The Role of Serum Albumin and Blood Urea Nitrogen to Serum Albumin Ratio in Prediction of Disease Severity and Thirty–day Mortality in Patients with COVID–19

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Abstract

Background: Considering the role of higher blood urea nitrogen and lower serum albumin (SA) levels in deceased COVID-19 patients, increased blood urea nitrogen to SA (B/A) ratio may help to determine those at higher risk of becoming critically ill. This study evaluated the association of SA level and B/A ratio with disease severity and 30–day mortality and also their predictive value for disease severity in COVID–19 patients. Methods: 433 adult patients with COVID–19, admitted to a referral medical center in Tehran, Iran, from February to May 2020 were included. The laboratory markers were measured on admission. Disease severity was categorized into mild disease, severe pneumonia, acute respiratory distress syndrome (ARDS), sepsis, and septic shock. The mortality was followed up for thirty days after admission. Results: Thirty–day mortality rate was 27.25%. The frequency of mild, severe pneumonia, ARDS, sepsis, and septic shock was 30.72%, 36.95%, 24.02%, 6.00%, and 2.31%, respectively. Mean B/A ratio was different among different disease severities. The odds of thirty-day mortality increased by 16% by each unit increase in B/A ratio and decreased by 57% by each unit increase in SA level. B/A ratio had the AUC of 0.45 for disease severity prediction with 71% sensitivity and 22% specificity. Conclusion: The results showed that B/A ratio and SA levels are associated with mortality in COVID–19 patient, while they had low predictive value for disease severity. High B/A ratio is, additionally, associated with disease severity. Therefore, we suggest to use this marker for clinical assessment of patients with COVID–19.

INTRODUCTION

Coronavirus disease 2019 (COVID–19), also known as 2019 novel Coronavirus (2019–n CoV), is today the most critical issue around the world (1). It started from Wuhan's city, China, in December 2019 and spread around the world quickly by human–to–human transmission (2, 3), announced as a pandemic respiratory disease by the World Health Organization (WHO) in March 2020. COVID-19 is infecting more patients each day with a worldwide mortality exceeding 4 million to date (August, 2021) (4).

The main site of infection in COVID–19 is the respiratory system and the main clinical presentations include cough, breathlessness, pneumonia (1). Nonspecific symptoms, which is fever, fatigue, malaise, headache and sore throat, are common among many of patients (5). In contrast, some may remain asymptomatic and act as carriers (6). In addition, COVID–19 may have a long incubation period (7). Severe cases with acute respiratory distress syndrome (ARDS) require intensive care unit (ICU) admission and mechanical ventilation. Multiple organ failure may occur in some cases of COVID-19 and result in death (1). Accordingly, it is important to predict the disease severity and clinical progression of COVID–19 (8).

It has been suggested that COVID–19 enters the body cells through binding to angiotensin converting enzyme-2 (ACE_2) receptor (9), which mainly helps in blood pressure regulation. This type I membrane

protein is expressed in epithelial tissues and other tissues including lungs, heart, kidneys and intestines at varying levels (10), which renders these tissues more vulnerable to damage by COVID–19 (11, 12). It has been shown that serum albumin (SA) levels results in down regulation of ACE_2 (13). Additionally, lower SA concentrations have been seen in severe forms of COVID-19 when compared to COVID-19 patients with low severity (14). Therefore, hypoalbuminemia is suggested as an important predictor of COVID–19 outcome, independent of age and comorbidities (15). Coagulopathy, an important complication during COVID–19, has been also associated with hypoalbuminemia (16, 17). Others have also emphasized on the significance of measuring this parameter in patients with COVID–19 (18). Therefore, it is valuable to study its predictive value for diagnosis of disease severity and mortality in COVID–19.

