Original Article

Characteristics of Albumin Levels and Liver Function in Patients With COVID-19 at H. Adam Malik Hospital, Medan

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Abstract

Background: COVID-19 (Corona Virus Disease-2019) pandemic has a high mortality rate especially in Medan, Indonesia. Serum albumin and liver function tests are believed to be predictive biomarkers for prognosis in patients with infectious diseases, including COVID-19. This study aimed to investigate the association between the mortality events and severely ill COVID-19 patients' serum albumin and liver enzymes.

Method: This is a cross-sectional study using secondary data from the medical records of H. Adam Malik Hospital patients with COVID-19 who were confirmed by RT-PCR from August to December 2020. All patients were analyzed for age, sex, hypoalbuminemia, increased liver enzymes and outcome using Chi-square tests (P<0.05).

Results: The average age of severe COVID-19 patients at H. Adam Malik Hospital ranged from 41 to 60 years, with more women prevalence than men. Most of the patients had hypoalbuminemia (84.2%), an increase in AST (59.4)% and ALT (45.5%). There was no significant association between hypoalbuminemia and the disease outcome (P=0.12). There was a significant association between elevated liver enzymes and mortality in severely ill COVID-19 patients (P<0.001).

Conclusion: We found that hypoalbuminemia is common in patients with severe COVID-19. However, we found that albumin levels had no association with the patients' mortality rate. Liver enzymes levels appear to be a predictive biomarker for outcomes in COVID-19 patients of H. Adam Malik Hospital. We found that higher ALT and AST levels were associated with significantly higher mortality.

Keywords: COVID-19, hypoalbuminemia, liver enzymes.

INTRODUCTION

In March 2020, COVID-19 (Corona Virus Disease-2019) was officially designated by WHO as a pandemic case with a mortality rate far exceeding MERS (Middle East Respiratory Syndrome) and SARS (Severe Acute Respiratory Syndrome).[1] In Indonesia, the city of Medan is the region with the most

extensive distribution of COVID-19 cases, namely 8,000 confirmed cases, 6,692 recovered cases and 326 death cases.[2]

In recent years, research has shown that specific biomarkers can provide additional information in determining pneumonia severity, aetiology, complications, and prognosis. Serum albumin is an examination that is often performed and is believed to be able to predict the prognosis in patients with infectious diseases. Low serum albumin levels are associated with morbidity and mortality in various diseases.[3]

In addition, the hepatocellular severity in COVID-19 patients was reported due to systemic inflammatory response, hypoxemia due to pneumonia (secondary infection) and liver injury due to side effects of drugs such as antibiotics, NSAIDs, herbal products and anti-viral agents.[4]

In a study conducted by J. Huang et al.,[5] severe COVID-19 patients with hypoalbuminemia at presentation increased the risk of death. The potential therapeutic value of albumin in COVID-19 needs urgent further evaluation.

Therefore, this study aims to assess albumin levels and liver function in severe COVID-19 patients at H. Adam Malik Hospital, Medan.

METHOD

This cross-sectional study was conducted in H. Adam Malik Hospital, starting from August to December 2020. This study was approved by the Ethics Committee of medical faculty of Universitas Sumatera Utara. The subjects were a population of 101 patients who were confirmed to be positive for COVID-19. Cross-sectional investigation of the correlates of COVID-19 outcome identified the following correlates: age, gender, low serum albumin and high liver enzyme levels. These data were obtained from the patients' medical records.

We applied 2 inclusion criteria: (i) all adult patients (>18 years of age) were diagnosed as having severe COVID-19 and were confirmed by real-time polymerase chain reaction (RT-PCR) (ii) patients with definite outcome of either survive or die due to COVID-19. Patients will be excluded for incomplete medical records.

Initial laboratory values on the day of admission were collected, including albumin, aspartate transaminase (AST) and alanine transaminase (ALT). Hypoalbuminemia was defined as a decreased albumin level below 3.5 g/dL, while a value above this was considered as normal. The normal range of values for ALT is about 0-55 u/L, while AST is about 5-34 u/L. Elevations were 2-3 times higher than the normal range. Outcomes recorded included discharges with no remaining symptoms and in-hospital mortality events.

Categorical variables were presented as frequencies and percentages. Univariate analyses were conducted using Chi-square tests, as well as Fisher's exact test to compare groups of patients with each variable to identify any significantly association with adverse outcomes. Tha value of $P<0.05$ was considered statistically

significant. Multivariate analysis was conducted using logistic regression.

RESULTS

The baseline characteristics of 101 patients with severe COVID-19 are provided in Table 1.

