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A Comparison of BUN/Albumin Ratio with PSI and CURB-65 for Predicting Mortality in COVID-19 Pneumonia in the Emergency Department

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ABSTRACT

Introduction: The coronavirus disease-2019 (COVID-19) pandemic was the leading cause of high mortality and morbidity in the previous two years. Rapid determination of the severity of the disease is important in terms of reducing the intensity and initiating effective treatment. Although the pneumonia severity index (PSI) and CURB-65 classifications are widely employed to predict mortality and morbidity in patients diagnosed with pneumonia, biomarkers predicting the mortality and severity of COVID-19 in the emergency department (ED) are also needed. This study investigated the relationship between the blood urea nitrogen (BUN)/albumin ratio (BAR) and mortality and disease severity.

Methods: Five hundred eighty-one patients presenting to the ED between March 2020 and January 2022 and diagnosed with COVID pneumonia were included in this observational study. Patients' BUN and albumin levels, and PSI and CURB-65 scores were calculated, and in-hospital mortality was recorded. The power of BAR in predicting mortality was compared with that of PSI and CURB-65 by using statistical analysis.

Results: A significant association was determined between increased BAR and mortality. The area under the curve (AUC) value of BAR was 0.684, with 76.6% selectivity and 53.4% sensitivity at a cut-off point of 6.85. The CURB-65 score AUC value was 0.571, with 56% selectivity and 55.9% sensitivity at a cut-off point of 1.5. The AUC value for the PSI score was 0.609, with 63.3% selectivity and 50.3% sensitivity at a cut-off point of 107.5.

Conclusion: BAR is a simple but independent marker of mortality and severity in COVID-19 viral pneumonia.

Keywords: BUN/albumin ratio, emergency department, COVID-19, mortality

Introduction

The coronavirus disease-2019 (COVID-19) has caused very considerable numbers of cases and deaths since it was first observed in December 2019. According to the World Health Organization, more than 500 million cases and 6 million deaths have been reported in the intervening period (1,2) Considering the disease's ability to mutate, insufficient availability of vaccines, especially in developing countries, and the constant threat of novel variants, it is still impossible to conclude that COVID-19 is no longer a part of daily life.

Hospital presentations due to COVID-19 reached extraordinary levels in all countries, and a large part of these involved emergency departments (EDs). Serious difficulties were encountered in patient management because of the resulting intensity and uncertainties concerning the prognosis of the disease. Although new guidelines aimed at treatment have been continuously published, studies regarding the management of EDs are still insufficient.

Easily calculated follow-up parameters and biomarkers for predicting mortality and mortality are required for the successful emergency management of patients with COVID-19. Predicting the severity of the disease will both facilitate the ED management of patients and enable accurate and effective treatment to be initiated without loss of time. Several biomarkers have been studied for this purpose, including D-dimer, troponin, and ferritin (3). The principal biomarkers in recent studies are albumin and blood urea nitrogen (BUN) levels. BUN is a component of CURB-65 used in pneumonia and exhibits a powerful correlation with disease severity. As a regulator of osmotic pressure and an acute phase reactant, albumin is a marker of mortality. These two critical markers have also been tested in conditions other than pneumonia and have been proved to be successful indicators of mortality in such different conditions as chronic obstructive pulmonary disease (4), pancreatitis (5, 6), and acute myocardial infarction.

Recent studies have reported that the BUN/albumin ratio (BAR) is a more successful indicator of mortality than BUN and albumin in pneumonia,

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the elderly, and non-chronic kidney failure patients (7). The present study investigated the role of the BAR in predicting mortality in patients presenting to the ED and diagnosed with COVID-19. To determine its success in predicting mortality, we also compared it with CURB-65 and the pneumonia severity index (PSI), contemporary, and reliable follow-up parameters used in calculating early period mortality in pneumonia (8).

Methods

Study Design

This observational retrospective study was conducted in the ED of an affiliated tertiary university hospital in the province of İzmir, Turkey, between March 2020 and January 2022. The laboratory parameters of patients diagnosed with COVID-19 in the ED were analyzed. Data were calculated for predicting mortality and morbidity, and were compared with PSI and CURB-65 data.

Patients and Setting

Patients aged over 18, presenting with symptoms suggestive of COVID-19 pneumonia, and with positive polymerase chain reaction (PCR) test results were included in the study. Patients with additional diseases other than COVID-19 pneumonia, or with medical history of kidney failure or chronic liver diseases were excluded. Patients' whose data were inaccessible or with deficient laboratory data were also excluded.

Patients with findings in favor of COVID pneumonia on thoracic computed tomography (CT) and positive PCR tests for the confirmation of pneumonia were subjected to analysis.