Blood urea nitrogen (BUN), end product of nitrogen metabolism, has been previously suggested as a useful predictor of cardiovascular morbidity and mortality (19), as well as mortality in patients with H1N1 pneumonia (20). In terms of COVID–19, elevated baseline BUN levels were associated with severe COVID-19 and adverse outcomes (21). Additionally, BUN/creatinine ratio have been reported to predict disease severity and patients' survival (22). On the other hand, B/A ratio had shown a high predictive value for in-hospital mortality in COVID-19 patients (23). Therefore, we hypothesized that the combination of BUN and SA levels (BUN to SA [B/A] ratio), previously indicated as an important predictor of progression of pneumonia into critical conditions (24) and patients' mortality (25, 26), can be a valuable predictor of COVID–19 severity, as well. As far as we are concerned, the predictive value of B/A ratio for COVID–19 severity has not been studied, previously. Hence, the present study aimed to evaluate these two available serum parameters, namely SA level and B/A ratio, for prediction of disease severity of COVID–19 and 30− day mortality in patients admitted to the hospital with COVID–19.

MATERIALS AND METHODS

Study design

In this descriptive cross-sectional study, adult patients (above the age of 18 years), diagnosed with COVID–19 based on positive PCR results, admitted to Shohada–e–Tajrish Hospital, a referral medical center in Tehran, Iran, from Feb. to May 2020 were included. Cases with moderate to severe disease were indicated for hospitalization. Patients with a positive history of hospitalization in the past 90 days, chronic immunodeficiency (such as patients with human immunodeficiency virus, receiving chemotherapy or those who used prednisolone or other immunosuppressive agents), advanced liver disease, receiving dialysis or patients with chronic renal disease [serum creatinine level >1.5mg/dL], and patients with cancer or cachexia were not included into the study. As a result, 433 eligible patients were enrolled into the study consecutively after signing the written informed consent.

The demographic and clinical presentation of the patients were extracted from the hospital's medical records. The disease severity of COVID–19 in the participants was categorized into mild disease, severe pneumonia, ARDS, sepsis, and septic shock, based on WHO categorization (27). Mild cases included patients with COVID–19 with uncomplicated upper airway infection, presenting with fever, fatigue, cough (with or without sputum), anorexia, myalgia, sore throat, dyspnea, nasal congestion, headache, and rarely diarrhea and nausea/vomiting. Severe cases were defined as COVID–19 cases with severe pneumonia, presenting with fever or respiratory infection with a respiratory rate [?]30/min or SpO_2 [?]93% at room air.

One blood sample was taken from all patients within 4 hours of their admission in standing position, collected in plain tubes, and sent to the laboratory within 2 hours after collection. In the lab, the samples were kept at 2–8^{o}C. For testing, the serum/plasma was separated from the samples by centrifuge, and evaluated for the levels of BUN, albumin, and other electrolytes. BUN was measured using enzymatic method with urease and glutamate dehydrogenase and SA level using Bromocresol green method and Latex coagulating nephelometric assay; other biochemical markers were measured using standard methods. The B/A ratio (mg/g) was calculated by dividing the BUN level (mg/l) by the albumin level (g/l).

The clinical progression and outcome of the disease in terms of survival or mortality were assessed 30 days after hospitalization by telephone call and hospital's records. In case of post–hospitalization death, the cause

of death was asked from their first–degree relative.

The protocol of the study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (code: IR.SBMU.TETECH.REC.1399.466). Any patient who was referred to another center or patients who did not respond to the 30–day telephone call were considered as lost to follow–up and excluded from the study.

Statistical analysis

Most of the study variables were categorical and described by frequency (percentage). Comparison of these variables among the study groups were performed using chi square or fisher's exact test, logistic regression and ANOVA. Receiver operating characteristic (ROC) curve analysis was drawn and the area under curve (AUC) was used for determining the cut-point of SA level and B/A ratio and studying the specificity of serum parameters for the disease severity. Multiple logistic regression analysis was performed for studying the association of variables with the study outcome, mortality; adjusted odds ratio (AOR) with 95% confidence interval (CI) were reported. For the statistical analysis, SPSS software version 16 was used. P values of <0.05 were considered statistically significant.

