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Original Research Article

A Comparative Study between CRP/Albumin Ratio and Serum Procalcitonin as A Prognostic Marker in Sepsis

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Abstract:

Backgrounds: One of the most prevalent causes of death among hospitalized patients in the critical care unit is sepsis (ICU). Because of the various co-morbidities and underlying disorders that these people have, diagnosing them is very difficult. A combination of hematological, biochemical, and microbiological tests can be used to identify sepsis. PCT and CRP levels are commonly considered valid indicators of the degree of systemic inflammation. The ratio of CRP to albumin is increasingly used as a biomarker for both systemic inflammation and nutritional status. The current study aimed to see if the CRP/albumin ratio, combined with procalcitonin, could be used to predict sepsis.

Methods: This was a prospective cross-sectional study carried out with 150 patients. Baseline characteristics, biochemical investigations, and serum CRP/albumin ratios were done. The quantitative variables were expressed as mean and standard deviation compared by ANOVA followed by Bonferroni's correction. A p-value of <0.05 was considered significant.

Results: Serum procalcitonin levels were significantly higher on day-1 in non-survivors compared to survivors (P<0.0001). CRP/albumin ratio was substantially higher on day-1, day-3, and the day of discharge in non-survivors compared to survivors (P<0.0001).

Conclusion: Despite the use of optimal treatment and an improved approach, the death rate in sepsis has been proven to be high (56.2 percent). Patients with increased procalcitonin and CRP/albumin ratio at admission can be better classified and identified as having a higher risk of adverse outcomes.

Keywords: Meningitis, CSF studies, hospital mortality, and biochemical investigations.

Introduction

In (ICU), sepsis is one of the leading causes of mortality, and diagnosing these patients is difficult as they undergo several comorbidities. [1,2] Severe sepsis can be diagnosed based on understanding the disease pathophysiology, pro-inflammatory and anti-inflammatory responses are triggered, as well as routes that aren't altered. A complicated interplay between the infectious pathogen and the host characterizes sepsis, which results in a wide range of distinct symptoms.

Sepsis detection is based on the "SOFA score" (Sequential Assessment of Organ Failure in Sepsis). [3] As of 2016, the Quick SOFA (quick SOFA) platform existed. To diagnose sepsis, various laboratory tests are required, including those that the acid-base balance, organ function, and blood oxygenation should be assessed. Sepsis can be diagnosed by combining hematological, biochemical, and microbiological investigations. [4] Instead of waiting years for a culture-based diagnosis, scientists have been working hard in recent years to uncover biomarkers that could aid in the early detection of this disease.

Procalcitonin and CRP are two of the most often studied indicators because they have the potential to enhance or replace current ones. CRP and PCT (PCT). In order for them to be effective, they must be utilized in conjunction with comprehensive clinical examinations and other laboratory data. It is widely accepted that PCT and CRP levels are reliable measures of the severity of systemic inflammation. [5] Bacterial infections can boost the

synthesis of procalcitonin and CRP levels within a few hours because of their potent activation.

More seriously ill and hospitalized patients are at greater risk of hypoalbuminemia. In severe sepsis, capillary leakage causes an increase in intravascular albumin loss and the catabolism of albumin is increased in the presence of acute sepsis. [6] CRP/albumin ratio is now considered a biomarker for systemic inflammation and nutritional status; it's frequently used in the assessment of individuals with severe sepsis. [7]

Objective

The present study evaluated if CRP/albumin ratio could be used in conjunction with procalcitonin to predict sepsis.

Material and Methods

Study design

This prospective cross-sectional study was carried out in the Department of Medicine, IMS & SUM Hospital, Bhubaneswar, a tertiary care hospital catering to patients. Each of the 150 participants in the study was admitted to IMS & SUM Hospital met the inclusion criteria and supplied their written/informed consent. The Ethical Committee of IMS & SUM Hospital approved the study, and informed/written consent was obtained from the patients and/or their family members after thoroughly explaining the process. All patients above 18 years of age. All patients with suspected cases of sepsis (Inclusion criteria: suspected cases of sepsis who fulfilled the criteria as described in American College of Chest Physician guidelines.

Details of laboratory examinations

Detailed history and thorough clinical examination were made. Clinical data including demographics, presenting symptoms, co-morbidities, drug history, occupation, travel history, clinical examination findings, laboratory investigations, treatment and final outcome were recorded in a proper format. History of illness and symptoms was obtained from guardians or accompanying close relatives if the subject was unable to communicate. Investigations included a complete hemogram, renal function test with serum TLC, urea, Prothrombin time, procalcitonin, CRP/albumin ratio and blood culture & sensitivity were performed.

