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Predicting early mortality in critically ill patients: the role of the CRP/albumin ratio and its relationship with the APACHE II score

Doaa Bahrouz Mousa[1], Hany Hussein Moussa[2*], Mohammed Ahmed Elgazzar[3], Basma M. Hani[4] and Ahmed Mostafa Abd El-Hamid[5]

Abstract

Background The C-reactive protein (CRP)/albumin ratio is a valuable marker for assessing systemic inflammation and nutritional status. While it has been well studied as an independent prognostic factor in patients with infections, cancers, and various conditions, it has not yet been applied as a model for predicting early mortality in ICU settings. This study evaluates the potential of the CRP/albumin ratio as an early indicator of mortality risk in ICU patients.

Methods Our team conducted an observational prospective study involving 245 critically ill cases aged between 20 and 60 years, specifically patients suffering from sepsis, shock, cardiac emergencies, and respiratory failure. The patients were divided into two groups: Group A ($n=86$) consisted of non-survivors, while Group B ($n=159$) comprised survivors. We collected data on albumin and CRP levels within the first 24 h of admission.

Results There was a significant negative correlation between hemoglobin (Hb), hematocrit, and albumin levels and mortality ($P<0.05$). On the other hand, a positive association between the APACHE II score, white blood cells (WBCs), platelets, C-reactive protein (CRP), and the CRP/albumin ratio and mortality was observed ($P<0.05$). Notably, the APACHE II score, WBCs, platelets, CRP, and CRP/albumin ratio were significantly higher in the non-survivors' group than those who survived ($P<0.05$). Conversely, both Hb and hematocrit levels were substantially lower in non-survivors versus survivors ($P<0.05$). The ROC curve analyses for the APACHE II score, CRP, and CRP/albumin ratio revealed cut-off values of > 11, 56.5, and 21.06, respectively, with AUCs of 0.614, 0.876, and 0.895, indicating that these factors can significantly predict mortality ($P<0.05$), showing sensitivities of 61.63%, 89.5%, and 91.6% and specificities of 52.83%, 72.3%, and 77.4%.

Conclusions CRP/albumin ratio is a significant tool in early mortality prediction scores among cases with critical illness.

Keywords C-reactive protein, Albumin, Mortality, Critically ill, APACHE II score

*Correspondence:
Hany Hussein Moussa
hany_ahmed@med.kfs.edu.eg
Full list of author information is available at the end of the article

Introduction

The global consequences of mortality in intensive care units (ICUs) are significant, leading to substantial productivity losses and increased financial burdens. Mortality rates can differ widely around the world, influenced by factors such as the quality of ICU facilities, availability of trained personnel, and reasons for patient admissions to the ICU [1].

The urgent needs of patients in the ICU demand close observation of their vital signs and the support of expert healthcare professionals. This combination makes ICU care expensive, highlighting the need to prioritize investments in these critical areas [2].

The current mortality prediction and scoring systems for ICU patients typically only become valid after the first 24 to 48 h of admission, as specific data tends to be uncertain at entry [3].

Recently, mortality predictions have provided physicians with data to make crucial decisions about patient care, such as starting or continuing life-sustaining treatments and identifying patients at higher risk for adverse outcomes. By doing so, they can implement preventive measures or interventions to improve patient well-being [4]. The outcome prediction of cases requiring critical care in the ICU is essential for guiding treatment decisions [5].

The mortality rate in the ICU can vary significantly based on factors like patient demographics, geographic regions, and the specific type of illness. Before admission, it is crucial to evaluate any existing comorbidities related to cardiac, renal, hematologic, metabolic, and hepatic conditions [6].

- C-reactive protein: C-reactive protein (CRP) is well-recognized as a sensitive inflammation biomarker. The association of elevations in plasma/serum CRP levels with disease state has received considerable attention, even though CRP is not a specific indicator of a single disease state. Circulating CRP levels have been monitored with varying degrees of success to gauge disease severity or to predict disease progression and outcome. For inflammatory biomarkers at ICU admission, the concentration of CRP can be an independent risk factor for ICU mortality, and CRP can improve risk reclassification for prognosis prediction [7].
- Serum albumin: Albumin is the most abundant plasma protein, with normal serum levels between 3.5 and 5 g/dl. Recognition of low serum albumin as a predictor of morbidity and mortality is known and reported to be associated with poor prognosis and mortality. Based on this knowledge, speculations that the ratio of CRP to albumin could be used as a predictive marker for mortality [8].