RESULTS

Complete records of 433 COVID–19 patients were available. Mean ±SD of age was 60.38±18.26 years and 60.74% were male (n=263). The mean±SD of the duration of hospitalization was 4.45± 5.70 days; 11.78% (n=51) required intubation; 113 (26.1%) died during hospitalization and 5 others (1.15%) until 30 days after admission. There were 133 patients with mild disease (30.72%), 160 patients with severe pneumonia (36.95%), 104 patients with ARDS (24.02%), 26 patients with sepsis (6.00%), and 10 patients with septic shock (2.31%). The frequency of the study variables among patients with different disease severities and between alive and deceased participants are shown in table 1. As shown, the deceased patients had a greater male–to–female ratio (74/44), compared to the alive patients (189/126), higher mean age (68.7 vs. 57 years, respectively; P<0.0001), and longer duration of hospitalization (4.5 vs. 1.8 days, respectively; P<0.0001). Among deceased patients, 44.1% (n=51) required intubation, while none of the alive patients required intubation (P<0.0001). There was a significant difference in mean age of patients with different disease severities (P<0.0001); pairwise comparison showed that patients with mild disease, severe pneumonia and sepsis were younger than those with septic shock and ARDS (P<0.0001) (Table 1).

There was no difference in mean SA level among patients with different stages of disease severity (P=0.237), while it was significantly lower in deceased patients compared to alive ones (3.85 vs. 4.31 g/dL, P<0.0001). Mean B/A ratio was significantly higher in deceased patients, compared to alive ones (11.57 vs. 5.06; P<0.0001) and different among patients with different disease severities (P<0.0001); post hoc comparisons showed significant differences in mean B/A ratio between patients with mild and ARDS (P=0.008), mild and sepsis (P=0.029), severe pneumonia and sepsis (P=0.016), and severe pneumonia and ARDS (P=0.002) (Table 2).

Results of the logistic regression model on the study outcomes showed 16% increase in the odds of 30-day mortality by each unit increase in B/A ratio (AOR=1.16, 95%CI [1.11, 1.21]), 4% increase by each year increase in age (AOR=1.04, 95%CI [1.02, 1.05]), 7% increase by each day of more hospitalization (AOR=1.07, 95%CI [1.02, 1.12]), 80% increase with having diabetes mellitus (AOR=1.80, 95%CI [1.05,3.08]) and 87% increase with having hypertension (AOR=1.87, 95%CI [1.14,3.06]) as a comorbidity. It also showed 57% decrease in the odds of 30-day mortality by each unit increase in SA level (AOR=0.43, 95%CI [0.31, 0.58]). The odds of ARDS increased by 3% per each year increase in age (AOR=1.03, 95%CI [1.00, 1.06]) and 17% per each unit increase in B/A ratio (AOR=1.17, 95%CI [1.04, 1.32]). Additionally, there is a 70% decrease in the odds of ARDS per each unit increase in SA level (AOR=0.30, 95%CI [0.16, 0.56]). Moreover, the odds of sepsis is increased by 15% per each unit increase in B/A ratio (OR=1.15, 95%CI [1.00, 1.33]) and 11% per each year increase in age (AOR=1.11, 95%CI [1.02, 1.20]). The analysis also revealed the odds of severe pneumonia is decreased by 78% per each unit increase in SA level (AOR=0.22, 95%CI [0.11, 0.41]) and 4% per each unit increase in B/A ratio (AOR=0.96, 95%CI [0.92, 1.00]). In addition, the odds of severe

pneumonia is increased by 5% per each year of increase in age (AOR=1.05, 95%CI [1.02, 1.07]) and 8% per each day of more hospitalization (AOR=1.08, 95%CI [1.02, 1.15]). The odds of mild disease, also, is increased by 49% by each day of more hospitalization (AOR=1.49, 95%CI [1.18, 1.87]). Furthermore, the analysis showed that intubation decreased the odds of mild disease by 85% (AOR=0.15, 95%CI [0.09, 0.27]), severe pneumonia by 47% (AOR=0.53, 95%CI [0.46, 0.62]), ARDS by 76% (AOR=0.24, 95%CI [0.15,0.39]), sepsis by 30% (AOR=0.70, CI95% [0.55, 0.90]) and 30-day mortality by 67% (AOR=0.33, 95%CI [0.27,0.40]) (Table 3).

