



Evaluation of C - Reactive Protein and Serum Albumin Ratio as a Predictor of Morbidity and Mortality in Patients with Sepsis and Septic Shock

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Abstract

Background & Objectives

Sepsis is defined as " A life-threatening organ dysfunction caused by a dysregulated host response to infection". A simple, quick, and accessible parameter is needed to confirm treatment response and predict mortality and morbidity. Hence present study aimed to know whether C-reactive protein/Serum albumin ratio can be used to predict clinical outcomes in patients with sepsis and septic shock.

Methods

This is a hospital based cross sectional observational study conducted in the department of general medicine, GSL Medical College &

Hospital, Rajahmundry. The study was done from 1st October 2019 - 31st March 2021.

Results

Among the total patients, 71.9% recovered and remaining 28.1% of patients succumbed to death. Among the study population, 8 (9%) patients were placed on ventilators, 24 (27%) patients were diagnosed as having septic shock and were on vasopressors. There was a statistically significant difference between survivors and non-survivors with respect to mean CRP, mean serum albumin, and ratio between mean CRP and mean serum albumin. The area under the ROC curve for CRP was 0.931, for serum albumin was 0.848 and for CRP/Serum albumin was 0.963 in the present study.

Conclusion

Parameters like CRP and serum albumin and their ratio were found to have predictive value in evaluating morbidity and mortality in sepsis and septic shock.

Keywords

Sepsis, Septic shock, CRP, serum albumin, mortality

Introduction

Sepsis is defined as " A life-threatening organ dysfunction caused by a dysregulated host response to infection". Septic shock is defined as " A subset of sepsis in which underlying circulatory and cellular or metabolic abnormalities lead to substantially increased mortality risk." ¹

The inflammatory response is vital in the pathophysiology of sepsis and the impact of inflammation that can worsen chronic illness, which is a significant determinant of adverse and long-term outcomes. Though diagnostic factors like Interleukins (beta 1,6, 8, 11, 18) and prognostic factors like Urokinase plasminogen activator (UPAR), Highly selective cardiac Troponin T are available, it is difficult to determine, and the immediate application of such prognostic information is complicated when dealing with unstable patients. Hence a simple, quick, and accessible parameter is needed to confirm treatment response and predict mortality and morbidity.

CRP is an acute-phase reactant protein that is produced following stimulation by various cytokines in response to infection, ischemia, trauma, and other inflammatory conditions.²Albumin is also a potent prognostic marker of outcomes in infection-related diseases, as its levels decrease during a response to acute-phase infections.³

Hence CRP/SERUM ALBUMIN ratio, a combination of markers for systemic inflammation and nutritional

status are used as predictors of morbidity and mortality in patients with sepsis and septic shock.

Aim & Objectives

To study whether C-reactive protein/Serum albumin ratio can be used to predict clinical outcomes in patients with sepsis and septic shock.

Methodology

This is a hospital based cross sectional study conducted in the department of general medicine, GSL Medical College & Hospital, Rajahmundry. The study was done from 1st October 2019 - 31st March 2021 during which every patient admitted in the department of general Medicine who were diagnosed with sepsis were included.

3a. Inclusion Criteria

All patients aged 18 years and above with Suspected or documented infection. The SOFA score was used for defining sepsis.

3b. Exclusion Criteria

- Chronic lung disease.
- Chronic hepatitis/ chronic liver disease.
- Chronic renal failure.
- Connective tissue disorders.
- Acute cerebrovascular accidents.
- Acute coronary syndromes.
- Inflammatory diseases.

The study included all inpatients who presented with sepsis and septic shock as per inclusion criteria. A detailed history and thorough clinical examination were done in every study subject. Necessary relevant investigations were carried out. Written informed consent was taken from every study subject, and institutional ethics review committee approval was obtained before commencing the study.