Hypoalbuminemia is common in seriously ill patients, and serum albumin level has been associated with increased mortality in acutely ill patients in previous reports. The association between hypoalbuminemia and poor clinical outcomes appeared to be independent of both nutritional status and inflammation [8].

C-reactive protein/albumin ratio: The C-reactive protein/albumin ratio or CRP/alb ratio represents a new prognostic marker, the role of which has been examined and proved in different illnesses and conditions and which is based on well-known, basic characteristics of the C-reactive protein and serum albumins [9].

This work aimed at assessing the CRP/albumin ratio's efficacy as an early mortality prediction model within the ICU, supporting treatment decisions for cases with critical illnesses, prioritizing ICU admission requirements, and correlating the CRP/albumin ratio with APACHE II score.

Patients and methods

Our research team carried out an observational prospective study that involved 245 participants aged between 20 and 60 years, as older ages have lower albumin levels that could affect study results, encompassing both genders. This study was conducted at Benha University hospitals in the general ICU departments (medical and surgical ICU). This study specifically focused on the following:

Inclusion criteria

Critically ill patients are with the following criteria:

- Sepsis with shock or respiratory failure
- Cardiac emergencies include acute coronary syndrome, heart failure, arrhythmias, and post-cardiac arrest syndrome.
- Respiratory failure due to acute illness or exacerbation of chronic lung disease
- Acute renal failure
- Endocrine emergencies include electrolyte, hormonal, and acid–base disturbances
- Acute liver failure
- Neurological emergencies with reduced consciousness or respiratory failure
- Massive hemorrhage, for example, following major trauma, gastrointestinal bleeding, or during the peripartum period

Exclusion criteria

- Patients with chronic hepatitis or liver cirrhosis, to avoid hypoalbuminemia, which occurs in these patients and could affect study results
- Patients without major data or patients transferred from other ICUs
- Patients aged ≤ 20 years or ≥ 60 years due to a possible effect on albumin levels

The study was conducted from October 2022 to March 2024, following ethical approval from the Ethical Committee of Benha University Hospitals, Qalyubia, Egypt, under approval code MD 6–5–2022. Before starting our research, we ensured that all patients or their legal responsibility signed informed consent forms.

All participants were divided into two distinct groups: Group A ($n=86$), comprised of non-survivors, and Group B ($n=159$), consisting of survivors.

A comprehensive medical histories from all patients collected by our research team, followed by detailed physical examinations and the hemodynamic parameters of patients (heart rate, respiratory rate, systolic BP, diastolic BP, MAP, temperature) were done, and laboratory tests such as complete blood count (CBC), assessments of renal and hepatic function, and measurements of urea, creatinine, uric acid, serum bilirubin, serum albumin and enzymes as; alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), as well as evaluations of prothrombin time (PT), international normalized ratio (INR), electrolytes, arterial blood gas (ABG) analysis, CRP, and albumin concentrations. All these assessments were conducted within 24 h of ICU admission.

Albumin measurement

Its reaction with the green indicator dye bromocresol (BCG) determines the albumin level. The typical reference range for albumin, assessed via a colorimetric assay, is 3.5–5.5 g/dL.

C-reactive protein (CRP) measurement

Latex kit determines CRP level.

Scoring for health conditions

Assign 5 points for chronic health issues or nonoperative/emergency postoperative cases that show significant organ failure or immunocompromised status. Elective postoperative cases with considerable organ insufficiency or immunocompromised conditions receive 2 points.