Data Collection

Data for patients presenting to the ED were collected from the hospital information system. The vital parameters, demographic data, and laboratory test results of the patients included in the study were recorded for statistical analysis. Exitus and discharge information for patients admitted to COVID treatment and intensive care units from the ED was also noted. BAR and PSI and CURB-65 scores were calculated from the data obtained and were compared to analyze their value in predicting mortality.

Statistical Analysis

Number and percentage were calculated for categorical variables, and mean, standard deviation and interquartile range (IQR) for numerical variables. Histogram curves, kurtosis, skewness, and the Shapiro-Wilk test were employed to determine whether continuous variables were normally distributed. Receiver operating characteristic (ROC) analysis was performed to evaluate the power of the test to predict mortality. Since the data did not show a normal distribution, the Mann-Whitney U test was used when comparing the mean of the 2 independent groups. Logistic regression analysis was performed to evaluate the success of the BAR, PSI, CURB65 tests in predicting mortality. All statistical calculations were carried out on SPSS 22.0 software and at a 95% confidence interval.

Results

Examination revealed that 1086 patients presented to our ED between March 2020 and January 2022, and 581 patients who met the inclusion criteria were enrolled. The exclusion criteria are shown in the consult diagram (Figure 1).

Men constituted 281 (37.5%) patients included in the study and women 363 (62.5%). The patients' mean age was 65 (19-97) years.

One hundred seventy-nine (30.8%) of these patients were admitted to intensive care units and 207 (35.6%) to COVID treatment units. One hundred ninety-five patients (33.6%) were discharged after treatment planning in the ED. Worsening was observed during follow-up in 108 (52.1%) of the 207 patients admitted to COVID treatment units, and these were transferred to the intensive care unit. In-hospital mortality occurred in 175 (30.1%) patients treated in the intensive care units.

Laboratory results, BAR, PSI, and CURB-65 scores were compared between the in-hospital non-survivor and survivor patient groups. BAR, PSI, CURB-65, BUN, creatinine, albumin, sodium, hematocrit, white blood cell, neutrophil, lymphocyte and C-reactive protein, were statistically significant in predicting mortality (Table 1).

ROC analysis was performed to determine the predictive power of BAR, PSI, and CURB-65 in terms of in-hospital COVID-19 mortality (Figure 2). Cut-off values were determined for BAR, CURB-65, and PSI parameters. The area under the curve (AUC) value for BAR was 0.684, exhibiting 76.6% specificity and 53.4% sensitivity, with a cut-off value of 6.85. The AUC value for CURB-65 was 0.571, with specificity of 56%, sensitivity of 55.9%, and a cut-off value of 1.5. The equivalent values for PSI were AUC 0.609, specificity 63.3%, sensitivity 53%, and a cut-off value of 107.5 (Table 2).

Regression analysis was performed to determine the value of BAR and PSI and CURB-65 scores in predicting mortality. BAR and PSI emerged as significant indicators of in-hospital mortality. However, regression analysis also showed that the BAR variable was a more relevant predictor of mortality compared with the other markers for each standard deviation change (Table 3).

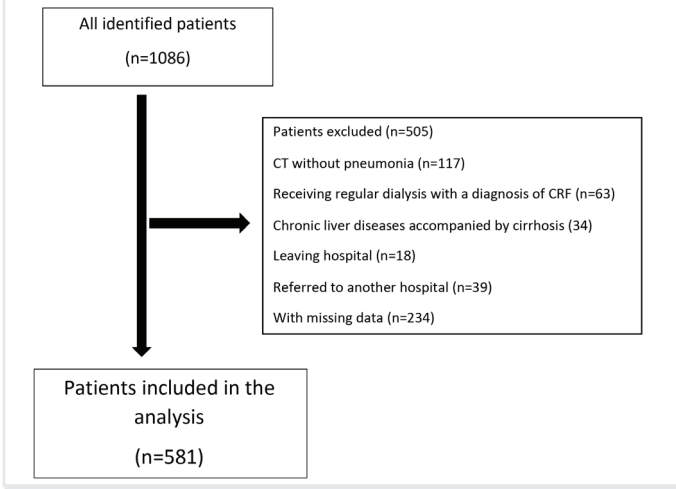

Figure 1. Consult diagram
CT: Computed tomography, CRF: Chronic renal failure

Table 1. Intragroup comparisons of variables in terms of in-hospital mortality

Parameters	Non-survivor, median (IQR)	Survivor, median (IQR)	p-value
BUN (mg/dL)	33 (40)	22 (17.25)	**0.001**
Albumin (g/dL)	3.2 (0.9)	3.4 (0.8)	**0.001**
Creatinine	1.32 (1.62)	1.07 (0.68)	**0.001**
Sodium	136 (7)	137 (6)	**0.036**
Glucose	136 (76)	132.50 (70.25)	0.882
Hematocrit	34.70 (9.30)	36.40 (8.80)	**0.004**
WBC	9.73 (7.15)	8.04 (6.24)	**0.001**
Neutrophil	7.71 (6.39)	5.76 (5.51)	**0.001**
Lymphocyte	1.15 (0.88)	1.30 (0.95)	**0.041**
Eosinophil	0.03 (0.11)	0.04 (0.11)	0.301
CRP	92.42 (124.50)	54.92 (113.55)	**0.006**
BAR (mg/g)	10.7 (13.7)	6.5 (5.5)	**0.001**
PSI	121 (46)	105 (45)	**0.001**
CURB-65	2 (1)	1 (1)	**0.005**

