

The Association Between C-Reactive Protein-to-Albumin Ratio and in-Hospital Mortality in Patients with *Klebsiella pneumoniae* Bloodstream Infection: A Retrospective Cohort Study

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Background: The C-reactive protein-to-albumin ratio (CAR), integrating inflammation (CRP) and physiological reserve (albumin), shows promise as a prognostic biomarker in critical illness, but its specific role in *Klebsiella pneumoniae* bloodstream infection (KP-BSI) mortality has not been confirmed.

Methods: Between 2019 and 2024, 264 adult patients with KP-BSI at a tertiary medical center were included in this retrospective cohort study. The primary endpoint was in-hospital mortality. Patients were categorized into three groups according to tertiles of the CAR: T1 < 3.91, T2 3.91–6.91, and T3 > 6.91. To assess the relationship between serum CAR levels and mortality risk, we applied multivariable Cox proportional hazards models and constructed Kaplan–Meier survival curves, with subgroup analyses incorporating interaction testing across sex, age, diabetes, septic shock, and CRKP status, as well as sensitivity analyses excluding patients with chronic liver disease, those with missing covariates, and including those with a length of hospital stay exceeding 180 days. The discriminatory performance of CAR was further assessed using receiver operating characteristic (ROC) curve analysis.

Results: Among the 264 patients included in the final analysis, 121 (45.8%) died during hospitalization. Non-survivors showed significantly higher CAR (7.1 ± 3.4) than survivors (4.8 ± 3.0) ($p < 0.001$). After adjusting for potential confounders, each unit increase in CAR was independently associated with a higher risk of in-hospital mortality (hazard ratio (HR)=1.12, 95% confidence interval (CI): 1.07–1.19, $p < 0.001$). When treated as a categorical variable, compared to the reference group (T1 group), patients in the highest tertile (T3) had a substantially elevated mortality risk (HR=3.12, 95% CI: 1.83–5.34, $P < 0.001$). Subgroup analyses and sensitivity analyses consistently supported the robustness of the results. The ROC analysis demonstrated that CAR had moderate discriminatory ability.

Conclusion: CAR is independently associated with in-hospital mortality in patients with KP-BSI. This readily available biomarker offers meaningful early risk stratification and may help identify patients at elevated risk who could benefit from closer monitoring and targeted clinical intervention.

Keywords: *Klebsiella pneumoniae*, bloodstream infection, C-reactive protein, albumin, CAR

Introduction

Klebsiella pneumoniae (KP) remains a leading cause of lethal bloodstream infections worldwide.¹ While its virulence is multifactorial, the polysaccharide capsule is paramount for initial immune evasion by inhibiting phagocytosis. Other key determinants, including LPS, siderophores, and adhesins, further drive the severe inflammatory response and tissue damage characteristic of invasive disease.² Critically, the convergence of hypervirulence and multidrug resistance in emerging KP lineages has created a double threat, driving more severe presentations and elevated mortality.^{3,4} KP bloodstream infection (KP-BSI) frequently triggers a rapid progression to sepsis and septic shock, a direct driver of multiorgan dysfunction. Consequently, mortality is substantial, typically quoted between 20% and 50%.^{3,5–7} Outcomes

are shaped by a confluence of factors. Host vulnerabilities (immunosuppression, advanced age, comorbidities) interact with treatment-related delays and high-risk bacterial phenotypes (eg., resistant strains) to synergistically increase mortality.^{8–12} Collectively, this clinical complexity drives the demand for better prognostic markers to support early risk stratification, guide clinical decision-making, and improve resource allocation.

Serum C-reactive protein (CRP) is an acute-phase reactant produced by the liver in response to proinflammatory cytokines, and elevated levels have been consistently associated with the severity of bloodstream infections.¹³ Incorporating CRP into the diagnostic assessment of suspected bacteremia has also been shown to improve clinical discrimination and risk stratification.¹⁴ Serum albumin, a negative acute-phase marker reflecting nutritional and physiological reserve, likewise functions as an important prognostic indicator in these patients. The CRP-to-albumin ratio (CAR) combines these complementary dimensions, thereby offering an integrated measure of inflammatory burden and host reserve that is relevant to sepsis and severe bacterial infections.¹⁵ CAR has gained increasing attention as a composite biomarker with superior predictive performance compared with CRP or albumin alone, demonstrating prognostic value in oncology and critical care populations.^{16,17} Preliminary studies suggest it may also predict adverse outcomes in community-acquired pneumonia, sepsis, and mixed bacteremia.¹⁸ However, evidence evaluating the prognostic significance of CAR specifically in *Klebsiella pneumoniae* bloodstream infections remains limited.

Previous studies in KP-BSI have explored individual prognostic biomarkers, including red cell distribution width (RDW), which was reported by our group to be associated with adverse outcomes.¹⁹ These findings underscore the relevance of host-related biomarkers in KP-BSI, yet they primarily reflect isolated pathophysiological dimensions. In contrast, the C-reactive protein-to-albumin ratio (CAR) integrates systemic inflammation and nutritional reserve, potentially offering a more comprehensive assessment of disease severity in this population.

Other inflammatory markers such as procalcitonin, presepsin, and interleukin-6 have also been investigated in bloodstream infections;^{20,21} however, their clinical utility may be constrained by cost and availability. Although these biomarkers highlight the importance of host response, most reflect single pathophysiological processes. In contrast, the C-reactive protein-to-albumin ratio (CAR) integrates systemic inflammation and nutritional status, potentially providing a more comprehensive and clinically accessible indicator of disease severity.

Despite increasing interest in composite inflammatory biomarkers, the prognostic value of CAR in KP-BSI remains insufficiently characterized. Given the wide variability in *Klebsiella* virulence, its frequent association with multidrug-resistant phenotypes, and its tendency to cause severe infections in vulnerable hosts, a pathogen-targeted evaluation is warranted. Therefore, we examined the relationship between CAR and in-hospital mortality among patients with KP-BSI, hypothesizing that higher CAR levels would independently predict in-hospital death beyond conventional clinical severity scores and comorbidity indices.

