

# PREDICTING MORTALITY AND CLINICAL OUTCOMES IN ICU PATIENTS USING CRP/ALBUMIN AND LACTATE/ALBUMIN RATIOS: A CROSS-SECTIONAL STUDY

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## Abstract

**Background:** Early risk stratification in critically ill patients is crucial for improving outcomes, and biomarker-based approaches, such as the CRP/Albumin and Lactate/Albumin ratios, offer potential prognostic value.

**Objectives:** To evaluate the prognostic accuracy of lactate/albumin ratio and the CRP/albumin ratio in critically ill patients during their ICU stay in predicting mortality, need for inotropic support, mechanical ventilation and duration of ICU stay.

**Methods:** This was a single centre, hospital based, analytical cross-sectional study conducted in the Department of Emergency Medicine and Medical ICU, Vinayaka Mission's Medical College & Hospital, Puducherry for a duration of 18 months.

**Results:** This study analyzed 50 critically ill patients, with 64% aged 60 years or older and 56% being male. More than half (54%) had an ICU stay of fewer than three days, while 66% had a hospital stay of fewer than seven days. Invasive or CPAP ventilation was required in 44% of cases, and 32% of patients needed inotropic support. The overall survival rate was 82%, with 18% of patients succumbing to their illness. Non-survivors had significantly elevated CRP levels ( $p=0.001$ ) and a higher CRP/albumin ratio ( $p=0.001$ ), while the lactate/albumin ratio showed a trend toward significance ( $p=0.062$ ). Patients requiring inotropic support exhibited significantly elevated CRP, CRP/albumin, and lactate/albumin ratios. Similarly, intubated patients had higher CRP ( $p=0.042$ ) and CRP/albumin ratios ( $p=0.042$ ). The CRP/albumin ratio correlated significantly with ICU stay ( $p=0.009$ ) but not with total hospital stay. It also demonstrated a strong predictive value for mortality (AUC=0.843,  $p=0.001$ ) and was superior to the lactate/albumin ratio in predicting inotropic support, invasive ventilation, and prolonged ICU stays.

**Conclusion:** The study highlights the CRP/albumin ratio as a strong prognostic marker for mortality, inotropic support, and invasive ventilation in critically ill patients. Its superior predictive value suggests its potential for early risk stratification and improved clinical decision-making.

**KEYWORDS:** CRP/Albumin Ratio, Lactate/Albumin Ratio, Prognostic Marker, Critical Illness, Mortality Prediction, Intensive Care Unit

## INTRODUCTION

Critically ill patients in intensive care units (ICUs) require precise prognostic assessments to guide treatment decisions and improve outcomes.<sup>[1]</sup>

Among the numerous biomarkers used in critical care, C-reactive protein (CRP) and albumin are particularly significant, reflecting inflammation and nutritional status, respectively.<sup>[2]</sup> Recent studies suggest that combining these markers into ratios, specifically the CRP/Albumin Ratio (CAR) and Lactate/Albumin Ratio (LAR), could enhance prognostic accuracy. CRP, an acute-phase protein produced in response to inflammation, is commonly used to assess infection severity and has been associated with adverse outcomes in conditions such as sepsis and trauma.<sup>[3]</sup> Albumin, the most abundant plasma protein, maintains oncotic pressure and serves as a marker of both nutritional status and systemic inflammation. Low albumin levels are linked to increased morbidity and mortality in critically ill patients.<sup>[4]</sup> CAR integrates CRP and albumin, providing a composite measure that reflects both inflammation and nutritional status. Studies have associated elevated CAR with worse outcomes in critical illnesses, including higher mortality rates.<sup>[5,6]</sup> Similarly, LAR combines lactate – a marker of metabolic stress and tissue hypoxia – with albumin, offering a broader assessment of a patient's physiological state.<sup>[7]</sup> Elevated LAR has been linked to increased mortality, potentially making it a more effective prognostic tool than lactate or albumin alone.<sup>[8]</sup>

Against this background, this study aims to evaluate the prognostic accuracy of lactate/albumin ratio and the c-reactive protein/albumin ratio in critically ill patients during their ICU stay in predicting mortality, need for inotropic support, mechanical ventilation and duration of ICU stay.