BUN: Blood urea nitrogen, IQR: Interquartile range, WBC: White blood cell, CRP: C-reactive protein, BAR: BUN/albumin ratio, PSI: Pneumonia severity index

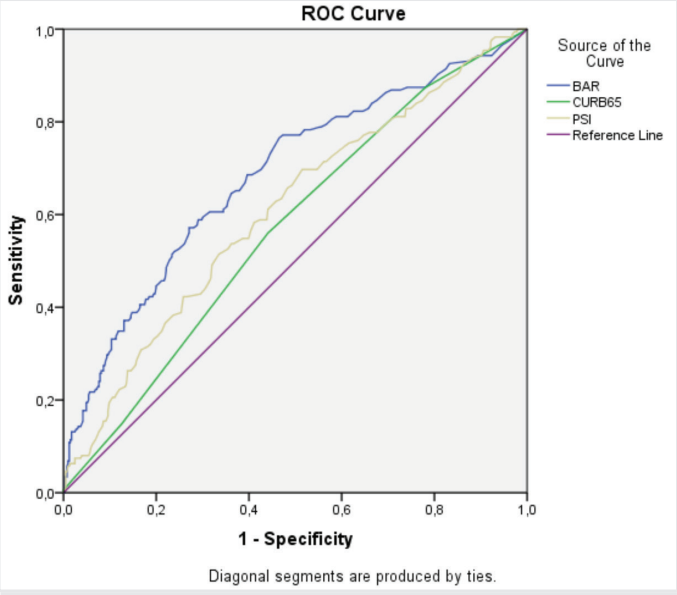

Figure 2. ROC curve for determining mortality prediction power
ROC: Receiver operating characteristic, BAR: BUN/albumin ratio, PSI: Pneumonia severity index

Discussion

The COVID-19 pandemic has resulted in significant research aimed at understanding viruses responsible for epidemics and at examining the characteristic findings of the disease. A significant study is also being performed on the development of powerful markers for determining the severity of existing viral pneumonia and predicting mortality. The objective is to be able to make predictions, not solely for the COVID pandemic, but also for subsequent epidemics.

This study analyzed many quantitative parameters potentially associated with the inflammatory response and potential markers associated with mortality. These novel biomarkers were then compared with classic scores such as CURB-65 and PSI.

Table 2. ROC analysis results by in-hospital mortality status

Test result variable(s)	AUC	Standard errora	Asymptotic Sig.b	Asymptotic 95% CI	
				Lower bound	Upper bound
BAR	0.684	0.025	0.001	0.635	0.732
CURB-65	0.571	0.025	0.007	0.521	0.620
PSI	0.609	0.026	0.001	0.559	0.659

ROC: Receiver operating characteristic, AUC: Area under the curve, Sig.: Significance, CI: Confidence interval, BAR: BUN/albumin ratio, PSI: Pneumonia severity index

Table 3. Regression analysis of BAR, PSI and CURB-65

	Beta	Six.	Exp (beta)	95% CI for EXP (B)	
				Lower	Upper
BAR	1.1	0.001	3.0	2.0	4.5
CURB-65	-0.1	0.601	0.891	0.6	1.4
PSI	0.5	0.035	1.6	1.1	2.4

BAR: BUN/albumin ratio, PSI: Pneumonia severity index, CI: Confidence interval

BUN is a valuable marker of mortality in several diseases, and particularly emerges in association with sepsis-related dehydration (9,10). It is also a component of the CURB-65 scoring system (11). Cheng et al. (12) reported that BUN values predicted mortality in a study investigating the validity of the infective parameters BUN and D-dimer in patients with COVID-19. In their meta-analysis, Shao et al. (13) suggested that acute kidney failure and increased BUN levels were useful in predicting mortality in patients with COVID-19. Liu et al. (14) calculated BUN-creatinine ratios and found that these were correlated with mortality. The mean BUN levels calculated in this study were significantly higher in the non-survivor patient group than in the surviving group, and the results were consistent with the current literature [median (IQR): exitus group: 33 (40); discharged group: 22 (17.25); p<0.001)].