Materials and Methods

Data Source

A retrospective cohort of patients with KP-BSI was assembled at Beijing Luhe Hospital, Capital Medical University, a tertiary referral center located in Beijing, China. Beijing Luhe Hospital is a tertiary care center with 1,300 inpatient beds, located in eastern Beijing, China. According to the Centers for Disease Control and Prevention (CDC), a bloodstream infection (BSI) is defined by the isolation of pathogenic organisms from a blood culture.²⁰ In the present study, only the first KP isolate detected in the bloodstream of each patient was included for analysis. All individuals meeting the diagnostic standards for KP-BSI at the hospital were systematically included over the six-year period from January 2019 to December 2024. The protocol for this study was approved by the Ethics Committee of Beijing Luhe Hospital, Capital Medical University (NO. 2025-LHKY-017-01). Given the retrospective and anonymous nature of the study, the ethics committee waived the requirement for informed consent. All procedures were carried out in accordance with institutional and local regulatory requirements, as well as the ethical principles of the Declaration of Helsinki. The reporting process complied with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) standards.²¹

Study Population

Clinical information for each patient was obtained from the electronic medical record system, and a de-identified database was subsequently created for analysis. Participants were eligible if they met the following condition: (1) KP was detected in blood culture, with the corresponding samples obtained and stored in our laboratory; 2) age >18 years; 3) length of stay was ≤ 180 days; and 4) availability of complete CRP and albumin data. For patients with multiple positive cultures, only the first isolate was included in the analysis. Exclusion criteria included patients under 18 years of age, those with missing data, or individuals with unspecified infections. [Figure 1](#) presents the study flowchart.

Microbiological Tests

Blood cultures were processed using the Bact/ALERT 3D automated blood culture system (bioMérieux, Marcy-l'Étoile, France). Aerobic and anaerobic adult bottles (Bact/ALERT FA/FN) were used according to clinical indication and the manufacturer's instructions. Bottles were incubated continuously at 35 ± 1 °C and monitored for up to 5 days; bottles flagged as positive by the instrument were subcultured immediately onto solid media and further processed for species identification and antimicrobial susceptibility testing. All patient-derived isolates were characterized at the species level and tested for antibiotic susceptibility using the VITEK 2 Compact platform (bioMérieux, France). Antimicrobial resistance was assessed in accordance with the Clinical and Laboratory Standards Institute (CLSI-M100) guidelines 2017–2019 to ensure consistency.²² *Klebsiella pneumoniae* ATCC 700603 was used as the quality control strain. The interpretation of results was conducted following the standards of the National Committee for Clinical Laboratory Standards (NCCLS).

Variable Extraction and Outcome

The C-reactive protein-to-albumin ratio (CAR, mg/g) was calculated by dividing serum CRP levels (mg/L) by albumin concentrations (g/L), consistent with previous studies. Both CRP and albumin measurements were obtained within

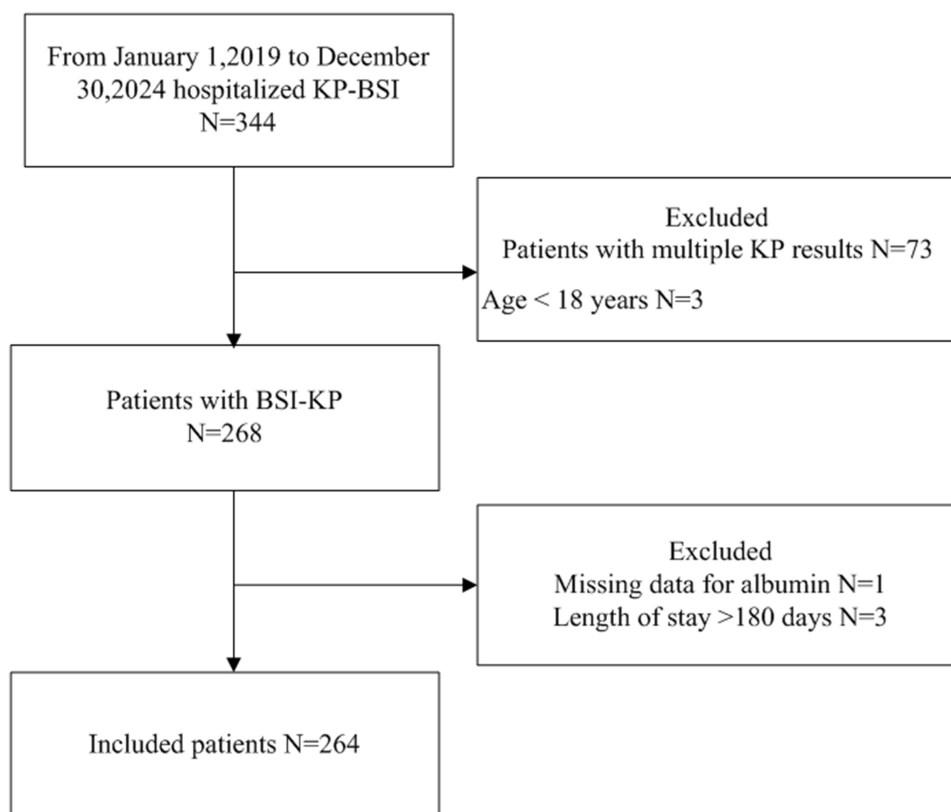


Figure 1 The flowchart of study.

Abbreviations: KP, *Klebsiella pneumoniae*; KP-BSI, *Klebsiella pneumoniae* bloodstream infection.

24 hours of obtaining the blood culture. CAR was analyzed as a categorical variable, with patients stratified into three tertiles: T1 < 3.91, T2 3.91–6.91, and T3 > 6.91. The primary endpoint of the study was in-hospital mortality.

Covariates

Demographic variables, including age and sex, and comorbidities such as diabetes, septic shock, and malignancy, were extracted from clinical records. Hematological and biochemical indices collected within 24 hours of obtaining the blood culture—such as creatinine, lactate, white blood cell (WBC) count, and platelet count—were also recorded. Treatment-related variables included use of continuous renal replacement therapy (CRRT) and mechanical ventilation. Microbiological factors encompassed carbapenem-resistant *Klebsiella pneumoniae* (CRKP). The Sequential Organ Failure Assessment (SOFA) score was employed to evaluate disease severity. The analysis also accounted for ICU admission, hospital-acquired infection, and the specific site of infection as covariates. Chronic liver disease in this study was defined as chronic viral hepatitis and liver cirrhosis due to various etiologies.

Statistical Analysis

Descriptive statistics were calculated for the entire cohort. Categorical variables were summarized as frequencies and percentages, while continuous variables were expressed as means \pm standard deviations (SD) for normally distributed data or as medians with interquartile ranges (IQR) for non-normally distributed data. Comparisons between groups were performed using the chi-square test for categorical variables, one-way ANOVA for normally distributed continuous variables, and the Kruskal–Wallis test for non-normally distributed continuous variables. Categorical variables were compared among the three groups using the chi-square test, while continuous variables were analyzed using one-way ANOVA if normally distributed and the Kruskal–Wallis test if not. Missing values for covariates with less than 30% incompleteness were imputed using the KNN algorithm to maintain data integrity. In our cohort, lactate levels were missing in 65 patients (~25%), while SOFA scores were missing in 32 patients (~12%).