Results of the ROC analysis showed B/A ratio had the area under the curve (AUC) value of 0.45 (95%CI [0.35, 0.46]) for predicting disease severity at the cut–point of B/A ratio of 8.88 with 71% sensitivity and 22% specificity. The AUC value of SA level was found to be 0.44 (95%CI [0.39, 0.50]) and sensitivity of 65.97% and specificity of 30.75% were reached with the cut–point of SA level of 3.91 (Table 4) (Figure 1).

DISCUSSION

The results of the present study showed the findings of the 433 patients admitted to the hospital with diagnosis of COVID–19. As shown above, the majority of the study population were male, in general and in both groups (deceased and alive patients), and mean age of deceased patients was higher. These results showed the importance of COVID–19 in the elderly and male individuals, which is consistent with the results of previous studies. In a study performed by Goyal, et al., 393 patients admitted with confirmed COVID–19, the median age was 62.2 years and 60.74% were male (28), which is similar to the results of our study. Others have also revealed that older males with comorbidities are more susceptible to COVID–19 incidence (29).

The results of the present study showed that mean duration of hospitalization was significantly longer in deceased group (4.5 vs. 1.8 days) and none of the alive patients required intubation; a total of 118 died (27.2%): 26.1% during their hospitalization period and 1.1% until 30 days after admission. Categorizing patients according to WHO classification showed that the frequency of mild disease, severe pneumonia, ARDS, sepsis, and septic shock was 30.72%, 36.95%, 24.02%, 6.00%, and 2.31%, respectively. Therefore, most of our studied patients had mild to moderate disease severity. In a study on 16,000 patients in Tehran, Iran, median duration of hospitalization was 5 days in deceased patients and 3 days in alive patients and the total case fatality rate (CFR) was 10.05%, higher in patients >65 years old (25.32%) and ICU patients (41.7%) (30). The median duration of hospitalization reported in this study was similar to that of ours, while the CFR was much higher in our study, which can be due to the difference in the factors affecting the mortality of the patients, such as age, comorbidities, and disease severity.

Serum parameters have been suggested as an easy and available assessment tool for prediction of disease severity of COVID–19 and the role of low SA levels (<3.5 g/dL) on progression of COVID–19 to respiratory failure (14) and its significance as predictor of COVID–19 outcome, independent of age and comorbidities (15, 18), has been well described. The underlying mechanism of this association has been suggested to be related to the down regulation of ACE_2 by SA (13), as well as the association of hypoalbuminemia with coagulopathy (16, 17). A study by Kheir, et al. on 181 COVID-19 pneumonia patients showed higher SA levels on admission were associated with a 72% decreased risk of developing venous thromboembolism for every 1 g/dL increase of SA level and a lower risk of developing ARDS, admission to the ICU, readmission to hospital within 90 days (31). In the present study, we also showed that mean SA levels was lower in deceased patients and each unit increase in SA decreased the odds of 30-day mortality, ARDS and severe pneumonia. The results of a meta–analysis on 4659 patients also showed that non–survivors had a significantly lower SA and higher BUN levels, suggesting these parameters as important predictors of mortality in patients with COVID–19 (32). This confirms the results in the present study on the predictive role of lower SA levels for mortality of patients with COVID–19. A cohort study by Liu, et al., conducted on 12,413 COVID-19 patients, showed that among the three markers that was studied, which are serum creatinine level, blood uric acid and blood urea nitrogen, an elevated baseline BUN level was associated with the highest risk of adverse outcomes. They also demonstrated that all-cause mortality risk was increased with elevated baseline levels of BUN (21). Another study also showed BUN/creatinine ratio as an independent predictor of COVID–19 disease severity and survival (OR=1.7 and 1.17, respectively) (22). The underlying mechanism of this

