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Original Article

C-reactive protein to albumin ratio: A new score for predicting the recurrence of spontaneous bacterial peritonitis in cirrhotic patients with ascites

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Abstract

Background and aim. *Spontaneous bacterial peritonitis (SBP) is a severe infection in cirrhotic patients with ascites causing high morbidity and mortality. Recurrent SBP is a significant concern due to the lack of reliable predictors. This study proposes a composite score using C-reactive protein (CRP) and serum albumin levels as potential biomarkers for predicting SBP recurrence in cirrhotic patients.* ***Methods.*** *The study involved 318 patients with ascites who experienced their first episode of SBP. Data on demographics, clinical features and laboratory results, including CRP and albumin levels, were collected. The predictive accuracy of the score was assessed using receiver operating characteristic curve (AUC) analysis and multivariate logistic regression.* ***Results.*** *Out of 318 included in study, 254 had continued the study. During the follow-up, 58 patients (22.84%) had recurrent SBP while 196 patients (77.16%) did not. Patients with recurrent SBP had higher CRP and lower albumin levels compared to those without recurrent SBP with p<0.001 for both. The composite CRP to albumin score was significantly higher in the recurrent SBP group (p=0.003). The ROC analysis indicated that a cut-off score of ≥3 had 80% sensitivity and 72% specificity (AUC = 0.84, p<0.001) for predicting recurrent SBP. Multivariate logistic regression analysis identified the CRP to albumin score, age, presence of diabetes, and renal dysfunction as significant predictors of SBP recurrence.* ***Conclusions****. The CRP to albumin composite score is a promising tool for predicting SBP recurrence in cirrhotic patients, with high sensitivity and specificity.*

Introduction

Spontaneous bacterial peritonitis (SBP) is a serious infection of ascites in patients with cirrhosis, leading to high morbidity and mortality rates[1,2]. Despite improved treatment, the mortality rate remains around 30%[3,4]. SBP requires significant resources, with an average hospital stay of six days and costs of approximately USD seventeen thousand per patient[5]. After surviving a first SBP, the risk of recurrence within a year can be as high as 70% without secondary prophylaxis[6]. The one-year survival rate after SBP is 30-50%, which drops to 25-30% at two years. However, using secondary prophylaxis reduces the recurrence rate to 20%[7,8]. The gold standard method for diagnosing spontaneous bacterial peritonitis is ascitic fluid analysis[6]. However, this procedure is invasive and may have complications. While many markers have been studied for diagnosing SBP[9-11], there are currently no universally accepted biomarkers or clinical scores to predict SBP recurrence. Factors such as age, liver disease severity, bacterial resistance, immune dysfunction, and poor nutritional status have been linked to SBP recurrence. However, these factors alone are not enough for early identification, making clinical decision-making complex. This knowledge gap necessitates the need for novel biomarkers and clinical parameters to effectively predict SBP recurrence. C-reactive protein (CRP) and serum albumin are promising markers for detecting inflammation and infection. CRP is commonly elevated in infectious and inflammatory conditions, including SBP[12,13]. CRP levels are indicative of disease severity and can predict patient outcomes in cirrhosis. Conversely, serum albumin, reflecting hepatic synthetic capacity and nutritional status, is often reduced in cirrhotic patients and has been linked to worse prognosis in liver-related infections such as SBP[14,15]. CRP and albumin levels independently impact clinical outcomes in SBP, but their combined predictive value for SBP recurrence needs further investigation. This study aims to evaluate the clinical characteristics of cirrhotic patients with recurrent spontaneous

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bacterial peritonitis and investigate the predictive value of CRP and albumin levels in predicting SBP recurrence. We propose a composite score based on these biomarkers to improve risk stratification and guide personalized treatment strategies for high-risk patients.

Patients and Methods

This prospective cohort study took place at the Egyptian Liver Research Institute and Hospital (ELRIAH) joint with Tropical and Internal Medicine Mansoura University Hospital in Egypt from October 2023 to December 2024. Patient confidentiality was strictly upheld, with all data de-identified prior to analysis. After calculation of sample size, the study included 318 cirrhosis patients with ascites (≥18 years).

Exclusion criteria

Patients under 18 years old, those with non-cirrhotic liver disease, significant infections at the time of SBP diagnosis, a history of malignancy or active cancer treatment, lack of available clinical data, patients with previous SBP or on secondary prophylaxis and follow-up of less than one year were excluded from the study.