Table 1. Basic Characteristics of COVID-19 Patients

Characteristics	N	f (%)
Sex		
Male	48	47.5
Female	53	52.5
Age (years)		
18-40	27	26.7
41-60	53	52.5
>60	21	20.8
Laboratory values Albumin		
Decreased	85	84.2
Normal	16	15.8
ALT		
Elevated	46	45.5
Normal	55	54.5
AST		
Elevated	60	59.4
Normal	41	40.6
Clinical outcome		
Discharged	76	75.2
Died	25	24.8

Forty-eight (47.5%) patients were male. There were 53 (52.5%) patients included in 41 to 60 years of age group, and 27 (26.7%) patients in 18 to 40 years of age group. Among the patients, 85 (84.2%) subjects had a low serum albumin level. Most patients had normal ALT value (55 of 101 subjects: 54.5%). In terms of AST, the 60 (59.4%) had an elevated AST level. Mortality events were found on the 25 (24.8%) of subjects.

We examined the association of clinical outcomes with serum albumin, ALT, and AST levels using statistical analysis (Table 2). The outcomes showed no significant association with serum albumin (P=0.12). A significant association was found between the clinical outcomes and ALT levels, as well as AST levels.

DISCUSSION

Several studies demonstrated that serum albumin levels are predictive of adverse outcomes in patients with confirmed COVID-19. Decreased albumin levels were associated with poor outcomes, including more venous thromboembolism events, ARDS development, ICU admissions, readmissions within 90 days, and total adverse events.[6,7]

Table 2. Serum albumin and liver enzymes levels of patients with severe COVID-19.

Characteristics	Outcome		P
	Died	Survived	
Albumin			
Decreased	25 (100%)	60 (78.9%)	0.012
Normal	0 (0%)	16 (21.1%)	
ALT			
Elevated	23 (92%)	23 (30.2%)	<0.001
Normal	2 (8%)	53 (69.8%)	
AST			
Elevated	23 (92%)	37 (48.7%)	<0.001
Normal	2 (8%)	39 (51.3%)	

A study conducted by Violi et al.[8] also found that serum albumin of less than 35 g/L was detected in 74% of the COVID-19 patients with a higher ICU prevalence and is associated with vascular disorders.[7]

The mechanism of hypoalbuminemia in COVID-19 has not been thoroughly studied. Albumin is a protein produced by the liver with a serum half-life of approximately 21 days.[5] Serum albumin levels can be decreased by many factors, including hepatocellular injury, malnourishment, inflammation, and renal losses.[6]

Albumin is synthesized less and extravasated into the interstitial space due to capillary leakage during a state of severe illness. Adequate albumin levels appear to have significant antioxidant properties, such as scavenging oxygen free radicals (OFR), which is critical in preventing tissue ischemia, reperfusion injury, and intense systemic inflammatory response. This implies that severely ill COVID-19 patients with hypoalbuminemia may have a diminished immunological response and can lead to mortality.[6]

In this study, the results showed that severe COVID-19 patients had a higher rate of decreased albumin levels (84.2%) than normal albumin levels. This is in line with the previous research conducted by Zhang,[4] which showed that hypoalbuminemia was seen mainly in severe cases of COVID-19 compared to mild cases.[4]

In addition, the study of J. Huang et al.[5] also showed that severe COVID-19 patients with hypoalbuminemia had a mortality rate of 13.2%. In this study, the survival rate for severe COVID-19 patients with hypoalbuminemia was 70.5% (P=0.12), which means that there was no significant association between hypoalbuminemia and the mortality rate in severe cases of COVID-19. The increased survival rate is caused by albumin therapy that have been administered in COVID-19 patients in H. Adam Malik Hospital.

Elevation of ALT and AST levels have also been noted in patients with COVID-19. Evidence suggests a strong correlation between the severity of liver impairment caused by viral infections and the degree of liver enzyme elevation. Up to 11% of patients with COVID-19 have liver comorbidities, and 14% to 53% show elevated transaminase levels (ALT and AST) during the progression of the illness. Patients with a mild illness may have normal or only slightly elevated aminotransferase levels, while those with more severe cases can present with higher elevations.[9,10]

In this study, we also found that the value of ALT and AST increased in severe COVID-19 patients who died, with P<0.001, which means that there is a significant relationship between elevated transaminase levels and mortality rate of severe COVID-19 patients. This is supported by a study conducted by Zhang et al.,[4] which stated that the hepatocellular severity in COVID-19 patients is due to a systemic inflammatory response, hypoxemia and the adverse effects of hepatotoxic therapy during hospitalization.

CONCLUSION

In this research, it can be concluded that severe cases of COVID-19 are mostly experienced by women aged 41-60 years. Hypoalbuminemia and increased liver function are predictors of mortality for severe COVID-19 in H. Adam Malik Hospital, Medan.

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