Procalcitonin to Albumin Ratio as A Biomarker for Predicting Mortality in Sepsis

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ABSTRACT

Objective: To investigate the ability of the procalcitonin to albumin ratio to predict mortality in patients with sepsis.
Study Design: Observational study.
Place and Duration of Study: Department of Intensive care, Samsun Training and Research Hospital, Samsun, Turkiye, from September to December 2022.
Methodology: Patients diagnosed with sepsis admitted to the intensive care unit were included in the study. They were divided into two groups based on their prognosis (expiry/survival). The procalcitonin, albumin, procalcitonin to albumin ratio, C-reactive protein (CRP), lactate, neutrophil, lymphocyte, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) levels of sepsis patients admitted to the intensive care unit were evaluated. A comparison was made between those who survived and those who expired.
Results: The procalcitonin, AST levels, and procalcitonin to albumin ratio of the sepsis patients who expired were higher than those of the sepsis patients who survived. Albumin and lymphocyte levels of patients who expired were lower than those in the patients who survived. In the ROC analysis, the sensitivity of the procalcitonin to albumin ratio was 79.20%, and the specificity was 81.80%. The procalcitonin to albumin ratio was positively related with procalcitonin, C-reactive protein, and aspartate aminotransferase levels, and negatively related with albumin and lymphocyte levels.
Conclusion: A procalcitonin to albumin ratio of 0.185 and above was found to be risky in terms of mortality in sepsis patients.

Key Words: *Procalcitonin to albumin ratio, Procalcitonin, Albumin, Sepsis.*

How to cite this article: Keskin A, Aci R. Procalcitonin to Albumin Ratio as A Biomarker for Predicting Mortality in Sepsis. *J Coll Physicians Surg Pak* 2024; **34(03)**:360-363.

INTRODUCTION

Sepsis is a global health problem, the leading cause of death from infection. Sepsis should be detected and diagnosed as soon as possible, so that, it does not turn into septic shock with mortality rate of 40% or more.[1] Early detection and treatment management of sepsis, which is the most widespread reason for intensive care unit (ICU) admissions, has always challenged healthcare professionals.[2]

The level of procalcitonin in the blood rises in answer to a pro-inflammatory stimulant, particularly caused by bacteria, and is generally classified as an acute phase reactant.[3] Procalcitonin levels may allow sepsis patients to be evaluated for ICU admission or mortality.[4]

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Received: March 07, 2023; Revised: July 08, 2023;
Accepted: October 23, 2023
DOI: https://doi.org/10.29271/jcpsp.2024.03.360

Albumin the most plentiful protein in the blood, has a regulative and important impact in acid-base physiology, dispersion of body fluids, and binding of main constituents in the blood circulation.[5] Additionally, albumin, an acute-phase protein, is a general biomarker for disease severity. Therefore, in critically ill patients, their levels fluctuate with fluctuations in the illness. During intensive care patient follow-up, serum albumin levels are analysed to monitor nutrition and assess disease severity.[6]

In inflammation, albumin levels decrease on one side and procalcitonin levels increase on the other. Sepsis is the leading cause of infection-related death. Predicting mortality in patients with sepsis and managing treatment accordingly can reduce the infection-related mortality rate. This study was conducted to investigate the procalcitonin to albumin ratio as a biomarker for predicting mortality in patients admitted to the ICU due to sepsis.

METHODOLOGY

The Ethics Committee approval was taken from the Human Research Ethics Committee of the Samsun Training and Research Hospital, Samsun, Turkiye (number GOKA/2022-8-8; dated 16th August 2022). The study period was from September to December 2022. The patients' data were retrospectively scanned and retrieved from the Hospital Information Management System.

The study was a single-centre observational retrospective study. Patients with sepsis in Internal Medicine ICU with positive microbial culture growth in the blood samples, were included in the study. Patients with no growth in their blood cultures were excluded from the study. In addition, patients younger than 18 years of age, and patients with malnutrition, malignancy or systemic haematological disease were excluded from the study as the results may be misleading. Patients were divided into two groups according to their prognosis (expiry/survival). The expiry group consisted of 53 patients and the survival group consisted of 33 patients. The procalcitonin, albumin, and procalcitonin to albumin ratio of the two groups were evaluated. C-reactive protein (CRP), lactate, neutrophil, lymphocyte, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) levels were also evaluated. The initial laboratory findings examined on the day of admission to the ICU were evaluated.

Procalcitonin levels were studied by electrochemiluminescence method using Elecsys BRAHMS procalcitonin kit on a Roche Diagnostic Cobas E601 device (Basel, Switzerland). Albumin levels were studied using a photometric colour test used for the quantitative determination of albumin in human plasma and serum on a Beckman Coulter AU5800 (Brea, California, USA) analyzer.