Multivariable Cox proportional hazards regression models were employed to assess the independent association between CAR levels and in-hospital mortality. The proportional hazards assumption was tested using the Schoenfeld residuals method, and the assumption was satisfied. Covariates for adjustment were selected based on evidence from the literature. The crude model (Model 1) included no covariates, whereas Model 2 incorporated age and sex. In addition to the variables included in Model 2, Model 3 further accounted for septic shock, diabetes, malignancy, mechanical ventilation, CRRT, lactate, and SOFA score. For trend testing, the median values corresponding to each CAR tertile were incorporated into the regression models as a continuous variable. Kaplan–Meier survival curves were generated and compared using the Log rank test. Subgroup analyses were conducted to examine the robustness of the associations across different patient subpopulations, and sensitivity analyses were performed by excluding patients with chronic liver disease, those with a length of hospital stay exceeding 180 days, and those with missing covariates. The predictive performance of CAR was further evaluated using receiver operating characteristic (ROC) curve analysis.

All statistical analyses were conducted using R software (version 4.2.2; <http://www.R-project.org>, The R Foundation) and Free Statistics software (version 1.9.2)²³. Two-tailed tests were applied, and a p-value < 0.05 was considered statistically significant.

Results

Baseline Characteristics of Participants

The study cohort of KP-BSI patients was stratified by CAR tertiles, and patient characteristics were compared across these groups (Table 1). The study included 264 patients, with an average age of 66.1 years, of whom 67.8% were male. Overall, 121 patients died during hospitalization, yielding an in-hospital mortality rate of 45.8%. Among the study population, CRKP accounted for 32.2% (n = 85). Non-survivors exhibited significantly higher CAR levels (7.1 ± 3.4) compared with survivors (4.8 ± 3.0 ; $p < 0.001$).

Table 1 Baseline Characteristic of Patients with KP-BSI

| Characteristics | Total (n = 264) | CAR (mg/g) | | | P value |
|----------------------------------|--------------------|---------------|---------------|---------------|---------|
| | | T1 (n = 88) | T2 (n = 88) | T3 (n = 88) | |
| Age, years | 66.1 ± 13.6 | 63.2 ± 14.9 | 66.7 ± 13.3 | 68.6 ± 11.9 | 0.029 |
| Sex, male, n (%) | 179 (67.8) | 65 (73.9) | 58 (65.9) | 56 (63.6) | 0.313 |
| CRKP, n (%) | 85 (32.2) | 29 (33) | 27 (30.7) | 29 (33) | 0.933 |
| Diabetes, n (%) | 117 (44.3) | 28 (31.8) | 39 (44.3) | 50 (56.8) | 0.004 |
| Chronic liver disease, n (%) | 26 (9.8) | 11 (12.5) | 10 (11.4) | 5 (5.7) | 0.266 |
| Chronic kidney disease, n (%) | 38 (14.4) | 13 (14.8) | 13 (14.8) | 12 (13.6) | 0.97 |
| Hematological disease, n (%) | 30 (11.4) | 8 (9.1) | 15 (17) | 7 (8) | 0.117 |
| Malignant tumor, n (%) | 48 (18.2) | 13 (14.8) | 19 (21.6) | 16 (18.2) | 0.503 |
| CVC, n (%) | 117 (44.3) | 49 (55.7) | 38 (43.2) | 30 (34.1) | 0.015 |
| Pneumonia, n (%) | 139 (52.7) | 54 (61.4) | 42 (47.7) | 43 (48.9) | 0.133 |
| Urinary tract infection, n (%) | 58 (22.0) | 20 (22.7) | 21 (23.9) | 17 (19.3) | 0.75 |
| Intra-abdominal infection, n (%) | 27 (10.2) | 8 (9.1) | 9 (10.2) | 10 (11.4) | 0.884 |
| Liver abscess, n (%) | 38 (14.4) | 7 (8) | 10 (11.4) | 21 (23.9) | 0.007 |
| Soft tissue infection, n (%) | 23 (8.7) | 4 (4.5) | 7 (8) | 12 (13.6) | 0.097 |
| ICU admission, n (%) | 158 (59.8) | 48 (54.5) | 48 (54.5) | 62 (70.5) | 0.046 |
| Ventilator use, n (%) | 136 (51.5) | 44 (50) | 38 (43.2) | 54 (61.4) | 0.051 |
| CRRT, n (%) | 46 (17.4) | 14 (15.9) | 15 (17) | 17 (19.3) | 0.832 |
| Nosocomial infection, n (%) | 110 (41.7) | 48 (54.5) | 33 (37.5) | 29 (33) | 0.009 |
| Septic shock, n(%) | 133 (50.4) | 24 (27.3) | 46 (52.3) | 63 (71.6) | < 0.001 |
| WBC, 10 ⁹ /L | 12.1 ± 9.4 | 10.3 ± 7.9 | 11.7 ± 8.9 | 14.3 ± 11.0 | 0.017 |
| Hematocrit | 0.3 ± 0.1 | 0.3 ± 0.1 | 0.3 ± 0.1 | 0.3 ± 0.1 | 0.837 |
| Platelet, 10 ⁹ /L | 138.1 ± 99.8 | 152.5 ± 94.4 | 140.1 ± 102.5 | 121.5 ± 101.2 | 0.116 |
| CRP, mg/L | 162.8 ± 82.2 | 80.0 ± 40.0 | 159.4 ± 35.4 | 249.1 ± 55.4 | < 0.001 |
| Procalcitonin, ng/mL | 19.6 ± 29.5 | 7.2 ± 12.5 | 13.7 ± 15.0 | 38.0 ± 41.4 | < 0.001 |
| Albumin, g/L | 29.9 ± 12.2 | 33.8 ± 19.4 | 30.0 ± 4.7 | 25.7 ± 4.2 | < 0.001 |
| Creatinine, μmol/L | 152.4 ± 134.3 | 123.7 ± 123.8 | 146.0 ± 135.5 | 187.4 ± 136.7 | 0.006 |
| BUN, mmol/L | 15.3 ± 12.6 | 11.5 ± 10.6 | 13.9 ± 11.2 | 20.5 ± 14.2 | < 0.001 |
| Lactate, mmol/L | 4.9 ± 4.1 | 3.9 ± 4.1 | 5.1 ± 4.4 | 5.4 ± 3.7 | 0.128 |
| SOFA score | 7.3 ± 4.4 | 5.6 ± 4.3 | 7.2 ± 4.7 | 8.9 ± 3.5 | < 0.001 |
| Empirical treatment | | | | | |
| Quinolones, n (%) | 32 (12.1) | 12 (13.6) | 8 (9.1) | 12 (13.6) | 0.566 |

(Continued)

Table 1 (Continued).