Statistical analysis

Data were entered into Microsoft® Excel workbook 2019 and exported into SPSS v21.0 (IBM, USA) for statistical analysis. Categorical data were expressed as frequency and compared the percentile using the Chi-square test. The normality of data was determined using the Shapiro Wilk test. Non-normative data were expressed as median and IQR and compared using the Mann-Whitney U test. Normative data were compared using a student t-test. The area under the curve and respective 95% confidence interval values were calculated. The calculated p-value <0.05 was considered significant.

Results

Baseline parameters

A total of 150 patients were included from the Department of Medicine and the Department of Gastroenterology, IMS & SUM hospital. The majority of the patients were aged <51-60 years (22%), followed by 21-30 years (21.3%) and 41-50 years (20%). Approximately 65% of patients were elderly. About 55.3% of patients were male, and 44.7 patients were female summarized (Table 1). In the present study, the incidence of overall mortality in patients with sepsis was 15.4%. Among expired patients, 30% were males, and 70% were females. Sex-based distribution was not significantly different between both outcomes (p=0.400). Blood culture was positive in 42 patients. Klebsiella species was the most in non-survivors (n=11), while Escherichia coli was the most common among survivors (n=9) summarised in the last section of the table (Table 2).

Table1: Frequency distribution of age, gender and the outcome of the study participants

Age (years)	Frequency	Percent (%)
18-20	6	4.0
21-30	32	21.3
31-40	29	19.3
41-50	30	20.0
51-60	33	22.0
61-70	20	13.3
Gender		
Male	83	55.3
Female	67	44.7
Outcome		
Alive	130	86.7
Expired	20	13.3

Clinical parameters

Patients who expired were older than the alive patients; however, the age difference was not significantly different (p=0.404). Among expired patients, 30% were males, and 70% were females.

Sex-based distribution was not entirely different between both outcomes (p=0.400). Results showed that total leukocyte count was not statistically significant between expired and alive patients (p=0.418). Similarly, urea levels were comparable between expired and survived patients (p=0.132). However, prothrombin time was statistically lower in survivors in comparison to non-survivors (p<0.0001). Our study observed that both ICU and hospital stays were significantly lower in survivors in comparison to non-survivors (p<0.0001) (Table 2). Our study observed that serum procalcitonin levels were considerably higher on day-1 in non-survivors in comparison to survivors (p<0.0001) summarised (Table 2).

Table 2: Clinical parameters and their outcome

Clinical Parameters	Alive (n=130)	Expired (n=20)	*p*-Value
Age	42.50	46.00	0.404
Gender [M: F], n	28:102	6:14	0.400
Renal dysfunction	52 (40%)	13 (65%)	0.035
TLC/mm^3	15405.0	14990.0	0.418
Urea (mg/dL)	59	68	0.132
Prothrombin time (sec)	12.7 ± 3.8	17.9 ± 7.2	<0.0001
Duration of ICU stay (days)	10.2 ± 2.1	2.4 ± 1.1	<0.0001
Duration of hospital stay (days)	14.6 ± 6.1	5.1 ± 3.5	<0.0001
Procalcitonin Levels			
Day 1	7.00	16.00	<0.0001
Day 3	4.00	6.00	0.072
Day 5	5.00	4.00	0.309
Day of discharge	5.00	6.00	0.085
CRP/albumin ratio			
Day 1	6.00	8.25	<0.0001
Day 3	4.70	6.10	<0.0001
Day 5	4.00	4.60	0.288
Day of discharge	1.95	2.70	<0.0001
SOFA score	6.00	11.5	<0.0001
APACHE II score	22.00	28.00	<0.0001
Microorganisms			
Acinetobacter	4	0	
E. coli	9	0	
Enterococci	1	0	
Enterococcus	2	1	
Klebsiella	2	11	
Pseudomonas	1	0	
Staphylococcus	7	0	
Streptococcus	3	1	

Comparison of CRP/albumin ratio: A higher CRP/albumin ratio on day-1, day-3, at the day of discharge in non-survivors in comparison to survivors (p<0.0001) was found in the current study displayed (Figure1). It was observed that APACHE II and SOFA scores were significantly higher on day-1 in expired in comparison to alive patients (p<0.0001) summarised (Table 2).