In most of the scoring systems, scores are calculated from data collected on the first ICU day — Acute Physiology and Chronic Health Evaluation (APACHE), Simplified Acute Physiology Score (SAPS), and mortality prediction model (MPM). Others are repetitive and collect data every day throughout the ICU stay or for the first 3 days — organ dysfunction and infection system (ODIN), Sequential Organ Failure Assessment (SOFA), multiple organs dysfunction score (MODS), logistic organ dysfunction (LOD) model, and Glasgow coma score (GCS). Scores can be subjective or objective [10].

The total APACHE II score, which included the acute physiology score (APS), age points, and chronic health points, was calculated within 24 h of admission.

Sample size calculation

We employed the statistical software Epi-info 2002, designed by the Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO), Atlanta, Georgia, USA. The sample size calculation is set

Table 1 Demographic data of patients at day 0 of ICU admission and disease severity of the studied groups

		Non-survivors ($n=86$)	Survivors ($n=159$)	*P*
Age (years)		50.91 ± 7.80	50.68 ± 7.67	0.826
Sex	**Male**	51 (59.3%)	92 (57.86)	0.786
	Female	34 (39.53)	67 (42.14)	
APACHE II score		14.14 ± 5.71	12.01 ± 6.10	**0.008***

Data are presented as mean ± SD

ICU intensive care unit, *APACHE II* Acute Physiology and Chronic Health Evaluation II

*Significant *P*-value < 0.05

Table 2 Laboratory investigations of the groups

	Non-survivors ($n=86$)	Survivors ($n=159$)	*P*
WBCs (10^3/μL)	16.37 ± 7.87	11.34 ± 5.88	**< 0.001***
Hb (g/dL)	10.82 ± 2.20	11.84 ± 2.33	**0.001***
HCT (%)	31.40 ± 5.75	33.92 ± 6.12	**0.002***
Platelets (10^2/mm^3)	263.48 ± 138.38	219.07 ± 97.20	**0.009***
Albumin (g/dL)	2.82 ± 0.57	4.02 ± 7.04	0.116
Creatinine (mg/dL)	2.14 ± 1.773	1.95 ± 2.028	0.469
CRP (mg/L)	133.60 ± 76.54	42.90 ± 42.01	**< 0.001***
CRP/albumin ratio	49.39 ± 30.13	13.25 ± 14.01	**< 0.001***
Na (mEq/L)	136.36 ± 6.54	136.78 ± 6.22	0.616
K (mEq/L)	4.30 ± 0.77	4.18 ± 0.81	0.255

Data are presented as mean ± SD

ICU intensive care unit, *WBCs* white blood count, *Hb* hemoglobin, *HCT* hematocrit, *CRP* C-reactive protein, *Na* sodium, *K* potassium

*Significant *P*-value < 0.05

Table 3 Hemodynamic parameters of the groups

	Non-survivors ($n=86$)	Survivors ($n=159$)	*P*
HR (beats/min)	106.28 ± 15.11	103.08 ± 17.09	0.147
RR (beats/min)	26.01 ± 4.64	25.74 ± 5.10	0.685
SBP (mmHg)	113.37 ± 21.17	115.28 ± 21.28	0.502
DBP (mmHg)	73.49 ± 15.16	74.97 ± 14.66	0.457
MAP (mmHg)	86.78 ± 16.87	88.41 ± 16.51	0.467
Temperature (°C)	37.81 ± 0.76	37.86 ± 0.81	0.673

Data are presented as mean ± SD

HR heart rate, *RR* respiratory rate, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *MAP* mean arterial pressure

at a minimum of 245 cases. We calculated the sample size following these criteria: 95% confidence limit, 80% power of the research, and 30% expected outcome.

Statistical analysis

We conducted statistical analysis utilizing SPSS v26 produced by IBM Inc. (Chicago, IL, USA). Quantitative variables were showcased as mean and standard deviation (SD), while the two groups were compared using an unpaired Student's *t*-test. Qualitative variables were showcased as frequency and percentage (%), while analysis was carried out utilizing the chi-square or Fisher's exact test when appropriate. The degree of correlation between two quantitative variables is measured by Pearson correlation. The degree of correlation between quantitative and qualitative variables is measured by Spearman correlation. The ROC curve measures diagnostic performance, such as sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). A two-tailed *P*-value of below 0.05 was deemed statistically significant.