The following investigations were carried out in all study subjects: Complete blood picture (CBP), Liver

function tests (LFT), Renal function tests (RFT), C-reactive protein (CRP), 12 Lead ECG, Chest x-ray PA, Blood culture and sensitivity.

All statistical analyses were performed by Epi- info software version 7.0 and MS Excel-2019. P-value <0.05 was considered as statistically significant.

Results

A total of 89 subjects were included. The mean age at presentation in this study was 55.11 ± 13.33 years. Most of the cases (26 patients) were 51-60 years of age group. Out of 89 patients, 56 (63%) were males and 33 (37%) were females.

The most common symptom observed in the present study was fever seen in 73% patients, shortness of breath seen in 31.5% patients. Cough with expectoration was found in 29.2% patients. 27% of patients presented with pain abdomen, 20.2% of patients presented with decreased urine output.

Among the total patients, 71.9% had recovered with aggressive supportive care and treatment with broad-spectrum antibiotics and were discharged from the hospital after organ dysfunction subsided. They were classified as survivors. The remaining 28.1% of patients succumbed to death and were called non-survivors.

Both hypertension and diabetes were present in 34.8% of individuals, only diabetes was seen in 24.7% and only hypertension was seen in 10.1% whereas 30.3% of study subjects had no comorbidities. There was no statistically significant association between comorbidities and the outcome of the study.

In the present study, cultures were not done in 4.5% of study subjects and were done in remaining patients. Among which, positive cultures were seen in 73.1% of samples, among which sputum has the highest positivity (24.7%) followed by urine (23.65%), pus

(14.6%) and blood (8.9%). CSF culture was positive in 1.1%. E. coli was the most common pathogen isolated in the present study (n=17, 26.2%) followed by pseudomonas (n=13, 30%), pneumococcus and Staphylococcus (each constituted 15.4%, n=10). Klebsiella constituted 13.8%, n=9. Candida (n=3, 4.6%) and Proteus (n=2, 3.1%) were detected in urine and acid-fast bacilli (1.5%) was isolated in sputum.

Prediction of Morbidity

To assess the morbidity in the present study, the Mean CRP/Serum albumin ratio was compared with the requirement of mechanical ventilation, inotropic support, and duration of hospital stay.

Among the study population, 81 individuals (91%) had no requirement for mechanical ventilation. 8 (9%) patients were placed on ventilators among them none was revived contributing to 100% mortality among ventilated patients and 32% mortality among total study subjects. There was a statistically significant association between the use of mechanical ventilation and the outcome of the study.

Among the study population, 24 (27%) patients were diagnosed as having septic shock and were on vasopressors. Out of which, 5 (7.8%) have survived and 19 (76%) have expired, contributing to 79.1% mortality among patients on inotropes and 76% mortality among total subjects. Thus, the mortality rate of septic shock was 76%. There was a statistically significant difference between survivors and non-survivors with respect to inotropic support.

There was a statistically significant association between mean CRP/serum albumin ratio and mechanical ventilation, inotropic support, and duration of hospital stay.

Prediction of Mortality

There was a statistically significant difference between survivors and non-survivors with respect to mean CRP, mean serum albumin, and ratio between mean CRP and mean serum albumin shown in table 2. CRP, Serum albumin, and CRP/Serum albumin ratio were significantly associated with the outcome of the study. ROC analysis was done to predict mortality among sepsis and septic shock patients. In this analysis, CRP had a sensitivity of 76% and specificity of 95.31% with a PPV of 86.36%, and an NPV of 91.04%. Serum albumin had a sensitivity of 48% and specificity of 90.6% with a PPV of 66.67%, and an NPV of 81.69%. CRP/Serum albumin ratio was found to have a sensitivity of 87.5% and specificity of 93.85% with a PPV of 84%, and an NPV of 95.31%. CRP/Serum albumin ratio had maximum sensitivity and NPV when compared to CRP and serum albumin alone. The area under the ROC curve for CRP was 0.931, for serum albumin was 0.848 and for CRP/Serum albumin was 0.963 in the present study.