| Characteristics | Total (n = 264) | CAR (mg/g) | | | P value |
|--------------------|--------------------|-------------|-------------|-------------|---------|
| | | T1 (n = 88) | T2 (n = 88) | T3 (n = 88) | |
| Carbapenems, n (%) | 97 (36.7) | 22 (25) | 36 (40.9) | 39 (44.3) | 0.018 |
| β-lactams, n (%) | 169 (64.0) | 65 (73.9) | 55 (62.5) | 49 (55.7) | 0.04 |
| Other drugs, n (%) | 57 (21.6) | 17 (19.3) | 24 (27.3) | 16 (18.2) | 0.279 |
| Outcome | | | | | |
| Mortality, n (%) | 121 (45.8) | 23 (26.1) | 37 (42) | 61 (69.3) | < 0.001 |

Abbreviations: CAR, C-reactive protein to albumin ratio; KP-BSI, *Klebsiella pneumoniae* bloodstream infections; CRKP, Carbapenem-resistant *Klebsiella pneumoniae*; CVC, central venous catheter placement; CRRT, continuous renal replacement therapy; ICU, intensive care unit; BUN, blood urea nitrogen; CRP, C-reactive protein; WBC, white blood cell; SOFA, sequential organ failure assessment.

Kaplan-Meier Survival Analysis

In Kaplan–Meier survival analysis, patients in the T2 and T3 tertiles exhibited significantly lower survival rates compared with those in the T1 tertile ($p < 0.0001$) (Figure 2).

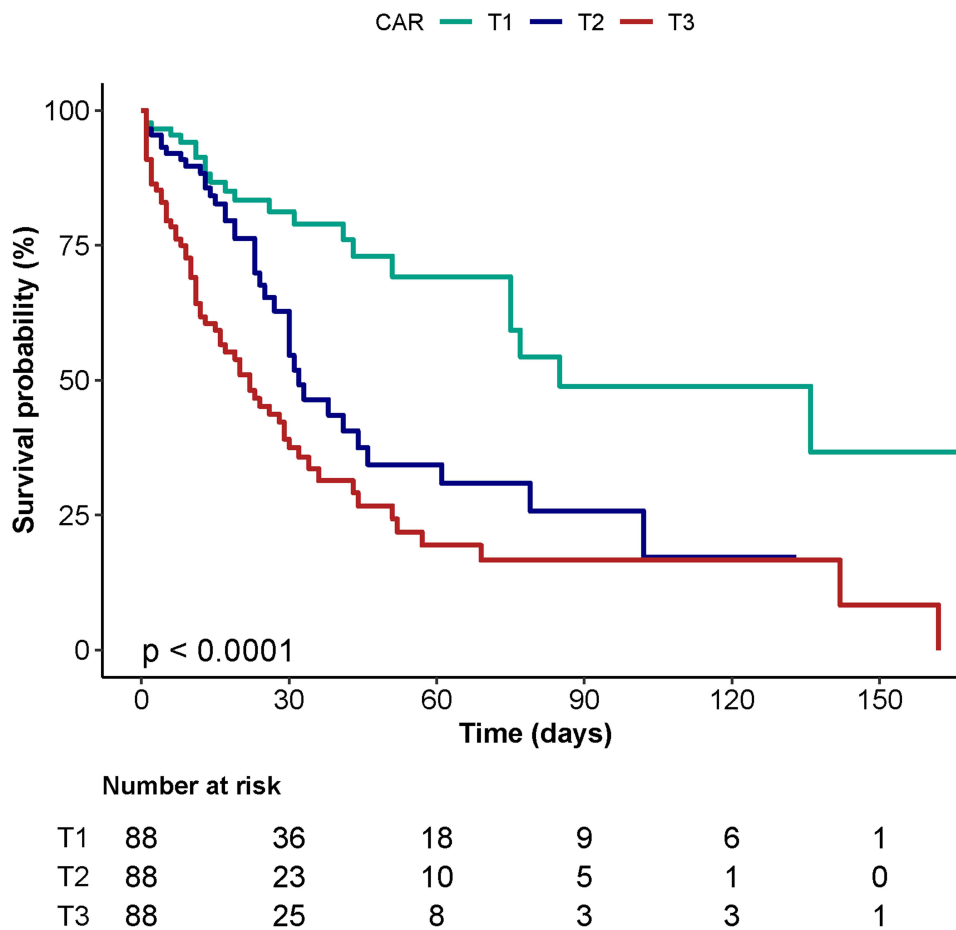


Figure 2 Kaplan-Meier survival curves were plotted for patients stratified by CAR tertiles.
Abbreviation: CAR, C-Reactive Protein-to-Albumin Ratio.

Table 2 Association Between CAR and Mortality in Patients with KP-BSI

| Variable | n.event_% | Model 1 | | Model 2 | | Model 3 | |
|--------------------------|------------|------------------|---------|------------------|---------|------------------|---------|
| | | HR (95% CI) | P value | HR (95% CI) | P value | HR (95% CI) | P value |
| CAR (mg/g) continuous | 121 (45.8) | 1.12 (1.07~1.18) | <0.001 | 1.12 (1.07~1.18) | <0.001 | 1.12 (1.07~1.19) | <0.001 |
| CAR tertile | | | | | | | |
| T1 | 23 (26.1) | 1(Ref) | | 1(Ref) | | 1(Ref) | |
| T2 | 37 (42) | 2.13 (1.25~3.62) | 0.005 | 2.13 (1.25~3.63) | 0.006 | 1.37 (0.79~2.4) | 0.262 |
| T3 | 61 (69.3) | 3.73 (2.29~6.09) | <0.001 | 3.59 (2.19~5.89) | <0.001 | 3.12 (1.83~5.34) | <0.001 |
| P for trend | | | <0.001 | | <0.001 | | <0.001 |

Note: Model 1: Unadjusted. Model 2: Adjusted for sex, age. Model 3: Adjusted for sex, age, CRKP, septic shock, diabetes, tumor, ventilator use, CRRT, SOFA score, lactate.

Abbreviations: CAR, C-reactive protein to albumin ratio; KP-BSI, *Klebsiella pneumoniae* bloodstream infections; CRKP, Continuous Renal Replacement Therapy; CRRT, continuous renal replacement therapy; SOFA, sequential organ failure assessment.

Relationship Between CAR and In-Hospital Mortality

The association between CAR and in-hospital mortality in KP-BSI patients was examined using multivariable Cox regression, with results summarized in Table 2. In the unadjusted Model 1, each one-unit increase in CAR was associated with a 12% higher risk of mortality (hazard ratio [HR] = 1.12; 95% confidence interval [CI]: 1.07–1.18; $p < 0.001$). This association remained significant after adjustment for age and sex in Model 2. Even after further adjustment for additional potential confounders in Model 3, the association persisted (HR = 1.12; 95% CI: 1.07–1.19; $p < 0.001$).