Results

Age and sex exhibited an insignificant variance among both groups. APACHE II score showed a significant increase within the non-survivor's group as opposed to the survivors' group ($P=0.008$) (Table 1).

Creatinine, albumin, Na, and K exhibited an insignificant variance among both groups. WBCs, platelets, CRP, and CRP/albumin ratio showed a significant increase within the non-survivor group as opposed to the survivors' group ($P<0.05$). Hb and HCT exhibited a substantial reduction within the non-survivors' group as opposed to the survivors' group ($P<0.05$) (Table 2).

Hemodynamic parameters exhibited an insignificant variance among both groups (Table 3).

There was a negative correlation between Hb, HCT, and albumin and mortality ($P<0.05$). A positive association was documented between APACHE II score, WBCs, platelets, CRP, and CRP/albumin ratio and mortality ($P<0.05$). Also, no association was documented between age, sex, creatinine, Na, K, HR, RR, SBP, DBP, MAP, and temperature and mortality (Table 4).

Table 4 Spearman correlation between different parameters and mortality of the studied groups

	r	*P*
Age (years)	0.014	0.825
Sex	0.058	0.367
APACHE II score	0.188	**0.003***
WBCs (10^3/μL)	0.331	**< 0.001***
Hb (g/dL)	−0.218	**0.001***
HCT (%)	−0.218	**0.001***
Platelets (10^2/mm^3)	0.171	**0.007***
Albumin (g/dL)	−0.456	**< 0.001***
Creatinine (mg/dL)	0.108	0.091
CRP (mg/L)	0.622	**< 0.001***
CRP/albumin ratio	0.654	**< 0.001***
Na (mEq/L)	−0.064	0.319
K (mEq/L)	0.099	0.122
HR (beat/min)	0.086	0.181
SBP (mmHg)	−0.031	0.627
DBP (mmHg)	−0.035	0.587
MAP (mmHg)	−0.032	0.618
RR (beat/min)	0.037	0.569
Temperature (°C)	−0.015	0.820

r correlation coefficient

APACHE II Acute Physiology and Chronic Health Evaluation II, *WBCs* white blood count, *Hb* hemoglobin, *HCT* hematocrit, *CRP* C-reactive protein, *Na* sodium, *K* potassium, *HR* heart rate, *RR* respiratory rate, *DBP* diastolic blood pressure, *SBP* systolic blood pressure, and *MAP* mean arterial pressure

*Significant *P*-value < 0.05

ROC curve of APACHE II score, CRP, and CRP/albumin ratio can significantly predict mortality respectively ($AUC=0.614$, 0.876, and 0.895, $P<0.05$) at cut-off > 11, > 56.5, and > 21.06 with 61.63%, 89.5%, and 91.6% sensitivity and 52.83%, 72.3%, and 77.4% specificity (Fig. 1).

