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RESEARCH ARTICLE

Relationship between serum albumin values and severity and length of stay in type 2 DM patients with COVID-19 at Bina Kasih Hospital

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is a significant health problem in Indonesia, increasing the risk of death and costs, especially in patients with type 2 diabetes mellitus (type 2 DM). Albumin, a protein with anti-inflammatory and antioxidant roles, is suspected to be associated with disease severity and length of hospitalization. Conditions such as poor glucose control in type 2 DM and a high viral load in COVID-19 can lead to hypoalbuminemia, which is thought to worsen the condition.

Methods: *This observational analytical study with a cross-sectional design was conducted at Bina Kasih Medan Regional Hospital (August–October 2021) on 34 inpatients with type 2 DM and COVID-19. The independent variable was albumin levels, while disease severity (moderate and severe) and length of hospitalization (≤ and ≥ 11 days) were the dependent variables. Bivariate analysis using the Chi-Square test was performed on secondary medical record data.*

Results: *The majority of subjects were male (76.4%). A significant inverse relationship was found between serum albumin levels and disease severity (P<0.032). However, no significant relationship was found between albumin levels and hospitalization duration (P<0.350).*

Conclusion: *Decreased albumin levels were associated with increased disease severity but not with hospitalization duration in patients with type 2 diabetes mellitus (DM) with COVID-19.*

Keywords: Albumin, disease severity, hospitalization duration, type 2 diabetes mellitus (DM), COVID-19.

INTRODUCTION

COVID-19 is spreading rapidly, and the World Health Organization (WHO) reports that approximately 44,351,506 people worldwide have been infected with the virus, with a death rate of over 1,171,255, with a fatality rate of around 0.5-1.0%.1

In Indonesia, the COVID-19 Task Force reported in 2020 that the rapid spread of COVID-19 has resulted in more than 500,000 cases and over 16,000 deaths.2

Clinical symptoms of COVID-19 infection range from asymptomatic to mild, moderate, and severe. Mild symptoms are respiratory rate <24/min with SpO2 >94%, moderate symptoms are respiratory rate 24-30/min with SpO2 90-94%, and severe symptoms are respiratory rate >30/min with SpO2 <90%.3

Managing COVID-19 in Indonesia requires significant funding. The length of hospitalization and severity of COVID-19 disease will increase the risk of death and costs, which will certainly burden both patients and the government.2

Several studies have shown that several factors can influence the length of hospitalization for COVID-19 patients, including age, gender, comorbidities such as hypertension, cardiovascular disease, renal disease, pulmonary disease, diabetes, clinical symptoms or disease severity, and laboratory parameters.4

One laboratory parameter is albumin, which is produced in the liver with a lifespan of approximately 2 weeks and is predominantly present in plasma (90%).5 Hypoalbuminemia is considered when the serum albumin value is <3.5 g/dL.6

Albumin has many functions besides maintaining oncotic pressure. It also acts as an anti-inflammatory, anti-oxidative, anti-thrombotic agent, fights infection, and acts as a drug transporter. Therefore, reduced albumin will increase inflammation, oxidative stress, thrombosis, and susceptibility to infection, which can worsen the severity of the disease and length of hospitalization.7,8

One comorbidity that causes hypoalbuminemia is Type 2 diabetes mellitus (DM) is caused by eight mechanisms: 1. Poor blood glucose control shortens the albumin half-life and results in albumin destruction. 2. Decreased insulin levels reduce albumin gene transcription and mRNA concentration, resulting in decreased albumin synthesis. 3. Insulin resistance increases low-grade inflammation. Inflammation increases capillary permeability, leading to albumin migration into the extravascular space. 8

Albumin is a predictor and prognostic factor for COVID-19. The higher the inflammatory process, the greater the shift of albumin from the intravascular to the extravascular space, leading to hypoalbuminemia. This inflammation leads to increased viral replication and an increased viral load. Increased replication and viral load in COVID-19 increase the severity, length of stay, and even death in COVID-19 patients. 9

In accordance with the above observations and several literature reviews, we can reasonably suspect that serum albumin levels play a role in increasing the severity and length of stay in patients with type 2 DM with COVID-19.

Given that the majority of people with diabetes in Indonesia have poor glucose control (>70%) and the persistence of COVID-19 cases, healthcare providers need to be prepared for a future surge in COVID-19 cases.

Our understanding of serum albumin levels and their relationship to the severity and length of hospitalization in people with diabetes with COVID-19 is still limited. Therefore, we need to conduct research on the relationship between serum albumin levels and the severity and length of hospitalization in type 2 diabetes patients with COVID-19.

METHOD

The data collected were secondary inpatient data. This observational study used a cross-sectional study design with type 2 diabetes patients confirmed with COVID-19 from August to October 2021. The sampling technique met inclusion and exclusion criteria.

