2018).

Meanwhile, according to researchers, hemoglobin has an effect where oxyhemoglobin decreases, bonds with hydrogen ions increase, and CO2-carrying capacity decreases (Clayton-Smith & Sharma, 2021). It is related to hemoglobin as an active protein that binds and transports oxygen and carbon dioxide (Zheng et al., 2018; Colombo et al., 2020). In addition, the Bohr effect may also apply where the affinity of hemoglobin for oxygen depends on the pH of the solution (Evans et al., 2021). So with these two effects, excess CO2 cannot be removed immediately, resulting in an increase in H2CO3 and a decrease in oxyhemoglobin. Hb-deoxygenated is a strong base, and an increase in pH occurs in venous blood containing 1.68 mmol/L extra arterial CO2, of which 65% is as HCO3 (Hb bound), 27% as carbamino-Hb, and 8% dissolved (Feher, 2017). Hb-deoxygenation can occur due to anemia, sepsis, transfusion toxicity, injury, and inhalation toxicity through various mechanisms (Oh et al., 2019). n addition, proteins as intracellular buffers have limitations in their role as buffers in regulating blood pH (Clayton-Smith & Sharma, 2021).

The results of the simultaneous influence test using the F test obtained a significant value of 0.041 < 0.05, so H1 is accepted. The joint increase in PaCO2, hemoglobin, and albumin affects respiratory acidosis. The three variables have a coefficient of determination of 0.267. In this study, 26.7% of conditions of increased blood acidity could be influenced by PaCO2, hemoglobin, and albumin. In comparison, the remaining 73.3% is influenced by other variables that have not been studied in this study. These other factors can be psychosocial and pathological. Psychosocial factors are framed in caring behavior, such as therapeutic communication, hard and soft skills, responsibility, and morals to ethics in nursing care (Ariani & Aini, 2018). These psychosocial factors greatly support patient satisfaction and accelerate the healing process. While pathologically, one of them is related to pathogenesis, especially during the Covid-19 pandemic, it also supports patient satisfaction. Covid-19 impacts health services and the quality of life for patients and health workers (Sholicha & Ratna, 2021). Several studies have shown that Covid-19 is highly susceptible to respiratory acidosis, especially in pulmonary vascular thrombosis (Diehl et al., 2020; Chen Etchison et al., 2021), cytokine storm, tubular necrosis, and septic shock (Barro et al., 2020). This condition will increase CO2 retention and the risk of respiratory failure (Conti et al., 2020; Mohamed & Alawna, 2020). In infectious and septic conditions, hyperlactatemia can be induced due to inadequate oxygen delivery, leading to tissue hypoxia and increased anaerobic glycolysis (Figge et al., 2018). Blockage of oxidative phosphorylation also increases anaerobic metabolism, which increases the risk of accumulation of the by-product, namely lactate (Rena et al., 2017). That is the interaction between carbon dioxide, protein, and hemoglobin in the body when healthy or sick. It involves many factors in the regulation of blood acid bases. Nurses, as the

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provider of care, must be able to provide the best care and must be able to meet bio-psycho-social-spiritual needs.

4. Conclusion

Based on the results of this study, it can be concluded that together there is a substantial effect between the increase in CO2, plasma protein, and Hb on the pH value of the blood gas analysis results. Respiratory acidosis in patients admitted to the ICU is mainly based on increased CO2, while non-volatile acids (plasma protein and Hb) have no partial effect. The negative effect of malnutrition on blood acidity so that the albumen and Hb buffer system can maintain the normality of blood acidity.

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