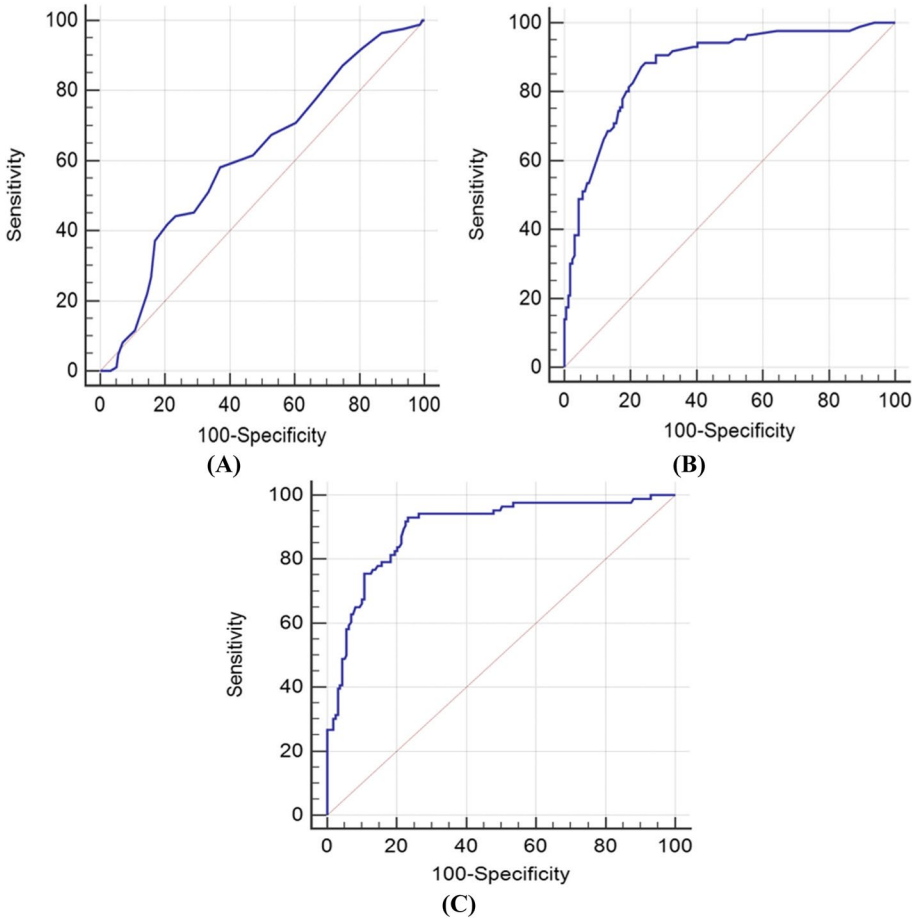

Fig. 1 ROC curve of **A** Acute Physiology and Chronic Health Evaluation II Score, **B** C-reactive protein, and **C** C-reactive protein/albumin ratio of the compared groups

Discussion

The C-reactive protein (CRP) represents a marker of the systemic inflammatory response (positive acute phase reactant), which are linked to worse clinical outcomes of various illnesses, especially in critically ill patients. Serum albumins are proteins with multiple roles, and their levels are used as a predictive marker (negative phase reactant), both in chronically and in critically ill patients [11].

The CRP/albumin ratio, a combination of markers for systemic inflammation and nutritional status, has been extensively studied as an independent prognostic marker in patients with infection, malignancy, and other diseases. However, relatively few studies focus on critical care patients in the ICU. This study aimed to evaluate the association between the CRP/albumin ratio and prognosis in critically ill patients in the ICU [12].

In this study, the APACHE II score significantly rose among the non-survivors (14.14 ± 5.71) versus the survivors (12.01 ± 6.10). Supporting this observation, Ahmed et al. [13], Basile-Filho et al. [14], and Park et al. [8] also reported that the APACHE II score was significantly higher in the non-survivors relative to the survivors. These results represent the efficacy of the APACHE II score in the prediction of high mortality as it is high.

In this study, we observed significant differences in the blood parameters of the non-survivors compared to the survivors. The levels of WBCs and platelets were significantly higher in the non-survivors. In contrast, the survivors presented lower values. Also, the levels of hemoglobin (Hb) and hematocrit (HCT) were significantly lower in the non-survivors compared to the survivors, supporting these observations (Ranzani et al. [5] and Park et al. [8]).

In this study, CRP and CRP/albumin ratio significantly rose among the non-survivors with values of 133.60 ± 76.54 and 49.39 ± 30.13, respectively, versus the

survivors with values of 42.90 ± 42.01 and 13.25 ± 14.01, respectively. Albumin in this study was significantly lower among the non-survivors (2.82 ± 0.57) versus the survivors (4.02 ± 7.04). These findings are compatible with the research by Loinjak et al. [9], who reported a substantial increase in the CRP/albumin ratio among non-survivors. Basile-Filho et al. [14] also corroborated this study, noting a considerable rise in CRP in the non-survivor group versus their survivor counterparts. Moreover, Park et al. [8] also reported that CRP and CRP/albumin ratios were significantly higher in the non-survivor group compared to the survivors' group, and albumin was also significantly lower in the non-survivor group compared to the survivors' group. Confirming these results, Ranzani et al. [5] reported that CRP and CRP/albumin ratio were significantly higher in the non-survivors group compared to the survivors' group and reported that albumin was also significantly lower in the non-survivors group compared to the survivors' group.