When CAR was analyzed as a categorical variable, patients in the T2 and T3 tertiles exhibited significantly higher mortality compared with the reference T1 tertile, with HRs of 2.13 (95% CI: 1.25–3.62) and 3.73 (95% CI: 2.29–6.09), respectively. After full adjustment in Model 3, the HR for T2 was 1.37 (95% CI: 0.79–2.40; $p = 0.262$), while the HR for T3 remained significantly elevated at 3.12 (95% CI: 1.83–5.34; $p < 0.001$). All models demonstrated statistically significant trends across CAR tertiles, with p -values < 0.05 .

Subgroup Analysis

To examine the robustness of the association between CAR and mortality, stratified and interaction analyses were performed. Stratified analyses revealed that the association was generally consistent across subgroups based on sex, age, diabetes, septic shock, and CRKP status. No significant interactions were identified for sex, age, or CRKP, while diabetes and septic shock demonstrated significant interaction effects (p for interaction < 0.05) (Figure 3).

Sensitivity Analysis

Sensitivity analyses excluding patients with chronic liver disease, those with missing covariates, and including those with a length of hospital stay exceeding 180 days. To address the potential confounding effect of chronic liver disease, a sensitivity analysis was performed excluding patients with this condition. Multivariable analysis demonstrated that CAR remained positively associated with in-hospital mortality among patients with KP-BSI. After adjustment for potential confounders, each one-unit increase in CAR was associated with an 11% higher risk of mortality (HR = 1.11; 95% CI: 1.04–1.17; $p = 0.001$). Furthermore, patients in the T3 tertile exhibited a significantly higher risk of death compared with those in the T1 tertile (HR = 2.89; 95% CI: 1.62–5.16; $p < 0.001$) (Table 3). Sensitivity analyses including patients with LOS >180 days and excluding missing data for covariates yielded consistent results (Table 3).

Receiver Operating Characteristic Analysis

The results of the ROC analysis indicate that the model has a moderate level of discrimination ability. The Area Under the Curve (AUC) value is 0.702, with a 95% CI ranging from 0.639 to 0.765 (a sensitivity of 50.4% and a specificity of 82.5%) (Figure 4).

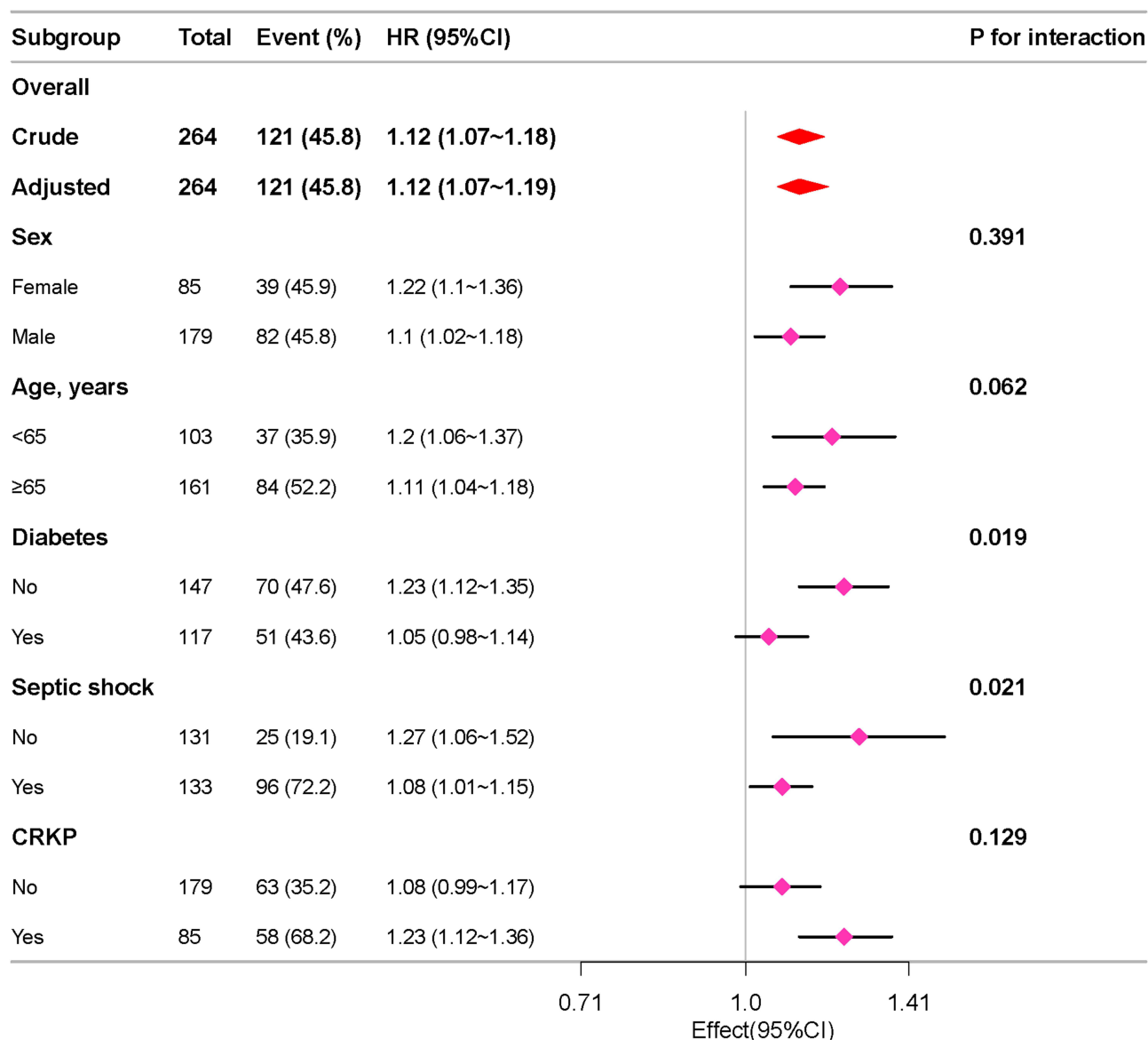


Figure 3 Subgroup Analysis of the Association Between CAR and Mortality in Patients with KP-BSI.

Discussion

In this pathogen-specific cohort, CAR was independently associated with in-hospital mortality among patients with KP-BSI after adjustment for potential confounders. To the best of our knowledge, this study is the first to specifically investigate the relationship between CAR and in-hospital mortality in individuals with KP-BSI.