## MATERIALS AND METHODS

**Study settings:** This was a single centre, hospital based, cross-sectional study conducted in the Department of Emergency Medicine and Medical Intensive Care Unit (MICU), Vinayaka Mission's Medical College & Hospital, Puducherry for a duration of 18 months. The study was approved by the Institutional Human Ethics Committee (IHEC) with reference number VMMC/GENMED/2022/JULY/02 dated 25/07/2022. The participants (or their attenders) were given the Participant Information Sheet (PIS) in their native language, and its contents were verbally explained to ensure their understanding and satisfaction. Enrolment into the study proceeded upon receipt of written informed consent.

**Study population:** Patients admitted for critical care who were at least 18 years old met the inclusion criteria. Exclusion criteria included protein-losing diseases, chronic kidney disease (CKD), chronic liver disease, protein-losing enteropathies, and severe malnutrition.

**Sample size and sampling technique:** The minimum required sample size was calculated as 50, based on an overall sensitivity of 0.70, specificity of 0.80, and a prevalence of 0.5. Sample size accounted for a 10% non-response rate. We used nonprobability sampling technique – purposive sampling/consecutive enumeration to enrol patients.

**Method of data collection:** Demographic data, clinical history, and laboratory investigations were obtained for all eligible patients. Blood samples were obtained to measure serum lactate, CRP, and serum albumin levels. CRP levels were determined using the Turbilatex method, an immunoturbidimetric assay in which anti-CRP antibody-coated latex particles agglutinate in the presence of CRP, leading to an increase in turbidity that is measured photometrically. Serum lactate levels were assessed using the lactate oxidase method, where lactate oxidase catalyzes the oxidation of lactate to pyruvate and hydrogen peroxide, with the latter reacting with a chromogen to produce a colour change measurable by spectrophotometry. Serum albumin levels were determined using an automated analyzer with a standard kit, employing the bromocresol green method, in which albumin binds to the dye, resulting in a colour change proportional to the albumin concentration.

**Statistical analysis:** The data obtained was manually entered into Microsoft Excel and analysed using Statistical Package for Social Sciences (SPSS) v23. All the categorical variables were summarised using frequencies and percentages. Continuous variables were summarized using mean (standard deviation) after testing for data normality, using Kolmogorov–Smirnov test and the Shapiro–Wilk test. To test for statistical significance, Chi square test or Fisher exact test (for categorical variables) and independent ‘t’ test (for continuous variables) was used. Pearson's correlation coefficient was estimated. Receiver operating characteristics (ROC) analysis was conducted to determine the area under the curve (AUC) of lactate/albumin and CRP/albumin in predicting study outcomes. Statistical significance was considered at p value less than 0.05.

## RESULTS

**Sociodemographic and clinical characteristics:** The study included 50 critically ill patients, with a majority (64%) aged 60 years or older. Males constituted 56% of the sample. Laboratory investigations revealed a mean haemoglobin level of 11.0 g/dL (SD 2.5), total count of  $11.7 \times 10^9/L$  (SD 6.0), and serum albumin of 3.3 g/dL (SD 0.5). The mean serum lactate was 20.6 mmol/L (SD 21.1), while the mean CRP was 51.8 mg/L (SD 38.8). The lactate/albumin ratio had a mean of 6.6 (SD 6.5), and the CRP/albumin ratio had a mean of 16.7 (SD 13.1). More than half of the patients (54%) had an ICU stay of fewer than three days, while 66% had a total hospital stay of fewer than seven days. Regarding respiratory support, 44% required invasive or CPAP ventilation. Inotropic support was required in 32% of cases. The overall survival rate was 82%, with 18% of patients succumbing to their illness.