Regarding such findings, there was a positive substantial correlation between APACHE II score, WBCs, platelets, CRP, and CRP/albumin ratio and mortality. A negative association was documented between HB, HCT, albumin, and mortality. Also, the APACHE II score could be a significant mortality predictor ($AUC = 0.614$), indicating a cut-off value of > 11 with a sensitivity of 61.63% and a specificity of 52.83%. CRP showed a significant mortality predictor ($AUC = 0.876$) at cut-off > 56.5, indicating a sensitivity of 89.5% and a specificity of 72.3%. Additionally, CRP/albumin ratio showed a significant mortality predictor ($AUC = 0.895$) at cut-off > 21.06, indicating a sensitivity of 91.6% and a specificity of 77.4%.

Recent findings align with those of Patel et al. [15], who established the APACHE II score as a notable predictor of mortality in ICU patients with AKI, achieving an AUC of 0.79 at a cut-off of > 23. This score exhibited a sensitivity of 57.14% and a specificity of 86.15%. On the other hand, Kim et al. [16] highlighted that CRP serves as a strong predictor for 180-day mortality with a cut-off > 67.5, showing a sensitivity of 84.86% (ranging from 79.70 to 90.03%) and a specificity of 30.95% (between 26.79 and 35.10%). Additionally, the CRP/albumin ratio was identified as a favorable predictor for mortality, with a cut-off of > 5.09, demonstrating a sensitivity of 61.08% (from 54.06 to 68.11%) and a specificity of 61.05% (from 56.67 to 65.44%). In the work of Ranzani et al. [5], CRP was a reasonable mortality predictor ($AUC = 0.590$) at a cut-off of 196, with a sensitivity of 52% and a specificity of 67%. Likewise, the CRP/albumin ratio was again noted as a viable predictor ($AUC = 0.612$) with a cut-off of 8.7, yielding a sensitivity of 54% and a specificity of 66%.

Acknowledging our study's limitations, particularly the relatively small sample size, is essential. Furthermore, our research did not incorporate other markers that could contribute to mortality prediction.

Conclusions

A negative correlation was observed between Hb, Hct, and albumin levels with mortality ($P < 0.05$). Also, a substantial positive correlation was found between the APACHE II score, WBC counts, platelets, CRP levels, and the CRP/albumin ratio with mortality ($P < 0.05$). The CRP/albumin ratio presented a strong ability to predict mortality, demonstrating a sensitivity of 91.6% and a specificity of 77.4% with a cut-off value of 21.06.

Authors' contributions

Doaa Bahrouz Mousa: collecting samples, writing the article draft. Hany Hussein Moussa: idea and concept, supervision of the work, reviewing results, and modification of the article, and final revision and approval of the article. Mohammed Ahmed Elgazzar: supervision the work, final revision, and approval of the article. Basma M Hani: statistical analysis, formulation of results, and article review. Ahmed Mostafa Abd El-Hamid: idea and concept, reviewing the sample collection, statistical and result preparation, supervision of the work, reviewing and modification of the article, and final revision and approval of the article.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Competing interests

The authors declare no competing interests.

Author details

[1]Critical Care Medicine Department, Faculty of Medicine, Kafr Elsheikh University, Kafr Elsheikh, Egypt. [2]Pulmonology Department, Faculty of Medicine, Kafr Elsheikh University, Kafr Elsheikh, Egypt. [3]Cardiothoracic Surgery Department, Faculty of Medicine, Benha University, Banha, Qalyubia, Egypt. [4]Public Health and Community Medicine Department, Benha, Faculty of Medicineaq, Benha University, Banha, Egypt. [5]Critical Care Medicine Surgery Department, Faculty of Medicine, Benha University, Banha, Qalyubia, Egypt.

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