Recently, CAR has been identified as a new prognostic indicator in multiple clinical contexts, including sepsis,¹⁵ coronavirus disease 2019 (COVID-19),^{24,25} acute pancreatitis,²⁶ stroke,²⁷ and hospitalized older adults.²⁸ Kim et al²⁹ reported that preoperative CAR (≥ 0.34) was independently associated with increased one-year and overall mortality after liver transplantation. Zhang and colleagues³⁰ demonstrated that elevated CAR was significantly associated with higher risks of mortality and major adverse cardiovascular events (MACE) in patients with valvular heart disease, with an adjusted HR of 1.89 (95% CI: 1.56–2.28; $P < 0.001$) for mortality and 1.40 (95% CI: 1.30–1.82; $P < 0.001$) for MACE. This broad applicability underscores CAR’s role as a sensitive marker reflecting the balance between systemic inflammation (CRP) and metabolic/nutritional status (albumin).

Table 3 Sensitivity Analysis

| Variable | Crude model | | Adjusted model | |
|---|------------------|---------|------------------|---------|
| | HR (95% CI) | P value | HR (95% CI) | P value |
| Excluding Patients with Chronic Liver Disease (N=238) | | | | |
| CAR continuous | 1.13 (1.07~1.18) | <0.001 | 1.11 (1.04~1.17) | 0.001 |
| CAR tertile | | | | |
| T1 | 1 (Ref) | | 1 (Ref) | |
| T2 | 2.38 (1.33~4.27) | 0.003 | 1.3 (0.7~2.4) | 0.411 |
| T3 | 4.18 (2.45~7.12) | <0.001 | 2.89 (1.62~5.16) | <0.001 |
| P for trend | 1.99 (1.55~2.54) | <0.001 | 1.8 (1.35~2.39) | <0.001 |
| Including patients LOS>180 days (N=267) | | | | |
| CAR continuous | 1.13 (1.08~1.18) | <0.001 | 1.12 (1.07~1.19) | <0.001 |
| CAR tertile | | | | |
| T1 | 1 (Ref) | | 1 (Ref) | |
| T2 | 2.03 (1.2~3.42) | 0.008 | 1.55 (0.88~2.74) | 0.131 |
| T3 | 3.86 (2.38~6.26) | <0.001 | 3.4 (1.97~5.86) | <0.001 |
| P for trend | | <0.001 | | <0.001 |
| Excluding missing data for covariates (N=199) | | | | |
| CAR continuous | 1.09 (1.03~1.14) | 0.001 | 1.11 (1.04~1.17) | 0.001 |
| CAR tertile | | | | |
| T1 | 1 (Ref) | | 1 (Ref) | |
| T2 | 1.69 (0.97~2.96) | 0.065 | 1.16 (0.65~2.09) | 0.616 |
| T3 | 2.8 (1.66~4.72) | <0.001 | 2.78 (1.55~4.98) | 0.001 |
| P for trend | | <0.001 | | <0.001 |

Note: Adjusted for sex, age, CRKP, septic shock, diabetes, tumor, ventilator use, CRRT, SOFA score, lactate.

Abbreviations: CAR, C-reactive protein to albumin ratio; KP-BSI, *Klebsiella pneumoniae* bloodstream infections; CRKP, Continuous Renal Replacement Therapy, CRRT, continuous renal replacement therapy; SOFA, sequential organ failure assessment.

However, within the realm of bloodstream infection, the prognostic performance of CAR may vary depending on the severity of host response. Dimitrijević et al³¹ suggested that CAR is a valuable predictor of bacteremia, septicemia, and mortality in patients with febrile neutropenia, while Güneş et al³² reported that CAR is independently associated with Gram-negative sepsis in neonates. These findings highlight the potential of CAR as a reliable predictor of clinical outcomes across diverse patient populations. Our study extends these observations to a well-defined cohort of patients with KP-BSI, a population at high risk of progressing to sepsis. Our results align with and substantially expand the evidence supporting CAR as a robust prognostic marker in critical illness. They indicate that CAR may excel at identifying the dysregulated host response that marks the transition from infection to severe sepsis. By demonstrating this independent association after controlling for traditional risk factors, we highlight CAR's clinical utility as a bedside tool for early risk stratification in this lethal infection. The mechanistic basis for CAR's prognostic value likely lies in its dual reflection of the intensity of the inflammatory cascade and the host's physiological reserve. CRP, an acute-phase synthesized by hepatocytes primarily in response to IL-6, serves as a quantitative marker of systemic inflammation severity.³³ In KP-BSI, elevated CRP levels reflect the bacterial load (eg., lipopolysaccharide) and consequent cytokine release (eg., IL-1 β , IL-6, TNF- α), which drive tissue injury, organ dysfunction, and potentially immune dysregulation.³⁴ In contrast, hypoalbuminemia indicates malnutrition, chronic inflammation, impaired hepatic synthetic dysfunction, and importantly, increased vascular permeability, leading to albumin extravasation.^{35,36} This "capillary leak" is a hallmark of severe sepsis/septic shock, contributing to hypovolemia, tissue edema, and impaired oxygen delivery. Moreover, albumin possesses antioxidant and anti-inflammatory properties, its depletion diminishes these protective effects.³⁷ Thus, CAR integrates a synergistic pathophysiological insult:

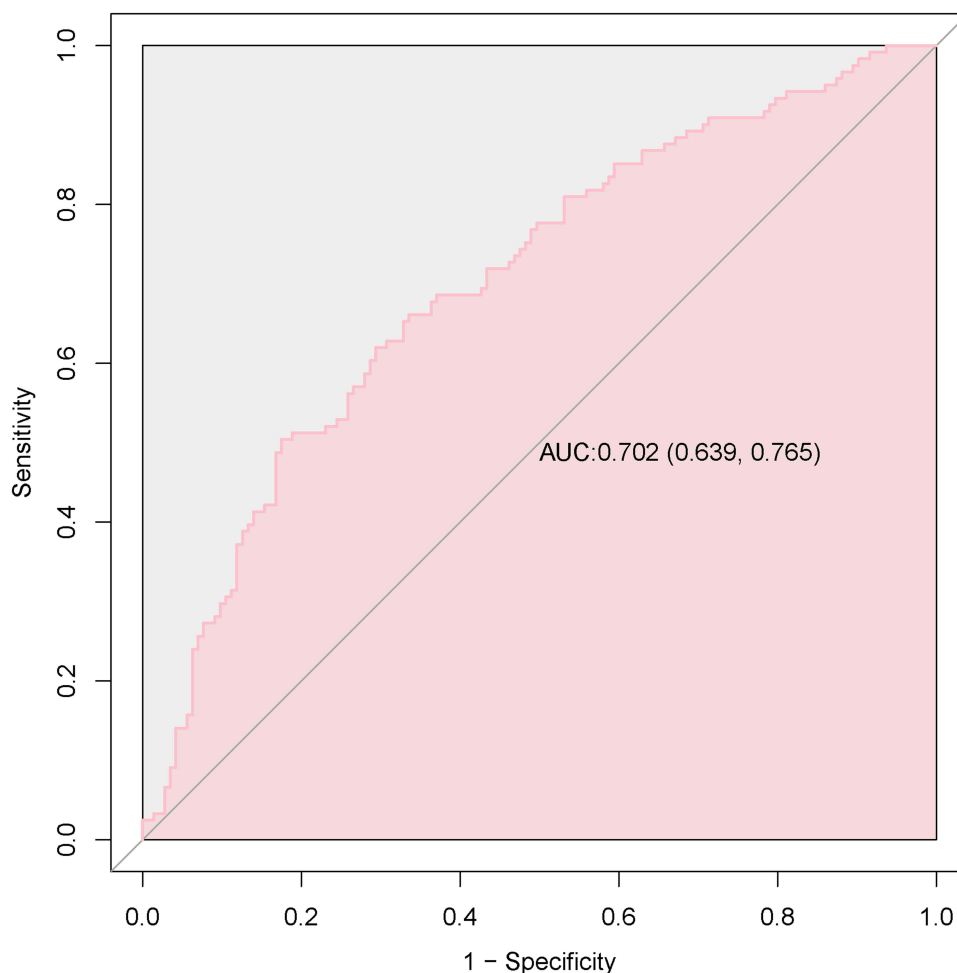


Figure 4 Receiver Operating Characteristic (ROC) Curves of the C-Reactive Protein-to-Albumin Ratio for Predicting In-Hospital Mortality.

heightened inflammation (high CRP) compounded by reduced physiological reserve and compromised endogenous defense mechanisms (low albumin). Its strong association between CAR and mortality can be attributed to CAR's role as a composite indicator, simultaneously reflecting systemic inflammatory response and nutritional condition. The hyperinflammatory state induced by *K. pneumoniae*, potentially exacerbated by specific virulence factors like hypermucoviscosity, coupled with the rapid depletion of albumin reserves, creates a vicious cycle that CAR effectively captures, explaining its strong association with mortality.

Several limitations should be acknowledged when interpreting our findings. First, the single-center retrospective design inherently limits generalizability and may introduce selection bias and unmeasured confounding, despite rigorous multivariable adjustment. Second, although admission CAR was utilized, serial CAR measurements could provide more dynamic insights into disease progression and treatment response, which were not captured in this study. Third, albumin levels can be transiently affected by fluid resuscitation, which was not consistently quantified in our dataset. Finally, the observational design precludes establishing causal relationships.

Despite these limitations, our study robustly demonstrates that an elevated CAR at admission is a strong, independent predictor of in-hospital mortality among patients with KP-BSI. By integrating both systemic inflammatory burden (CRP) and physiological reserve/endogenous defense capacity (albumin), CAR provides a simple, cost-effective, and clinically accessible tool for early identification of high-risk patients. Future prospective, multi-center studies incorporating serial CAR measurements, detailed pathogen characterization, and exploration of CAR-guided management strategies are warranted to validate and extend these findings, ultimately improving outcomes in this challenging infection.

Conclusion

In summary, CAR was independently associated with increased in-hospital mortality in patients with KP-BSI, supporting its role as a readily available biomarker for early risk stratification. Given that CAR reflects both systemic inflammation and nutritional status, it may have broader relevance across infectious diseases; however, caution is warranted when extrapolating these findings beyond KP-BSI. Prospective studies are needed to validate its clinical utility and to clarify its potential role in guiding risk-based management strategies.

Data Sharing Statement

The original contributions presented in this study are included in this article, further inquiries can be directed to the corresponding author.

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Author Contributions

YH: Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. TA: Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. MH: Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. PZ: Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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References

- Ikuta KS, Swetschinski LR, Robles Aguilar G.; GBD. 2019 antimicrobial resistance collaborators. global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the global burden of disease study 2019. *Lancet Lond Engl.* 2022;400:2221–2248. doi:10.1016/S0140-6736(22)02185-7
- Abbas R, Chakkour M, Zein El Dine H, et al. General overview of *Klebsiella pneumoniae*: epidemiology and the role of siderophores in its pathogenicity. *Biology.* 2024;13(2):78. doi:10.3390/biology13020078
- Li D, Huang X, Rao H, et al. *Klebsiella pneumoniae* bacteremia mortality: a systematic review and meta-analysis. *Front Cell Infect Microbiol.* 2023;13:1157010. doi:10.3389/fcimb.2023.1157010
- Hala S, Malaikah M, Huang J, et al. The emergence of highly resistant and hypervirulent *Klebsiella pneumoniae* CC14 clone in a tertiary hospital over 8 years. *Genome Med.* 2024;16(1):58. doi:10.1186/s13073-024-01332-5
- Yu X, Zhao Y, Sun X, et al. Association between clinical-biological characteristics of *Klebsiella pneumoniae* and 28-day mortality in patients with bloodstream infection. *BMC Microbiol.* 2024;24(1):552. doi:10.1186/s12866-024-03714-6
- Ramos-Castañeda JA, Ruano-Ravina A, Barbosa-Lorenzo R, et al. Mortality due to KPC carbapenemase-producing *Klebsiella pneumoniae* infections: systematic review and meta-analysis: mortality due to KPC *Klebsiella pneumoniae* infections. *J Infect.* 2018;76(5):438–448. doi:10.1016/j.jinf.2018.02.007
- Li Y, Li J, Hu T, et al. Five-year change of prevalence and risk factors for infection and mortality of carbapenem-resistant *Klebsiella pneumoniae* bloodstream infection in a tertiary hospital in North China. *Antimicrob Resist Infect Control.* 2020;9(1):79. doi:10.1186/s13756-020-00728-3
- Van Heuverswyn J, Valik JK, van der Werff S D, et al. Association between time to appropriate antimicrobial treatment and 30-day mortality in patients with bloodstream infections: a retrospective cohort study. *Clin Infect Dis off Publ Infect Dis Soc Am.* 2023;76:469–478. doi:10.1093/cid/ciac727
- Fostervold A, Raffelsberger N, Hetland MAK, et al. Risk of death in *Klebsiella pneumoniae* bloodstream infections is associated with specific phylogenetic lineages. *J Infect.* 2024;88(5):106155. doi:10.1016/j.jinf.2024.106155