association has been suggested to be related to the expression of ACE_2 receptors on kidneys, which results in activating the renin–angiotensin–aldosterone system and increases the absorption of water and sodium in the kidney tubules, causing passive reabsorption of BUN, renal vasoconstriction, and worse prognosis in patients with underlying renal function (33). The results of the study by Cheng et al. showed serum BUN [?]4.6mmol/L as an independent predictor of in–hospital mortality in patients with COVID–19 (34), which is in line with the results of the present study; although we considered SA level and B/A ratio.

The important predictive value of this parameter, B/A ratio, has been shown previously on progression of pneumonia into critical conditions (24) and patients' mortality (25, 26). Also, in a study performed by Kucukceran, among 602 COVID-19 patients, the BUN level and B/A ratio were significantly higher in deceased patients compared to alive patients. It also showed B/A ratio has higher predictive value for in-hospital COVID-19 mortality with AUC value of 0.809 with the cut-off value of 3.9 mg/g (23). However, none have studied its value for disease severity of COVID–19 and our study was the first to evaluate this issue, as far as we are concerned. Our study demonstrated not only higher mean values of B/A ratio in deceased patients, but also significant differences by different disease severities. The results of the present study suggest that B/A ratio is not able to predict disease severity in patients with COVID–19 since the AUC for B/A ratio was not statistically significant. As far as we are concerned, previous studies have not considered the predictive value of this indicator as a parameter for disease severity to be comparable to the results of the present study.

One of the limitations of the present study was non–randomized inclusion of patients into the study and to the groups. The non–randomized categorization of the patients into the groups was inevitable, as we had to categorize them according to the disease outcome. The study center is also a referral center, which reduces the bias of non–randomized inclusion of patients into the study; thus, we included all patients into the study by census method. The second limitation is that we have measured BUN and SA levels of participants once and did not consider the time dependent variations in these serum parameters. Another limitation of the study is the risk of bias in the results due to the effect of confounders on the results, for reducing of which we excluded conditions that can affect the serum parameters; however, there could be other factors confounding the results that have not been considered in this study. Last but not least, this was a single–center study and it is questionable, whether the results of this study are replicable in other regions of the country.

CONCLUSION

The results showed high B/A ratio and low SA levels is associated with higher odds of 30-day mortality in patients with COVID–19. In addition, high B/A ratio is also associated with severe forms of disease. The results also demonstrated high B/A ratio ([?]8.88) is not a significant predictor of COVID–19 severity. Considering the significant association of these two serum parameters in mortality and their ease of use, it is suggested to investigate this issue in larger populational studies, especially in patients with severe COVID–19.

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The authors of the present study declare that none of the authors have any conflict of interest.

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Table 1. Distribution of general characteristics according to disease severities and 30-day mortality