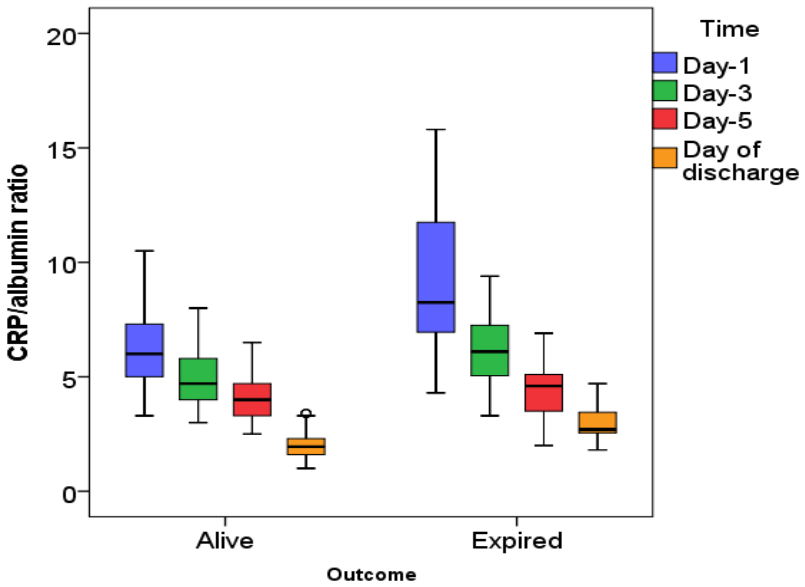

Figure 1: Comparison of CRP/albumin ratio at a different time with the outcome

Relation of CRP/albumin ratio and Procalcitonin

Our study observed a mild positive and significant correlation of CRP/albumin ratio and Procalcitonin with APACHE II and SOFA score on day-1 summarised (Table 3). Moreover, the area under the curve (AUC) for the CRP/albumin ratio for the prediction of mortality was 0.778 (95% CI, 0.703-0.842). Youden index analysis showed that CRP/albumin ratio >7.1 had 75% sensitivity and 72.31% sensitivity for the mortality prediction. The AUC for procalcitonin for mortality prediction was 0.547 (95% CI, 0.463-0.628). Youden index analysis showed procalcitonin >3 had 95% sensitivity and 22.31% sensitivity for mortality prediction displayed in ROC curve (Figure 2)

Table 3: Relation of CRP/albumin ratio and procalcitonin with Apache II and SOFA score at day-1

Parameters	CRP/Albumin ratio		Procalcitonin	
	Spearman coefficient	P value	Spearman coefficient	*p* value
APACHE II score	0.276	0.001	0.282	0.001
SOFA score	0.266	0.001	0.246	0.001

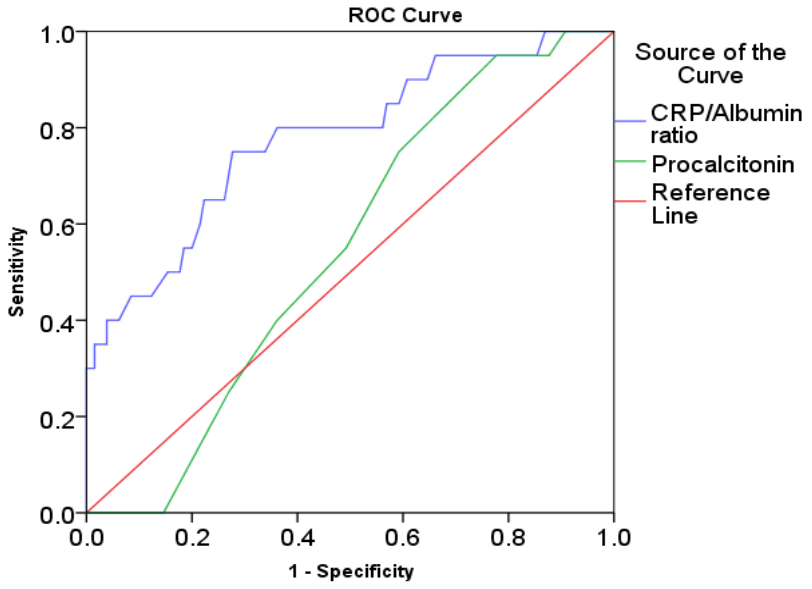

Figure 2: ROC curve analysis

Discussion

Infections and sepsis in hospitalized patients are common causes of admission and healthcare-associated diseases. According to the current consensus, in this group of patients, beginning effective antibiotic therapy early in the course of the illness reduces morbidity and mortality. [8] The capacity of a sepsis biomarker to enhance existing clinical assessments such as the history and physical examination such as CRP and white cell count determines its clinical value (WCC) and the CRP/albumin ratio with additional data. Patients in critical care have been treated with PCT for diagnostic and prognostic purposes. The CRP/albumin ratio can be used as a predictive marker in sepsis, but only if it is correlated with procalcitonin.