Correlation of CRP/Serum albumin ratio with SOFA score:

CRP/Serum albumin ratio as a predictor of mortality and morbidity in sepsis and septic shock patients in the present study was compared with well-known mortality score i.e., SOFA score in sepsis and septic shock. The mean CRP/Serum albumin ratio had a significant correlation with SOFA score assessed by Spearman correlation test r-value of 0.742.

Discussion

In the present study, there were 71.9% survivors and 28.1% non-survivors. Whereas, in Hamsa B.T et al.⁴ study, there were 61.3% survivors and 38.7% non-survivors. There were 37 patients in the survivor

group (63%) and 22 patients in the non-survivor group (37%) in the Na Cui et al.⁵ study. Overall, ninety-five (51.6%) patients have died in Krsto G et al.⁶ study. The variation in survival rates can be attributed to the severity of symptoms at the time of admission which varied in different studies.

In the present study, the SOFA score was higher in non-survivors compared to survivors (10.88±2.19 Vs. 4.30±1.7) and there was a significant difference (p<0.001) between survivors and non-survivors.

Similarly, a significant difference in the SOFA scores between survivors and non-survivors was found in Longxiang Su et al.⁷ and Qin X et al.⁸ studies.

Also in Min Hyung Kim et al.⁹ and Sun R et al.¹⁰ studies, the SOFA score was an independent predictor of mortality.

CRP/Serum albumin ratio as a predictor of mortality

Patients were followed up from the day of admission to assess primary outcomes. Among study participants (n=89), survivors were 64 (71.9%) among whom the mean admission CRP/Serum albumin ratio was 8.75 with a standard deviation of 4.38. Non-survivors were 25 (28.1%) patients among whom the mean CRP/Serum albumin ratio was 21.21 with a standard deviation of 5.39. There was a statistically significant difference between survivors and non-survivors for CRP/Serum albumin ratio (p<0.0001). A similar significant association was also found in Ji Eun Park et al.¹¹, Hamsa B.T et al.¹², and Sun R et al.¹⁰ studies. In the present study, the sensitivity of the CRP/Serum albumin ratio was 87.5% and specificity was 93.85% with a PPV of 84% and an NPV of 95.31%.

Similarly, in Sun R et al.¹⁰ study, CRP/Serum albumin ratio has higher specificity (73.2%) than sensitivity (71.4%). Whereas in Ji Eun Park et al.¹¹ study, the

sensitivity of CRP/Serum albumin ratio was 64.2% and specificity was 52.7% and in Min Hyung Kim et al.⁹ study, the sensitivity of CRP/Serum albumin ratio was 61.08%, specificity was 61.05%, PPV was 37.92% and NPV was 80.11%.

CRP/Serum albumin ratio as a predictor of morbidity

To identify the role of CRP/Serum albumin ratio in assessing morbidity, analysis of the need for ventilator support, length of hospital stay, vasopressor support was done.

Among the study population (n=89), 8 patients required ventilator support accounting for 9% of the study population. There was a statistically significant association between Ventilator Support and mean CRP/serum albumin ratio in the present study (p<0.001). The need for inotropic support was seen in 24 patients (27%). There was a statistically significant association between inotropic support and the mean CRP/Serum albumin ratio in the present study (p<0.001).

Based on the length of hospital stay, patients were assessed, 38 patients required up to 7 days of hospital

stay, and 51 patients required even prolonged duration of hospital stay. There was a statistically significant association between a hospital stay and the mean CRP/Serum albumin ratio in the present study (p = 0.013).