Variable	Category	Died (N=118)	Alive (N=315)	P	Outcome during hospitalization	Outcome during hospitalization	Outcome during hospitalization	Outcome during hospitalization	Outcome during hospitalizati
					Mild (N=133)	Severe pneumo-nia (N=160)	ARDS (N=104)	Sepsis (N=26)	Septic shock (N=10)
Gender	Male/female	74/44	189/126	0.650*	76/57	99/61	66/38	15/11	7/3
Age (years), Mean(SD)	Age (years), Mean(SD)	68.7 (1.5)	57.0 (18.1)	<0.0001^{+}	58.2 (18.4)	56.41 (18.5)	69.0 (15.8)	58.4 (18.5)	61.2 (14.7)
Hospital duration (days), Mean(SD)	Hospital duration (days), Mean(SD)	4.5 (6.6)	1.8 (3.4)	<0.0001^{+}	0.9 (1.8)	3.0 (4.9)	3.6 (4.6)	4.0 (9.5)	3.5 (4.9)
Diabetes Melli-tus, No.(%)	Diabetes Melli-tus, No.(%)	28 (23.7)	51 (16.1)	0.021*	19 (14.29)	28 (17.5)	28 (26.92)	4 (15.38)	0 (0)
Hypertension, No.(%)	Hypertension, No.(%)	37 (31.3)	70 (22.2)	0.013*	28 (21.5)	40 (25)	32 (30.77)	7 (26.92)	0 (0)
Intubation, No.(%)	No	66 (55.9)	315 (100)	<0.0001*	130 (97.7)	139 (86.9)	83 (79.8)	21 (80.8)	8 (80)
	Yes	51 (44.1)	0 (0)		3 (2.3)	21 (13.1)	21(20.2)	5 (19.2)	2 (20)

*The results of chi square test or Fisher exact test,$^{+}$The results of one–way ANOVA

Table 2. Bivariate comparison of mean SA levels and B/A ratio at different disease outcomes during hospitalization and final disease outcome

Variable	Disease Outcome	Disease Outcome	Disease Outcome	Outcome in alive patients	Outcome in alive patients	Outcome in alive patients	Outcome in alive patients	Outcome in alive patients	Ou in
	Alive (N=315)	Died (N=118)	P	Mild (N=133)	Severe pneu-monia (N=160)	ARDS (N=104)	Sepsis (N=26)	Septic shock (N=10)	P
Serum albumin (g/dL)	4.31 (0.73)	3.85 (0.72)	<0.0001^{+}	4.11 (0.07)	4.27 (0.75)	4.2 (0.7)	4.21 (0.8)	3.87 (0.4)	0.2
BUN/Albumin (mg/g)	5.06 (4.80)	11.57 (8.67)	<0.0001^{+}	5.85 (5.75)	5.67 (5.61)	8.96 (8.09)	10.5 (9.41)	7.35 (4.53)	<0

$^{+}$The results of one–way ANOVA

Post hoc for pairwise comparison of mean B/A ratio in different disease severities: mild with ARDS (P=0.008), severe pneumonia with ARDS (P=0.002), mild with sepsis (P=0.029), severe pneumonia with sepsis (P=0.016)

Table 3. Results of the logistic regression for the effect of study variables on disease severity