10. Varon B, Palacios-Baena ZR, de Kraker MEA, et al. Universal risk factors for mortality in bloodstream infections (UNIFORM): a systematic review and Delphi survey. *Clin Microbiol Infect off Publ Eur Soc Clin Microbiol Infect Dis.* 2024;30:453–461.
11. Şimşek BT, Bozok T, Şahinoğlu MS, et al. Bloodstream infections caused by carbapenem-resistant *Klebsiella pneumoniae*: analysis of risk factors, treatment responses and mortality. *Infect Dis Lond Engl.* 2025;57:350–360. doi:10.1080/23744235.2024.2436991
12. Meini S, Del Cesta R, Sbrana F, et al. Clinical outcomes of patients hospitalized in internal medicine wards adequately treated for bloodstream infections caused by NDM-producing *Klebsiella pneumoniae*. Results from a real-life retrospective multi-center study in an endemic area. *Infection.* 2025;53. 1737–1744. doi:10.1007/s15010-025-02488-x
13. Liang P, Yu F. Value of CRP, PCT, and NLR in prediction of severity and prognosis of patients with bloodstream infections and sepsis. *Front Surg.* 2022;9:857218. doi:10.3389/fsurg.2022.857218
14. Yu J, Shi X, Ma J, et al. C-reactive protein is an independent predictor of 30-day bacterial infection post-liver transplantation. *Biomolecules.* 2021;11(8):1195. doi:10.3390/biom11081195
15. Zhou X, Fu S, Wu Y, et al. C-reactive protein-to-albumin ratio as a biomarker in patients with sepsis: a novel LASSO-COX based prognostic nomogram. *Sci Rep.* 2023;13(1):15309. doi:10.1038/s41598-023-42601-4
16. Xu H-J, Ma Y, Deng F, et al. The prognostic value of C-reactive protein/albumin ratio in human malignancies: an updated meta-analysis. *Oncol Targets Ther.* 2017;10:3059–3070. doi:10.2147/OTT.S137002
17. Park JE, Chung KS, Song JH, et al. The C-reactive protein/albumin ratio as a predictor of mortality in critically ill patients. *J Clin Med.* 2018;7(10):333. doi:10.3390/jcm7100333
18. Kunutsor SK, Laukkanen JA. Serum C-reactive protein-to-albumin ratio is a potential risk indicator for pneumonia: findings from a prospective cohort study. *Respir Med.* 2022;199:106894. doi:10.1016/j.rmed.2022.106894
19. Huang Y, Ao T, Hu M, et al. Association between red cell distribution width and mortality in patients with *Klebsiella pneumoniae* bloodstream infection: a cohort study. *Infect Drug Resist.* 2025;18:5961–5971. doi:10.2147/IDR.S552844
20. Calandra T, Cohen J. International sepsis forum definition of infection in the ICU consensus conference. The international sepsis forum consensus conference on definitions of infection in the intensive care unit. *Crit Care Med.* 2005;33(7):1538–1548. doi:10.1097/01.CCM.0000168253.91200.83
21. von Elm E, Altman DG, Egger M, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet Lond Engl.* 2007;370:1453–1457. doi:10.1016/S0140-6736(07)61602-X
22. Chen J, Allel K, Zhuo C, et al. Extended-spectrum β -lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae*: risk factors and economic burden among patients with bloodstream infections. *Risk Manag Healthc Policy.* 2024;17:375–385. doi:10.2147/RMHP.S453686
23. Huang Y, Ao T, Zhen P, et al. Association between serum bicarbonate and 28-day mortality in critically ill patients with infective endocarditis: a cohort study from MIMIC-IV. *Sci Rep.* 2025;15:312. doi:10.1038/s41598-024-84385-1
24. Güneş BÇ, Taştan YÖ, Doğanekin B, et al. Predictive value of CAR for in-hospital mortality in patients with COVID-19 pneumonia: a retrospective cohort study. *Arch Med Res.* 2021;52(5):554. doi:10.1016/j.arcmed.2021.02.006
25. Rathore SS, Oberoi S, Iqbal K, et al. Prognostic value of novel serum biomarkers, including C-reactive protein to albumin ratio and fibrinogen to albumin ratio, in COVID-19 disease: a meta-analysis. *Rev Med Virol.* 2022;32(6):e2390. doi:10.1002/rmv.2390
26. Piñerúa-González JF, Ruiz Rebollo ML, Zambrano-Infantino RDC, et al. Value of CRP/albumin ratio as a prognostic marker of acute pancreatitis: a retrospective study. *Rev Esp Enferm Dig.* 2023;115:707–712. doi:10.17235/reed.2023.9345/2022
27. Yang J, Chen Y, Wan J, et al. Prognostic value of the C-reactive protein to albumin ratio in patients with stroke: a meta-analysis. *Sci Rep.* 2025;15(1):21150. doi:10.1038/s41598-025-07327-5
28. Capurso C, Lo Buglio A, Bellanti F, et al. C-reactive protein/albumin ratio vs. prognostic nutritional index as the best predictor of early mortality in hospitalized older patients, regardless of admitting diagnosis. *Nutrients.* 2025;17:2907. doi:10.3390/nu17172907
29. Kim K-S, Kwon H-M, Kim JH, et al. C-reactive protein-to-albumin ratio is a predictor of 1-year mortality following liver transplantation. *Anesth Pain Med.* 2022;17(4):420–428. doi:10.17085/apm.22176
30. Zhang B, Li Z, Ye Y, et al. Prognostic value of C-reactive protein to albumin ratio in patients with valvular heart disease: nationwide prospective cohort study. *Int J Surg Lond Engl.* 2025;111(8):5245–5254. doi:10.1097/JS9.0000000000002576
31. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. *J Clin Invest.* 2003;111(12):1805–1812. doi:10.1172/JCI200318921
32. Paczosa MK, Meccas J. *Klebsiella pneumoniae*: going on the offense with a strong defense. *Microbiol Mol Biol Rev MMBR.* 2016;80(3):629–661. doi:10.1128/MMBR.00078-15
33. Wiedermann CJ. Hypoalbuminemia as surrogate and culprit of infections. *Int J Mol Sci.* 2021;22(9):4496. doi:10.3390/ijms22094496
34. Allison SP, Lobo DN. The clinical significance of hypoalbuminaemia. *Clin Nutr Edinb Scotl.* 2024;43:909–914.
35. Roche M, Rondeau P, Singh NR, et al. The antioxidant properties of serum albumin. *FEBS Lett.* 2008;582:1783–1787. doi:10.1016/j.febslet.2008.04.057
36. Dimitrijević J, Čalamać M, Đurmez O, et al. PCT-to-albumin ratio and CRP-to-albumin ratio as predictors of febrile neutropenia complications: a prospective observational trial. *Support Care Cancer off J Multinatl Assoc Support Care Cancer.* 2025;33:262.
37. Güneş H, Yurttutan S, Çobanuşağı M, et al. CRP/albumin ratio: a promising marker of gram-negative bacteremia in late-onset neonatal sepsis. *Turk Arch Pediatr.* 2021;56:32–36. doi:10.14744/TurkPediatriArs.2020.99076

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