Data collection

Clinical, demographic, and laboratory data of patients were collected during the initial admission. Only patients who survived the first SBP episode and had complete 12-month follow-up records were included. The patients were divided into two groups: those with non-recurrent SBP (first episode only) and those with recurrent SBP (subsequent episodes after completing treatment for the first episode and the patient's adherent to prophylaxis treatment). The first episode was defined as no prior SBP diagnosis according to international guidelines (ascitic fluid contains ≥250/m3 polymorphonuclear leukocytes (PMNL) and the culture is positive or when the culture is negative but the neutrophil count ≥250/m3 with no other causes of peritonitis or hemorrhagic ascites [16]. SBP recurrence was identified as a new episode occurring after initial treatment.

Treatment and prophylaxis of SBP

All patients received initial intravenous antibiotics following diagnostic paracentesis according to EASL guidelines[16]. Ciprofloxacin was used for prophylaxis based on the 2021 American Association for the Study of Liver Disease recommendations due to norfloxacin being unavailable[17].

Laboratory investigations.

Laboratory included CBC, serum albumin, bilirubin, creatinine, sodium, and glucose levels. Ascitic fluid was obtained using a sterile method and WBC count, PMN percentage, and lymphocyte percentage were determined. CRP was measured using a Roche Diagnostics assay.

CRP to albumin sore

A composite score based on CRP and albumin levels was calculated for each patient to assess the risk of SBP recurrence. Serum albumin levels were categorized as follows: <2.5 g/dL (2 points), 2.5–3.5 g/dL (1 point), and >3.5 g/dL (0 points). CRP levels were categorized as follows: >50 mg/L (2 points), 20–50 mg/L (1 point), and < 20 mg/L (0 points). The total CRP/Albumin score was the sum of the points from both parameters, with higher scores indicating a greater risk of recurrence.

Ethics approval

This study was conducted with the approval of the Egyptian Liver Research Institute and Hospital (Approval# CT2023-005) in accordance with the guidelines of the Declaration of Helsinki.

Statistical analysis

Descriptive statistics were used to summarize the demographic and clinical characteristics of the non-recurrent and recurrent SBP groups. Continuous variables were presented as means ± SD, and categorical variables as frequencies (n) and percentages (%). Group differences were assessed using t-tests for continuous variables and chi-square tests for categorical variables ($p < 0.05$). The CRP/Albumin score was compared between the groups using an independent t-test. The diagnostic accuracy of the CRP/Albumin score was evaluated using the ROC curve, with sensitivity, specificity, and AUC values calculated. Multivariate logistic regression analysis identified independent predictors of SBP recurrence, including CRP/Albumin score, age, diabetes, and renal dysfunction. ORs with 95% CIs were reported. Pearson's correlation coefficient assessed relationships between CRP, albumin, age, renal dysfunction, and diabetes. Statistical analyses were performed using SPSS version 25.0 (IBM Corporation, Armonk, NY, USA).

Results

Among the 318 cirrhosis patients, **figure 1** with ascites experienced the first episode of SBP, 254 patients continued the study, while 64 patients were excluded. Out of the included patients, 58 (22.84%) had recurrent SBP during the follow-up period, while 196 did not have recurrent SBP.

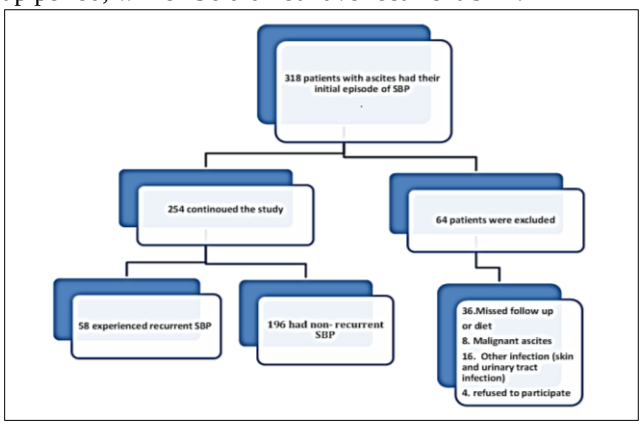

Figure 1: Flow chart of study

Demographic and clinical characteristics of non-recurrent vs. recurrent SBP groups

The demographic and clinical characteristics of the non-recurrent and recurrent SBP groups are summarized in **table 1**. Participants in the non-recurrent group had a mean age of 54.2 years (±9.1), while the recurrent group's mean age was 56.8 years (±8.4), with no significant difference between the two groups. The recurrent SBP group had higher CRP levels, ascitic WBC, bilirubin, and creatinine levels compared to the non-recurrent SBP group. However, they had lower albumin, platelet count, and sodium levels. No significant differences were observed in ascitic PMN%, ascitic lymphocytes, blood WBC, or blood lymphocytes.