Albumin is a negative acute phase reactant involved in the neutralization of endogenous and exogenous substances, antioxidation, immune system regulation, and anti-inflammatory processes (15,16). Albumin levels may decrease in cases of malnutrition, inflammation, and hepatocellular injury. Previous studies have reported that a decrease in albumin levels is associated with mortality in COPD, pancreatitis, acute coronary syndrome, and pneumonia (4,6,17,18). In their study of 319 patients, Violi et al. (19) reported a powerful negative correlation between mean albumin levels and mortality in patients with COVID-19. In another meta-analysis, Aziz et al. (20) reported a link between low albumin levels and mortality in COVID-19 patients. The results of this study were in agreement with the previous literature, with mean albumin levels significantly predicting non-survivor patients [median (IQR): exitus group: 3,2 (0.9); discharged group: 3.4 (0.8); p<0.001)].

BAR calculated using BUN and albumin is a powerful independent predictor of mortality and disease severity in current studies. Ugajin et al. (21) described BAR as significant in predicting in-hospital mortality

and determining the severity of community-acquired pneumonia. The odds ratio (OR) value calculated for BAR in that study was 1.10 (21). In a study of patients aged over 65 presenting to the ED, Dundar et al. (22) compared BUN, albumin, and epidermal growth factor receptor levels with BAR. Those authors concluded that the risk of hospitalization was higher in patients with increased BAR, and that BAR exhibited better correlation than other laboratory parameters studied in the ED in terms of determining disease severity. Dundar et al. (22) calculated an OR value of 2.82 for BAR. Küçükceran et al. (23) reported an OR value of 10.48 for BAR in the prediction of in-hospital mortality among patients with COVID-19 in the ED. The AUC value for BAR in that study was 0.809, with 87.5% sensitivity and 59.9% specificity and a cut-off point of 3.9 mg/g (23). The value for BAR in this study was 3 and was significantly higher in the non-survivor group than in the survivors [median (IQR): exitus group: 10.7 (13.7); discharged group: 6.5 (5.5); $p<0.001$)]. The AUC value for BAR in this study was 0.684, with selectivity of 76.6% and sensitivity of 53.4%. The threshold value for the cut-off point was 6.85.

BAR is a biomarker with results that provide a successful prediction recently. Ryu et al. (7) compared BAR and PSI and CURB-65 scores in patients with aspiration pneumonia and reported significant success. In an important study of patients receiving immunosuppressants, Xia et al. (24) reported that the use of classic biomarkers was not sufficient to show mortality and morbidity. The authors also concluded that BAR exhibited a powerful negative correlation with disease severity (24). The results in this study were similar to an AUC value of 0.684 for BAR, 0.571 for CURB-65, and 0.609 for PSI. BAR thus appears to exhibit a similar power to PSI scores in predicting in-hospital mortality in COVID-19 pneumonia. In the regression model established, the mortality risk increased three times for each one unit of standard deviation in the BAR value, and 1.6 times for each one unit of deviation in PSI values. However, CURB-65 was not statistically significant in the regression model. Additionally, PSI is an algorithm with many parameters, including patient characteristics, comorbidities, physical examination findings, radiographic findings, and laboratory results (25). In order for PSI to be use capable of as a predictor of mortality, it is therefore necessary to have a good knowledge of the patient's history, with parameters that can be calculated in routine clinical practice (26). CURB-65 is a simple and widely employed tool, particularly in EDs (11). However, the value of this scoring system decreases in young patient groups, and it is difficult to evaluate in patients with an uncertain mental state before infection (27) BAR represents an important biomarker for overcoming these difficulties in data acquisition.

Study Limitations

This study did not consider the possibility that patients with non-end-stage chronic kidney disease may have a high baseline BUN and that patients with liver disease without cirrhosis may have low baseline albumin levels.

The principal limitations of this study are its retrospective, single-center nature and the small patient numbers.

Conclusion

The results of this study showed that BAR can be used to predict mortality in patients with COVID-19 pneumonia since it can be calculated easily and quickly with simple laboratory parameters that can be obtained in all EDs. It also exhibited a strong predictive power compared with PSI and CURB-65 in predicting in-hospital mortality in patients with COVID-19 pneumonia.

Additionally, this is the first study to compare BAR with PSI and CURB-65 scores in terms of predicting in-hospital mortality in COVID-19 pneumonia.

Ethics Committee Approval: This study was approved by the Ethics Committee of İzmir Katip Çelebi University Non-Interventional Clinical Research Ethics Committee (approval number: 0596, date: 20.01.2022).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: M.G.E., O.S.Ç., A.K.; Design: M.G.E., H.A.; Data Collection or Processing: M.G.E., U.P., A.K.; Analysis or Interpretation: M.G.E., H.A., A.K.; Literature Search: M.G.E., U.P., H.A.; Writing: M.G.E., U.P., H.A.

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