In our study, 15.4 percent of patients died in the hospital. In a study, Chatterjee et al. reported that more than half of the 264 severe sepsis patients died within 28 days of being admitted to the ICU, with 148 (56%) of these deaths occurring in the ICU. There was a 63.6 percent rate of in-hospital death. [9] The mortality rate for sepsis in Indian research by Jain et al was 43%.10 Patients aged 51-60 comprised 22% of the total population, 21.3% of those aged 21-30, 20% aged 41-50, and 19.3% aged 31-40. Only 4% of subjects were under 18 to 20 years old. The age differences between deceased and living patients were insignificant (p=0.404). Jain et al findings align with our results. [10]

In our study, 30 percent of non-survivors were male, and 70 percent were female. Both outcomes had a sex-based distribution that was not substantially different (p=0.400). The current study corroborated with the previous study showing similar results. [10] Severe sepsis outcomes are not consistently different between men and women. Research in a critical surgical care unit found that, in patients with established infections, the female gender was an independent predictor of increased fatality rates (ICU). [11]

Non-survivors exhibited a greater rate of renal impairment than survivors (65% vs. 40%; p=0.035). According to a previous study, that the patient with septic acute renal failure had a greater risk of dying in the hospital. Septic shock (79.5 percent) or the sepsis syndrome on inclusion had an impact on mortality (70.8 percent). [12]

In our investigation, the total leukocyte count of expired and alive individuals did not differ statistically significantly (p=0.418). Similarly, urea levels (p=0.132) were similar between deceased and living patients. Non-survivors had a considerably higher prothrombin time than survivors (p=0.0001). The abnormalities in coagulation that are practically universal in septic patients are believed to have a significant role in the malfunctioning of multiple organ systems in these people (MODS). [13] Liu et colleagues; recently found that the prothrombin time (PT) was considerably reduced in the survivor group (median 15.6 s vs. 20.1 s, p = 0.030). [14]According to Jain et al., non-survivors have a considerably greater PT than non-survivors (p=0.005). [10]

The blood procalcitonin levels of non-survivors were substantially greater on day one than those of survivors in our study (p< 0.0001). In this investigation, procalcitonin levels of less than seven ng/mL on the first day predicted death. The results of previous, as well as Clec'h and Meng et al. investigations, are supported by this study. [15,16] According to recent research, sepsis can be diagnosed using PCT measures [17]. We also noticed a considerable decrease in procalcitonin levels in survivors following discharge. It has been found that procalcitonin levels are an excellent predictor of the prognosis in sepsis, according to a previous study. [18] According to the study by Meng et al, PCT-Q10 ng/mL (75.0 percent) had the highest sensitivity for death compared to CRP10 mg/dL or APACHE II25 (both 50.0 percent) (55.9 percent). [15]

At admission, the CRP/albumin ratio might be used to estimate mortality in patients with severe sepsis. Very few studies have examined the predictive significance of the CRP/albumin ratio in patients with sepsis. The primary objective of our study was in-hospital mortality for patients with severe sepsis; researchers also looked into the role of CRP as a prognostic marker. As a result, CRP and albumin were examined together rather than separately. Inflammatory and nutritional variables, which significantly impact prognosis, might be combined using these markers. [19] Inflammation can also be detected by measuring the CRP/albumin ratio. Patients with severe sepsis and septic shock treated with EGDT had a better prognosis if their CRP/albumin ratio was higher upon arrival. [20] Researchers have already proven that the relationship between CRP and albumin, which reflects the degree of chronic inflammation, could predict sepsis patient 90-day mortality following discharge. There is a correlation between the pretreatment CRP/albumin ratio and outcome. Pretreatment values were revealed to be the most significant predictor of physiological abnormalities.

In our investigation, 42 patients had positive blood cultures. Non-survivors (n=11) were more likely to have Klebsiella species, while survivors (n=9) were more likely to have Escherichia coli. Moreover; only 15% of blood cultures were positive. [10] In a large metropolis, a tertiary care center, some patients may be delayed referrals and thus have already received antibiotics before admission. This

could be a plausible explanation for reduced culture positivity.

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Author contribution

Conceptualization: Udaybhanu Rout
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Investigation: Aswini Kumar Sahoo
Methodology: Samir Sahu
Data collection: Rishab Garg and Abhirup Bagchi
Project administration: Udaybhanu Rout
Supervision: Girish Kumar Pati and Samir Sahu
Writing- original draft: Udaybhanu Rout and Kanishka Uthansingh
Writing - review & editing: Girish Kumar Pati

Ethical Approval: This study was conducted by the ethical principles laid down in the Declaration of Helsinki and its later amendments. The institutional review board approved the protocol of the study and the Institutional ethics committee of the Institute of Medical Sciences and SUM Hospital.

Data availability: The authors confirm that the data supporting the findings of this study are available with the corresponding author. Raw data supporting these study findings are available from the corresponding author upon reasonable request.

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