Similarly, in Hamsa B.T et al. study¹², for evaluation of the role of CRP/Serum albumin ratio in assessing morbidity, analysis of the need for ventilator support, length of ICU stay, vasopressor support was done. Among the study population, 86 patients required ventilator support accounting for 57.3% of the study population. The need for inotropic support was seen in 104 patients. There was a statistically significant association found between Ventilator Support (p=<0.001), and inotropic support (p= 0.025) with respect to CRP/Serum albumin ratio. Based on the length of ICU stay, patients were assessed, 138 patients required up to 5 days of ICU Stay, remaining 12 patients required even prolonged duration of ICU stay. There was no statistically significant association found between ICU Stay and CRP/serum albumin ratio (p= 0.484).

1. Tables & Figures

Variables	Frequency	Mean CRP/ albumin	P value
Ventilation support required	8(9%)	22.4 ± 4.72	<0.0001
Ventilation support not required	81(81%)	11.26 ± 6.77	
Inotropic support required	24 (27%)	19.19 ± 6.38	<0.0001
Inotropic support not required	65(73%)	9.69 ± 5.83	
Hospital Stay (1 to 7 days)	38 (42.7%)	14.45 ± 9.5	0.013
Hospital Stay (>7 days)	51 (57.3%)	10.61 ± 4.53	

Table 1: mean CRP/ Albumin values when addition support required.

VARIABLES	Outcome		Total (n=89)	p-value
	Survived (n=64)	Expired (n=25)		
CRP (mg/l)	21.87 ± 9.5	40.92 ± 8.85	27.22 ± 12.65	<0.0001
Serum albumin(g/dl)	2.63 ± 0.52	1.97 ± 0.36	2.44 ± 0.57	<0.0001
CRP/serum albumin ratio	8.75 ± 4.38	21.21 ± 5.39	12.25 ± 7.31	<0.0001

Table 2. Shows CRP, Serum albumin, and CRP/Serum albumin ratio levels in survivors and non-survivors.

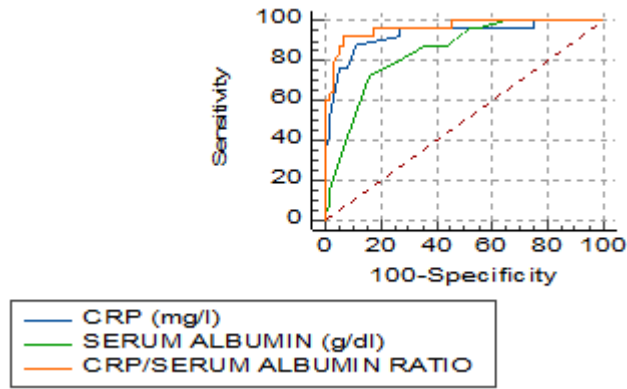


Figure 1. Shows ROC curves of CRP, Serum albumin, and CRP/Serum albumin ratio.

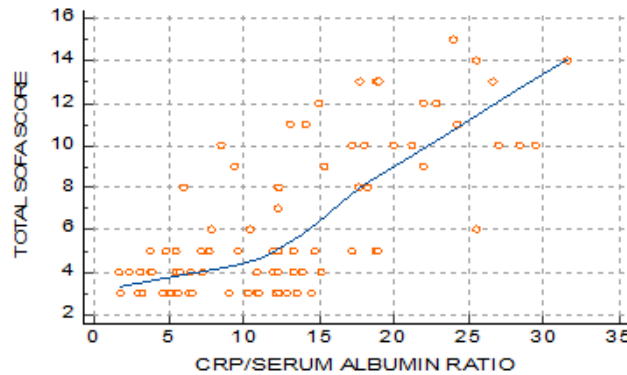


Figure 2. Shows correlation of CRP/Serum albumin ratio with SOFA score.

1. Conclusion

Parameters like CRP and serum albumin and their ratio were found to have predictive value in evaluating morbidity and mortality in sepsis and septic shock.

Limitations of the study

Study sample size was small which may not reflect the actual burden of the condition.

Recommendations

Future studies with a larger sample size are required to establish it as an independent predictor of morbidity and mortality in sepsis and septic shock patients.

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