Statistical analyses were performed using SPSS v22 for Windows (IBM Corporation, Armonk, New York, USA). Categorical data were presented as percentiles and continuous data as medians (25^{th} to 75^{th} percentiles (Q1-Q3)). Normally distributed continuous data were presented as mean ± standard deviation. The normality analysis for continuous data was performed using the Shapiro-Wilk analysis. Since the groups' data did not show normal distribution, they were compared with the Mann-Whitney U analysis. Binary logistic regression test (Method=Enter) was performed for the procalcitonin to albumin ratio. In addition, receiver operating characteristic (ROC) curve test was performed to evaluate the specificity and sensitivity of the procalcitonin to albumin ratio. Kaplan-Meier analysis was performed to determine the risk levels of procalcitonin to albumin ratio in terms of survival. Additionally, correlation analysis was performed using Spearman correlation analysis. Levels with a p-value less than 0.05 were considered significant.

RESULTS

A total of 86 sepsis patients aged between 44 and 91 years hospitalised in ICU were included in the study. Descriptive data of these patients is presented in Table I.

While the mean age of the patients in the expiry group was 70.77±9.52 years, the mean age of the patients in the survival group was 69.30±12.13 years. Eighteen (33.96%) of the patients in the expiry group were women and 35 (66.04%) were men. Twelve (36.36%) of the patients in the survival group were women and 21 (63.64%) were men. The median (Q1-Q3) hospitalisation days of the patients in the expiry group were 22 (12-32), and the median hospitalisation days of the patients in the survival group were 24 (14-32). Eighteen (33.96%) of the pathogens were gram (-) bacteria and 35 (66.04%) were gram (+) bacteria in patients in the expiry group. Nine (27.27%) of the pathogens were Gram (-) bacteria and 24 (72.73%) were Gram (+) bacteria in patients in the survival group. There was no significant difference in the mean age, gender, and pathogen factor ratios of these groups and the median hospitalisation days. Laboratory findings of these groups are presented in Table II.

The procalcitonin, procalcitonin to albumin ratio, and AST levels of the patients in the expiry group were higher than the patients in the survival group. In addition, the albumin and lymphocyte levels of the patients in the expiry group were lower than the patients in the survival group (Table II).

The levels of the survival group were taken as a reference in regression analysis. Nagelkerke R^2 was found to be 0.397, and the predicted ratio was 76.70% for procalcitonin to albumin ratio ($p<0.001$).

According to the ROC test results, the area under the curve (AUC) was 0.860, the specificity was 81.80%, and the sensitivity was 79.20% ($p<0.001$).

According to Kaplan-Meier analysis, the median level for procalcitonin-to-albumin ratio was determined as 0.185 (95% CI 0.088-0.282). Kaplan-Meier curve predicted that procalcitonin to albumin ratio of 0.185 and above is risky for mortality.

According to the correlation analysis, a positive correlation was determined between the procalcitonin to albumin ratio and procalcitonin (correlation coefficient (r)=0.993, p<0.001), CRP (r=0.286, p=0.008) and AST (r=0.215, p=0.047). Additionally, it was negatively correlated with albumin (r=-0.362, p=0.001) and lymphocyte (r=-0.358, p=0.001) levels.

Table I: Descriptive data of patients.

Parameters Median (Q1-Q3)	Patients (n=86)
Gender n (%)	
Men	56 (65.12)
Women	30 (34.88)
Age mean (X±SD)	70.21±10.55
Pathogen n (%)	
Gram (+) bacteria	59 (68.60)
Gram (-) bacteria	27 (31.40)
Length of stay days	23 (13-32)
Prognosis n (%)	
Expiry	53 (61.63)
Survival	33 (38.37)
Procalcitonin (µg/L)	1.47 (0.36-5.95)
Albumin (g/L) (X±SD)	24.73±5.39
Procalcitonin to albumin ratio	0.056 (0.01-0.23)
C-reactive protein (mg/L)	136.50 (81.20-268.00)
Lactate (blood gas) (mmol/L)	2.35 (1.60-3.40)
Neutrophil (10^9/L)	9.75 (6.50-15.60)
Lymphocyte (10^9/L)	0.90 (0.40-1.40)
Aspartate aminotransferase (U/L)	38.00 (20.00-56.00)
Alanine aminotransferase (U/L)	18.50 (10.00-45.00)

Table II. Laboratory findings of groups formed according to prognosis status.