**Association between serum lactate, CRP, lactate/albumin, CRP/albumin and study outcomes:** Patients who did not survive had higher mean serum lactate (23.9 vs. 19.9 mmol/L) and significantly elevated CRP levels (91.5 vs. 43.1 mg/L,  $p = 0.001$ ) compared to those who were discharged. Similarly, the CRP/albumin ratio was significantly higher in non-survivors (29.6 vs. 13.9,  $p = 0.001$ ), while the lactate/albumin ratio showed a trend toward higher values but did not reach statistical significance ( $p = 0.062$ ). Patients requiring inotropic support had significantly elevated serum lactate (29.5 vs. 16.5 mmol/L,  $p = 0.041$ ), CRP (74.4 vs. 41.2 mg/L,  $p < 0.001$ ), lactate/albumin ratio (9.0 vs. 5.4,  $p < 0.001$ ), and CRP/albumin ratio (24.1 vs. 13.2,  $p < 0.001$ ) compared to those who did not. Intubated patients also exhibited significantly higher CRP ( $p = 0.042$ ), lactate/albumin ratio ( $p = 0.031$ ), and CRP/albumin ratio ( $p = 0.042$ ), though serum lactate differences did not reach statistical significance ( $p = 0.073$ ). These findings suggest that elevated CRP and CRP/albumin ratios are strong predictors of mortality, inotropic support, and intubation in critically ill patients.

**Correlation between serum lactate, CRP, lactate/albumin, CRP/albumin and ICU/hospital stay:** Serum lactate showed no significant correlation with ICU stay ( $r_p = 0.127$ ,  $p = 0.378$ ) or hospital stay ( $r_p = -0.192$ ,  $p = 0.183$ ). CRP demonstrated a significant positive correlation with ICU stay ( $r_p = 0.319$ ,  $p = 0.024$ ), but no significant correlation with hospital stay ( $r_p = -0.108$ ,  $p = 0.455$ ). The lactate/albumin ratio had a weak, non-significant positive correlation with ICU stay ( $r_p = 0.258$ ,  $p = 0.071$ ) and a negative but non-significant correlation with hospital stay ( $r_p = -0.138$ ,  $p = 0.339$ ). The CRP/albumin ratio showed a significant positive correlation with ICU stay ( $r_p = 0.365$ ,  $p = 0.009$ ), but no significant correlation with

hospital stay ( $r_p = -0.071$ ,  $p = 0.624$ ). These findings suggest that higher CRP and CRP/albumin ratios are associated with prolonged ICU stays, while no significant associations were observed with total hospital stay.

**ROC analysis showing AUC of lactate/albumin and CRP/albumin in predicting study outcomes:** The CRP/albumin ratio demonstrated strong predictive value for mortality, with an AUC of 0.843 (95% CI: 0.731–0.954), a cutoff of 24.4, and a high sensitivity (88.9%) and specificity (78.1%) ( $p = 0.001$ ). In contrast, the lactate/albumin ratio had a lower AUC of 0.692 and did not reach statistical significance ( $p = 0.062$ ). Both ratios were significant predictors of inotropic support, with AUCs of 0.731 and 0.752 for lactate/albumin and CRP/albumin, respectively ( $p < 0.01$ ). Similarly, both ratios were effective in predicting the need for invasive ventilation, with CRP/albumin showing an AUC of 0.692 and lactate/albumin an AUC of 0.702 ( $p < 0.05$ ). For ICU stay  $>3$  days, CRP/albumin (AUC = 0.683,  $p = 0.023$ ) was a significant predictor, whereas lactate/albumin (AUC = 0.612,  $p = 0.153$ ) was not. These findings suggest that the CRP/albumin ratio is a stronger prognostic marker than the lactate/albumin ratio, particularly for predicting mortality and prolonged ICU stays.