Score for SBP recurrence based on CRP and albumin levels

Table 2 presents the scoring system based on CRP and albumin levels for predicting SBP recurrence. Serum albumin levels were categorized into three ranges: <2.5 g/dL (2 points), 2.5–3.5 g/dL (1 point), and >3.5 g/dL (0 points). CRP levels were also categorized: >50 mg/L (2 points), 20–50 mg/L (1 point), and <20 mg/L (0 points). This scoring system was designed to assess the risk of SBP recurrence based on these two critical inflammatory and nutritional markers.

Descriptive statistics for SBP recurrence using CRP/ Albumin score

Table 3 shows that the average CRP/Albumin score for non-recurrent SBP was 1.2 (±1.0), whereas the recurrent SBP group had a notably higher average score of 3.6 (±1.1), with a p-value of 0.003. This suggests that a higher CRP/Albumin score is linked to a higher chance of SBP recurrence, highlighting the effectiveness of this score in predicting recurrence risk.

ROC curve analysis for CRP/Albumin score

Table 4 displays the findings from the ROC curve analysis for the CRP/Albumin composite score. The optimal threshold for predicting SBP recurrence was ≥3, with a sensitivity of 80% and a specificity of 72%. The area under the curve (AUC) was 0.84 (p<0.001), indicating that the CRP/Albumin score is a robust predictor of SBP recurrence. **Figure 2** illustrates the ROC curve, highlighting the predictive precision of the score.

Multivariate logistic regression for SBP recurrence using CRP to albumin score.

Table 5 presents the results of the multivariate logistic regression analysis. The CRP to albumin composite score was found to be a significant independent predictor of SBP recurrence, with an odds ratio (OR) of 2.5 (95% CI: 1.8–3.2, p< 0.001), indicating that higher CRP/Albumin scores increase the likelihood of recurrent SBP. Additionally, age (OR: 1.05, 95% CI: 1.01–1.09, p=0.02), the presence of diabetes (OR: 1.8, 95% CI: 1.2–2.7, p=0.03), and renal dysfunction (OR: 2.1, 95% CI: 1.3–3.3, p=0.02) were also identified as significant predictors of recurrence. These findings suggest that older age, diabetes, and renal dysfunction are additional risk factors for recurrent SBP.

Correlations between CRP, albumin, and other key clinical parameters.

Table 6 displays the correlations among CRP, albumin, age, renal dysfunction, and diabetes. CRP exhibited a strong negative correlation with albumin (r = -0.45, p<0.001), indicating that higher CRP levels are linked to lower albumin levels, consistent with the relationship between systemic inflammation and nutritional status. Additionally, CRP showed a moderate positive correlation with renal dysfunction (r = 0.34, p<0.001), suggesting a potential association between elevated CRP levels and deteriorating renal function. Albumin was negatively correlated with renal dysfunction (r = -0.31, p<0.001), supporting the notion that decreased albumin levels may indicate renal impairment. Weak to moderate correlations were observed among age, renal dysfunction, and diabetes, implying interrelationships among these factors, albeit not as strongly associated with CRP or albumin levels.

Table 1: Demographic and clinical characteristics of Non-Recurrent vs. Recurrent SBP groups Recurrent SBP groups