Parameters	Reference range	Expiry n=53 Median (Q1-Q3)	Survival n=33 Median (Q1-Q3)	p*
Procalcitonin (µg/L)	0-0.046	3.56 (1.43-7.94)	0.36 (0.16-0.97)	<0.001
Albumin (g/L) (X±SD)	35-52	23.30±5.02	27.02±5.23	0.001
Procalcitonin to albumin ratio		0.14 (0.030-0.414)	0.014 (0.005-0.040)	<0.001
C-reactive protein (mg/L)	0-5	155.00 (104.00-291.00)	110.00 (65.50-251.00)	>0.05
Lactate (blood gas) (mmol/L)	0.50-1.60	2.40 (1.60-3.40)	2.10 (1.60-3.40)	>0.05
Neutrophil (10^9/L)	2.00-6.90	9.69 (6.40-16.30)	9.80 (7.80-14.40)	>0.05
Lymphocyte (10^9/L)	0.60-3.40	0.70 (0.40-1.10)	1.20 (0.80-1.50)	0.010
Aspartate aminotransferase (U/L)	0-35	43.00 (24.00-61.00)	28.00 (19.00-47.00)	0.044
Alanine aminotransferase (U/L)	0-35	27.00 (11.00-64.00)	16.00 (10.00-30.00)	>0.05

** Mann-Whitney U test.*

DISCUSSION

Sepsis is related with a high rate of inpatient mortality. Treatment in ICUs with more experience in treating patients with sepsis has a lower mortality rate.[7] However, sepsis is a common cause of ICU admission and death in the ICU.[8] Additionally, the early diagnosis of sepsis cases who are at risk of death in ICU continues to be a problem.[9]

Procalcitonin is a potential infection biomarker to evaluate the clearance, eradication, and presence of infection, guide antibiotic management, and predict mortality.[10] In addition, procalcitonin guidance in sepsis has been effective in reducing mortality, side effects due to infection, and hospitalisation costs.[11] However, owing to its secretion during non-infectious processes, procalcitonin has limited use to achieve its goal of high sensitivity, specificity, and ability to monitor the progression of sepsis.[12]

Procalcitonin levels are particularly elevated in patients with gram-negative infections, and the injection of endotoxin, a product of gram (-) bacteria, induces procalcitonin release in healthy human participants.[13] Procalcitonin levels are a valuable biomarker in distinguishing between Gram (+) and Gram (-) sepsis patients.[14] In this study, the procalcitonin levels in the expiry group were higher than those in the survival group. In addition, there was no significant difference in the rates of pathogenic agents (Gram (-) or Gram (+)) detected between the groups.

Albumin modulates the inflammatory response, can affect oxidative damage and maintain colloid osmotic pressure. Decrease in albumin values (hypoalbuminemia), which has very important features, is common in ICU.[15] In addition, although albumin synthesis rates in septic patients are similar to non-septic patients, mean plasma albumin levels are reduced.[16] Decreased albumin levels reverse their positive effects on vessel wall integrity and increase capillary permeability.[17] In this study, the albumin values in the expiry group were lower than those in the survival group.

A study of newborns with sepsis found that the procalcitonin to albumin ratio was a useful independent marker in determining the presence and severity of neonatal sepsis. It has also been found to be associated with disease severity.[18] In another study with patients with sepsis-induced acute kidney injury, it was stated that the procalcitonin albumin ratio was an independent risk factor with a robust and accurate risk assessment for poor prognosis.[19] In a recent study, it was stated that the procalcitonin albumin ratio was an important determinant of septic shock and 28-day mortality compared to procalcitonin or albumin alone in sepsis patients.[20]

In this study, the procalcitonin to albumin ratio detected in the expiry group was higher than those of the survival group. CRP and AST levels in the expiry group were higher than those of the survival group. Additionally, lymphocyte levels in the expiry group were lower than those in the survival group. Additionally, the procalcitonin to albumin ratio was positively correlated with procalcitonin, CRP and AST levels. It also showed a negative correlation with albumin and lymphocyte levels.

CONCLUSION

The procalcitonin to albumin ratio can be considered as a useful biomarker in predicting mortality in sepsis patients. A procalcitonin to albumin ratio of 0.185 and above should be considered risky for mortality.

ETHICAL APPROVAL:

The Ethics Committee approval was taken from the Human Research Ethics Committee of the Samsun Training and Research Hospital, Samsun, Turkiye (Number GOKA/2022-8-8; dated 16th August 2022).

PATIENTS' CONSENT:

Informed consents were taken from all patients included in the study.

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTION:

AK: Conception and designing of the study, creating the study plan, acquisition, analysis, and interpretation of data, writing the manuscript.

RA: Data processing, design of the work, and critical revision of the manuscript.

All authors approved the final version of the manuscript to be published.

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