## DISCUSSION

The distribution of age among participants demonstrated a higher prevalence of older adults, with 64% of the study population being 60 years of age or older. This observation aligns with the well-documented phenomenon that age-related physiological decline and the presence of comorbidities increase the susceptibility of older individuals to critical illness. Prior research by Nasa et al.<sup>[9]</sup> (2012) and Brummel et al.<sup>[10]</sup> (2022) similarly emphasizes the heightened vulnerability of elderly patients to severe medical conditions requiring intensive care. The gender distribution in this study revealed a slightly higher proportion of male patients (56%) compared to females (44%). This finding is consistent with previous literature, such as the study conducted by King et al.<sup>[11]</sup> (2019), which suggests that males may have a higher risk of developing critical illness. This gender disparity in critical care admission may be attributed to biological differences, lifestyle choices, and a higher prevalence of comorbid conditions, such as cardiovascular diseases, in males.<sup>[12]</sup>

The clinical and biochemical parameters observed in this study exhibited significant variation, reflecting the diverse nature of the underlying conditions among critically ill patients. Haematological markers, including mean haemoglobin levels and total leukocyte counts, showed substantial differences, which is consistent with the findings reported by Azoulay et al.<sup>[13]</sup> (2015). Similarly, renal function markers, such as serum urea and creatinine levels, displayed wide-ranging values, indicative of varying degrees of renal impairment in critically ill patients. Liver function tests, including total bilirubin, total protein, and serum albumin levels, also exhibited significant heterogeneity, underscoring the involvement of hepatic dysfunction in a subset of patients. This variation is in accordance with findings by Sausmarez et al.<sup>[14]</sup> (2021), who reported a broad spectrum of liver function abnormalities in critically ill individuals. The substantial differences in these biochemical parameters highlight the complexity and multifactorial nature of critical illness, wherein multiple organ systems are frequently compromised.<sup>[15]</sup>

The prognostic value of the CAR and LAR in predicting mortality, need for inotropic support, requirement for invasive ventilation, and prolonged ICU stay was examined in this study. The analysis revealed that the CAR was significantly elevated in patients who did not survive compared to those who were discharged ( $p = 0.001$ ), indicating a strong association with mortality. The ROC curve analysis demonstrated an AUC of 0.84, reflecting a high discriminative ability of this biomarker in predicting patient outcomes. A cut-off value of 24.35 was identified, with a sensitivity of 88.89% and specificity of 78.05%, suggesting that the CAR serves as a highly reliable predictor of mortality in critically ill patients. These findings are supported by prior studies conducted by Ranzani et al.<sup>[16]</sup> (2013) and Park et al. (2018), both of which established a strong correlation between elevated CAR values and increased mortality risk in ICU settings.

Similarly, the LAR demonstrated a statistically significant difference between patients who survived and those who did not ( $p = 0.06$ ), with an AUC of 0.69. Although its predictive accuracy was lower than that of the CAR, the LAR still exhibited a reasonable sensitivity of 88.89% and a specificity of 58.54%. These findings align with prior research by Bakker et al.<sup>[17]</sup> (2013), which highlighted the association between elevated lactate levels and adverse outcomes in critically ill patients. Additionally, Lau et al.<sup>[18]</sup> (2021) supported the use of the LAR as a mortality predictor, while suggesting that its prognostic value may be enhanced when combined with other biomarkers. The moderate predictive capability of the LAR observed in this study suggests that, while it provides useful prognostic insights, it should ideally be integrated into a broader panel of laboratory tests for a more comprehensive assessment of patient prognosis.<sup>[19]</sup>

Regarding the need for inotropic support, the CAR demonstrated a strong correlation with cardiovascular instability requiring inotropic intervention. The analysis revealed an AUC of 0.75 ( $p < 0.01$ ), with a sensitivity of 81.25% and specificity of 64.71% at a cut-off value of 13.28. These findings align with the study conducted by de Blake et al.<sup>[20]</sup> (2003), which suggested that inflammatory markers, such as CRP, play a critical role in cardiovascular instability in critically ill patients.<sup>[21]</sup> Since systemic inflammation is a key factor in hemodynamic compromise, CRP levels serve as an indicator of the need for inotropic support. Similarly, the Lactate/Albumin ratio was significantly elevated in patients requiring inotropic support ( $p < 0.01$ ), with an AUC of 0.73. A cut-off value of 3.83 provided sensitivity and specificity of 81.25% and 64.71%, respectively. This highlighted the prognostic significance of lactate levels in identifying patients at risk of requiring inotropic support.