The dependent variable was albumin. Serum albumin levels were considered normal and low if the serum albumin level was <3.5 g/dL.6

The independent variables were severity and length of stay. Patients were considered moderately severe if their respiratory rate was 24-30 beats/min and SpO2 90-94%, and severe if their respiratory rate was >30 beats/min and SpO2 <90%.11

Length of stay was defined as the number of days of hospitalization from the first day of admission until discharge. In this study, a duration of ≤11 days was categorized as a normal length of stay, while a length of stay >11 days was considered an increased length of stay.12

Antibodies are soluble substances classified as proteins called globulins and are now known as immunoglobulins. Two important characteristics are specificity and biological activity. Their primary function is to bind antigens and deliver them to the effector system for destruction.1

Immunoglobulins (Ig) are produced by plasma cells derived from the proliferation of B cells following contact with antigens. The antibodies produced specifically bind to other new antigens of the same type.1,8

RESULT

Of the 82 subjects, 34 patients met the inclusion and exclusion criteria: 26 men and 8 women (Table 1).

Table 1. Characteristics of the Study Subjects

Characteristics N: 34	
Male gender,n(%)	26 (76.4%)
Female gender,n (%)	8 (23.5%)
Length of stay <11 days, n(%)	15 (44.1%)
Length of stay ≥11 days, n(%)	19 (55.8%)
Moderate severity (patient)	15
Normal albumin value	5
Albumin value decreased by	10
Severity level (patient)	19
With:	
Normal albumin value	7
Albumin value decreased by	12
Length of treatment <11 days (patients)	15
With:	
Normal albumin value	6
Albumin value decreased by	9
Length of stay ≥ 11 days (patient)	19
With:	
Albumin values were normal	7
Albumin value decreased by	12

The relationship between albumin levels and the severity of COVID-19 in diabetic patients

There were 5 diabetic patients with moderate COVID-19 with normal albumin levels, 10 with low albumin levels, 7 diabetic patients with severe COVID-19 with normal albumin levels, and 12 patients with severe COVID-19 with low albumin levels (Table 1).

	Severity of the disease		Nilai P
Kadar albumin	Sedang	Berat	
Normal	5	7`	0,032
Menurun	10	12	
Total	15	19	

Statistically, there is a significant relationship between albumin levels and disease severity. (P<0.032)

The relationship between albumin values and length of stay in diabetes patients with COVID-19

Diabetic patients with COVID-19 with a length of stay of less than 11 days with normal albumin values were 6 people and 9 people with low albumin values, while diabetes patients with COVID-19 with a length of stay of ≥11 days with normal albumin levels were 7 people and albumin levels were less than 12 people. (table1)

The relationship between albumin levels and length of stay in diabetes patients with COVID-19

	Lama Masa Rawatan		Nilai P
Kadar albumin	<11 hari	≥11hari	
Normal	6	7	0,008
Kurang	9	12	
Total	15	19	

Statistically, there is no significant relationship between albumin levels and the length of treatment for diabetic patients with COVID-19.

DISCUSSION

This study showed that more men than women were diagnosed with COVID-19. These results align with those of other researchers in Indonesia and several other countries, where men outnumber women. 12 However, this study differs from the study by Wu et al., which showed a predominance of female patients. This is likely due to the presence of the X chromosome and sex hormones in women, which play a role in preventing viral infections. 13

This study demonstrated an inverse relationship between serum albumin levels and disease severity. This is consistent with the theory that albumin acts as an anti-inflammatory, prevents oxidative stress, acts as an anti-infective, and transports drugs throughout the body. A lack of albumin (hypoalbuminemia) increases susceptibility to infection, increases thrombosis, disrupts drug distribution, and increases inflammation and oxidative stress. Increased inflammation and oxidative stress lead to an increased cytokine storm and viral load in COVID-19 patients, which can lead to increased disease severity. 7,8

This study shows that decreasing albumin levels lead to increasingly severe disease severity, from moderate to severe. To our knowledge, this research has never been conducted before. A study conducted by Liang S et al. in 193 COVID-19 patients showed that decreased albumin levels increased the severity from mild to moderate. However, this study only assessed mild and moderate severity in non-diabetic COVID-19 patients.14 Therefore, hypoalbuminemia can be used as an indicator of COVID-19 disease severity in diabetics.15

However, this study did not show that decreased albumin levels led to longer hospital stays, which contradicts research by Arcas G., which found that hypoalbuminemia increased hospital stays.16 This may be due to other factors influencing the study results, such as age, gender, obesity, and smoking, comorbidities such as hypertension, liver disease, chronic lung disease, kidney disease, and cardiovascular disease.12

There are several limitations to this study. First, the study design was cross-sectional, which does not describe the course of the subjects' conditions and the causal relationships between the variables studied. Second, the sample only came from one location, namely inpatients at Bina Kasih Medan General Hospital. Third, the small sample size where the initial population of the study was 82 subjects, then selection was carried out based on inclusion and exclusion criteria, it turned out that only 34 subjects met the requirements to be included. Fourth, there are still other factors that have not been analyzed due to imperfect medical records. Fifth, there are factors such as age, gender, obesity, smoking, and other comorbidities.

CONCLUSION

This study found a significant association between hypoalbuminemia and disease severity, but hypoalbuminemia was not associated with length of stay in diabetic patients with COVID-19. Further research with a larger sample size and other influencing factors is needed to obtain more accurate results.

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