and 30-day mortality

Outcome	Predictor	β(SE)	OR (95%CI)	P
Mild	Albumin	-0.223 (0.458)	0.80 (0.32, 1.96)	0.62
	BUN/Albumin	0.028 (0.053)	1.02 (0.92, 1.14)	0.59
	Age	0.015 (0.021)	1.01 (0.97, 1.05)	0.49
	Being male	0.36 (0.73)	1.44 (0.34, 6.04)	0.61
	Diabetes Mellitus	1.07 (0.90)	2.94 (0.49, 17.32)	0.23
	Hypertension	0.61 (0.895)	1.84 (0.31, 10.63)	0.49
	Hospitalization	0.399 (0.118)	1.49 (1.18, 1.87)	0.001
	Intubation	-1.884 (0.292)	0.15(0.09,0.27)	<0.0001
Severe pneumonia	Albumin	-1.50 (0.323)	0.22 (0.11,0.41)	<0.0001
	BUN/Albumin	0.45 (0.086)	0.96 (0.92,1.00)	<0.0001
	Age	0.049 (0.012)	1.05 (1.02,1.07)	<0.0001
	Being male	0.239 (0.370)	1.27 (0.61,2.62)	0.51
	Diabetes Mellitus	0.67 (0.43)	1.96 (0.83,4.62)	0.12
	Hypertension	-1.145 (0.030)	1.88 (0.87,4.06)	0.10
	Hospitalization	0.082 (0.030)	1.08 (1.02,1.15)	0.007
	Intubation	-0.630 (0.078)	0.53 (0.46,0.62)	<0.0001
ARDS	Albumin	–1.196 (0.319)	0.30 (0.16, 0.56)	<0.0001
	BUN/Albumin	0.169 (0.059)	1.17 (1.04, 1.32)	<0.0001
	Age	0.034 (0.014)	1.03 (1.00, 1.06)	0.016
	Being male	-0.182 (0.408)	0.23 (0.065, 0.88)	0.65
	Diabetes Mellitus	-0.105 (0.468)	0.90 (0.31, 3.85)	0.82
	Hypertension	-0.055 (0.454)	0.94 (0.38, 2.30)	0.90
	Hospitalization	-0.022 (0.032)	0.97 (0.91, 1.04)	0.50
	Intubation	-1.435 (0.249)	0.24 (0.15,0.39)	<0.0001
Sepsis	Albumin	-0.989 (0.579)	0.37 (0.12, 1.15)	0.087
	BUN/Albumin	0.148 (0.073)	1.15 (1.00, 1.33)	0.043
	Age	0.105 (0.042)	1.11 (1.02, 1.20)	0.011
	Being male	-0.316 (0.797)	0.72 (0.15, 3.47)	0.69
	Diabetes Mellitus	1.099 (1.258)	3.00 (0.25, 35.33)	0.38
	Hypertension	2.262 (1.221)	9.60 (0.87, 105.16)	0.06
	Hospitalization	0.104 (0.086)	1.11 (0.93, 1.31)	0.22
	Intubation	-0.359 (0.124)	0.70 (0.55,0.90)	0.004
Septic shock	Albumin	5.21 (3.99)	0.55 (0.22, 1.39)	0.192
	BUN/Albumin	-0.040 (0.137)	0.96 (0.73, 1.25)	0.77
	Age	-0.040 (0.057)	0.96 (0.85, 1.07)	0.48
	Being male	0.98 (1.44)	1.24 (0.29, 5.16)	0.765
	Diabetes Mellitus	-	-	-
	Hypertension	-	-	-
	Hospitalization	0.046 (0.149)	1.04 (0.78, 1.40)	0.75
	Intubation	-0.277 (0.158)	0.76 (0.56,1.03)	0.080
30-day mortality	Albumin	-0.841 (0.158)	0.43 (0.31, 0.58)	< 0.0001
	BUN/Albumin	0.149 (0.021)	1.16 (1.11, 1.21)	< 0.0001
	Age	0.043 (0.007)	1.04 (1.02, 1.05)	< 0.0001
	Being male	0.161 (0.225)	1.17 (0.75, 1.82)	0.47
	Diabetes Mellitus	0.590 (0.274)	1.80 (1.05, 3.08)	0.03
	Hypertension	0.629 (0.251)	1.87 (1.14, 3.06)	0.012
	Hospitalization	0.071 (0.022)	1.07 (1.02, 1.12)	0.001
	Intubation	-1.098 (0.100)	0.33 (0.27, 0.40)	< 0.0001

Table 4. Validity indices for prediction of disease severity by B/A

Indices	Cut-off point	Area under curve (95% CI)	Sensitivity	Specificity
Albumin (g/dL)	3.91	0.4408 (0.39, 0.50)	65.97%	30.75%
BUN/Albumin (mg/g)	8.88	0.4521 (0.35,0.46)	71%	22%

Hosted file

`image1.emf` available at https://authorea.com/users/451244/articles/712194-the-role-of-serum-albumin-and-blood-urea-nitrogen-to-serum-albumin-ratio-in-prediction-of-disease-severity-and-thirty-day-mortality-in-patients-with-covid-19

Figures

Figure 1. ROC curve for SA levels (right) and B/A ratio (left) based on the disease severity in SARS-CoV-2 patients