The study also examined the predictive value of CAR and LAR for the requirement of invasive ventilation. The CRP/Albumin ratio was found to be significantly higher in patients requiring intubation ( $p = 0.04$ ), with an AUC of 0.69. The cut-off value of 10.73 yielded a sensitivity of 83.33% and specificity of 50.00%. These findings are supported by Herold et al.<sup>[22]</sup> (2020), who identified elevated CRP levels as a strong predictor of respiratory failure necessitating mechanical ventilation. This association emphasizes the role of systemic inflammation in respiratory compromise.

Similarly, the Lactate/Albumin ratio demonstrated a significant difference between intubated and non-intubated patients ( $p=0.03$ ), with an AUC of 0.70. A cut-off value of 3.83 provided sensitivity of 83.33% and specificity of 60.53%. These results corroborate the observations made by Shapiro et al.<sup>[23]</sup> (2005), who identified lactate as a crucial biomarker for predicting the need for mechanical ventilation, particularly in patients with sepsis.

Furthermore, the correlation between CRP/Albumin and Lactate/Albumin ratios with ICU and hospital length of stay was analyzed. The CRP/Albumin ratio exhibited a significant correlation with prolonged ICU stay ( $r=0.365$ ,  $p=0.009$ ), while CRP levels themselves were also significantly associated with longer ICU stays ( $r=0.319$ ,  $p=0.024$ ). These findings are in line with Grander et al.<sup>[24]</sup> (2010), who demonstrated that CRP levels serve as a predictor of prolonged ICU admissions. The results suggest that higher CAR values may indicate a greater severity of illness, necessitating extended intensive care. Although LAR also showed a correlation with ICU and hospital stays, the association was less pronounced compared to CAR, reinforcing the greater prognostic utility of CRP/Albumin in this context.

Finally, the analysis of the receiver operating characteristic (ROC) curve for predicting mortality, inotropic support, and invasive ventilation confirmed that both CRP/Albumin and Lactate/Albumin ratios possess significant predictive capabilities. However, the CRP/Albumin ratio consistently exhibited higher AUC values across different outcomes, indicating a stronger prognostic potential. This finding aligns with Ranzani et al.<sup>[16]</sup> (2013), who also demonstrated that the CRP/Albumin ratio had superior predictive performance compared to other biomarkers. Given its consistent performance in predicting multiple adverse outcomes, the CRP/Albumin ratio may serve as a valuable prognostic tool in ICU settings, facilitating early risk stratification and targeted clinical interventions for critically ill patients.

### Limitations

Despite the significant findings, this study has several limitations that should be acknowledged. The study was conducted in a single-centre setting, which may introduce selection bias and limit external validity. Another important limitation is the lack of consideration for potential confounding factors, such as underlying comorbidities, medication history, and pre-existing inflammatory conditions, which could influence CRP, lactate, and albumin levels. Furthermore, while CAR and LAR showed significant associations with clinical outcomes, their predictive value may be influenced by dynamic changes over time, which were not accounted for in this study.

### CONCLUSION

The results of this study underscore the potential of the CAR and LAR as valuable prognostic indicators in patients with severe illness. In particular, the CRP/Albumin ratio demonstrated a strong predictive ability for mortality, the need for inotropic support, and invasive ventilation. These biomarkers can serve as essential tools for clinicians in early risk stratification and clinical decision-making, ultimately contributing to improved patient outcomes. Integrating these markers into routine clinical practice has the potential to enhance the accuracy of prognostic assessments and facilitate timely, appropriate interventions for critically ill patients, thereby optimizing critical care management.

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