Variable	Non-Recurrent Mean (±SD) (N=196)	Recurrent Mean (±SD) (N=58)	p-Value
Age (years)	54.2 (±9.1)	56.8 (±8.4)	0.21
CRP (mg/L)	40.5 (±4.2)	58.2 (±6.3)	<0.001
Ascites WBC (cells/mL)	3.85 (±0.65)	4.92 (±0.56)	<0.001
Ascites PMN (%)	67.5 (±10.2)	72.3 (±9.5)	0.16
Ascites Lymph (%)	32.5 (±11.5)	27.7 (±8.9)	0.15
Blood WBC (cells/mL)	9.88 (±0.9)	10.42 (±0.7)	0.11
Blood PMN (%)	66.8 (±12.6)	73.2 (±11.4)	0.07
Blood Lymph (%)	19.4 (±9.9)	14.3 (±7.2)	0.09
Hemoglobin (g/dL)	10.5 (±1.9)	9.8 (±2.3)	0.25
Platelet (cells/mL)	98.2 (±6.5)	92.1 (±7.3)	0.04
Bilirubin (mg/dL)	1.2 (±0.4)	1.8 (±0.5)	<0.001
Creatinine (mg/dL)	0.9 (±0.3)	1.2 (±0.4)	0.03
Albumin (g/dL)	3.3 (±0.6)	2.7 (±0.5)	<0.001
Sodium (mEq/L)	136.1 (±3.2)	133.2 (±3.9)	0.02
Glucose (mg/dL)	100.3 (±15.1)	110.5 (±18.2)	0.06

Table 2: Score for SBP Recurrence based on CRP and Albumin levels

Parameter	Thresholds	Points Assigned
Serum Albumin (g/dL)	<2.5	2
	2.5–3.5	1
	>3.5	0
CRP (mg/L)	>50	2
	20–50	1
	<20	0

Table 3: Descriptive statistics for SBP Recurrence using CRP/Albumin score

Group	Mean score (±SD)	p-Value
Non-Recurrent SBP	1.2 (±1.0)	0.003
Recurrent SBP	3.6 (±1.1)	

Table 4: ROC curve Analysis for CRP/Albumin score

Parameter	Cut-off Score	Sensitivity (%)	Specificity (%)	AUC	p-Value
CRP/Albumin score	≥3	80	72	0.84	<0.001

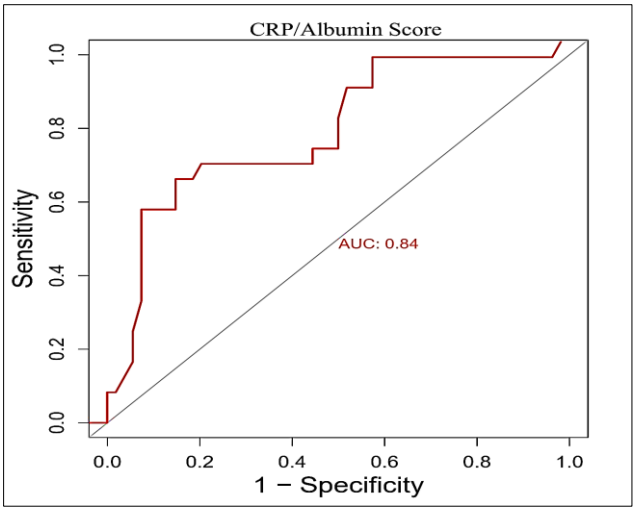

Figure 2: ROC curve of the score

Table 5: Multivariate Logistic Regression for SBP Recurrence Using CRP/Albumin Score

Predictor	OR (95% CI)	p-Value
CRP/Albumin Composite Score	2.5 (1.8–3.2)	<0.001
Age (years)	1.05 (1.01–1.09)	0.02
Presence of Diabetes	1.8 (1.2–2.7)	0.03
Renal Dysfunction (HRS)	2.1 (1.3–3.3)	0.02

Table 6: Correlations between CRP, albumin, and other key clinical parameters

Parameter	CRP (mg/L)	Albumin (g/dL)	Age (years)	Renal Dysfunction (HRS)	Diabetes (Yes/No)
CRP (mg/L)	1.00	-0.45	0.12	0.34	0.15
Albumin (g/dL)	-0.45	1.00	-0.22	-0.31	-0.10
Age (years)	0.12	-0.22	1.00	0.28	0.18
Renal Dysfunction (HRS)	0.34	-0.31	0.28	1.00	0.30

Discussion

This study assesses the predictive value of CRP to albumin ratio in predicting recurrent SBP. Significant differences were observed in CRP levels, ascitic white blood cell count, bilirubin, creatinine, albumin, and sodium levels, suggesting that recurrent SBP is associated with a more severe clinical condition marked by heightened systemic inflammation and organ dysfunction[18]. CRP is a marker of inflammation that rises in response to infections. Our study found that the recurrent SBP group had higher CRP levels than the non-recurrent group, suggesting CRP's role in predicting infections in cirrhotic patients. This aligns with previous research linking elevated CRP levels to SBP in cirrhotic patients[11-13]. Albumin is a vital protein in the human circulatory system, regulating osmotic pressure, binding and transporting ligands, and offering antioxidant and anti-inflammatory properties[19]. Our study revealed a higher prevalence of hypoalbuminemia in cases of recurrent SBP compared to non-recurrent SBP, indicating compromised nutritional status in cirrhotic patients with complications like SBP. Hypoalbuminemia is considered a crucial factor in SBP patients, as it is associated with decreased serum complement levels, potentially increasing susceptibility to infections. These findings support the conclusion that hypoalbuminemia is associated with SBP recurrence[16, 20,21]. This study introduced a composite score, the CRP to albumin score to predict SBP recurrence. The recurrent SBP group had a significantly higher mean score (3.6 ± 1.1) compared to the non-recurrent group (1.2 ± 1.0), indicating its potential to identify high-risk patients. The ROC curve analysis showed a sensitivity of 80% and specificity of 72% for the CRP/Albumin score at a cut-off of ≥3, with an AUC of 0.84,

demonstrating solid predictive accuracy. This score, based on CRP and albumin levels, offers a practical and accessible tool for predicting SBP recurrence, comparable to established scoring systems like the MELD score. Our composite score is derived from two key markers linked to SBP: serum albumin and CRP. CRP is produced by the liver in response to inflammation, including SBP. Elevated CRP levels in serum and ascitic fluid are associated with bacterial infections in cirrhosis, like SBP[11,22, 23]. Albumin is essential in the development and treatment of SBP due to its scavenging and antioxidant properties and regulation of endothelial function. These functions help modulate immune responses, inflammation, and oxidative stress, key factors in sepsis and SBP pathogenesis. Low serum albumin levels (<2.85 g/dl) before discharge are a significant predictor of SBP recurrence in cirrhotic patients, impacting long-term outcomes and mortality[24,25]. The ease of measuring CRP to albumin levels in routine clinical practice makes our score a rapid and dependable tool for evaluating the risk of recurrent SBP in cirrhotic patients. This score can help clinicians make prompt therapeutic decisions, such as initiating more aggressive prophylactic treatments or closely monitoring high-risk patients. The multivariate logistic regression analysis revealed that the CRP to albumin score is the most significant independent predictor of SBP recurrence, with an odds ratio (OR) of 2.5 (95% CI: 1.8–3.2). These underscores the importance of utilizing this composite score in clinical settings. Age, diabetes, and renal dysfunction were identified as significant predictors of recurrent SBP. The association between age and SBP recurrence may be attributed to the increased frailty and weakened immune responses in older patients[26]. Diabetes poses a risk for infections by exacerbating inflammation and compromising the immune system, leading to recurrent infections. It has been observed as a significant factor in patients with recurrent spontaneous bacterial peritonitis, potentially due to immune system alterations and deficiencies in the complement system. Studies have indicated that cirrhotic patients with lower levels of serum C3 and C4 are at a higher risk of bacterial translocation[27]. Renal dysfunction, indicated by creatinine levels and the presence of hepatorenal syndrome acute kidney injury (HRS-AKI), is associated with worse outcomes in cirrhotic patients and is a significant predictor of recurrent SBP. Previous studies have also identified old age and renal dysfunction as independent risk factors for SBP recurrence and hospital readmission[28]. Spontaneous bacterial peritonitis is a widespread global problem that results in substantial medical expenses and severe complications like acute kidney injury, hepatic encephalopathy and bleeding. In the USA, the in-hospital mortality rate for SBP patients was 17.6%[1]. It is essential to recognize SBP patients at risk of recurring episodes who need timely monitoring and preventive treatment with targeted drugs. Our score can lower hospitalizations and ease the financial strain on healthcare institutions and could greatly influence the management of SBP by offering a straightforward, non-invasive method for risk assessment. This has several important implications:

(1) Early identification of high-risk patients for SBP recurrence can lead to prioritized follow-up and improved outcomes.

(2) Focusing on high-risk patients, potentially reducing costs and can enhance patient management strategies. There are some limitations to consider. *Firstly*, the sample size may not be large enough to detect minor differences in some clinical parameters. *The second* is lack of external validation. Future studies with larger, multi-center cohorts are needed to confirm these findings and validate the CRP to Albumin score as a predictive tool for SBP recurrence.

Conclusion

The CRP to albumin score shows promise in predicting recurrent SBP in cirrhotic patients. This simple and clinically relevant score could help guide treatment decisions and improve patient outcomes.

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