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Comparative Analysis of Lactate to Albumin Ratio versus CRP to Albumin Ratio in Mechanically Ventilated Patients

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Abstract

Mechanically ventilated patients in intensive care units (ICUs) often suffer from severe, life-threatening conditions that need close monitoring and precise therapeutic interventions. Biomarkers are crucial in investigating the prognosis, guiding treatment decisions, and predicting outcomes in these critically ill patients. Among these biomarkers, the Lactate to Albumin Ratio (LAR) and the C-Reactive Protein to Albumin Ratio (CAR) have emerged as significant predictors of morbidity and mortality. The present study focuses on conducting a comparative analysis of LAR versus CAR in mechanically ventilated patients. An observational study was conducted on 50 mechanically ventilated patients, aged between 25 to 80 years, in the intensive care unit (ICU). The serum biomarkers like Lactate, CRP and albumin levels, were measured upon admission to the intensive care unit (ICU). Additionally, the other outcomes were assessed such as ICU mortality and length of stay. The findings revealed that the mean age of the patient was 55.64±16.52 years. Both the lactate-to-albumin ratio (0.70) and the CRP-to-albumin ratio (0.69) were significantly associated with ICU mortality. The p values of these two parameters were 0.03 and 0.04 respectively in lactate to albumin ratio and CRP to albumin ratio. The lactate-to-albumin ratio was more strongly correlated with markers of metabolic stress and tissue hypoxia, while the CRP-to-albumin ratio was a stronger predictor of inflammation severity. Both ratios provide valuable prognostic insights for mechanically ventilated patients. However, the lactate to albumin ratio is more indicative of metabolic stress and CRP to albumin ratio reflects inflammatory status, with lactate to albumin ratio being a more reliable indicator of prognosis in mechanically ventilated patients.

Keywords: *CRP to Albumin Ratio, Lactate to Albumin Ratio, Ventilated Patients.*

Introduction

Mechanical ventilation is an essential component of critical care, providing life-sustaining support for patients with severe respiratory failure and other life-threatening conditions that impair breathing [1]. While this intervention is often necessary, it is not without significant risks and complications, such as ventilator-associated pneumonia, barotrauma, and ventilator-induced lung injury, all of which can contribute to increased morbidity and mortality [2, 3]. The ability to accurately assess the severity of illness and predict outcomes in mechanically ventilated patients is crucial for optimizing care, tailoring interventions, and improving survival rates [4]. Biomarkers have emerged as valuable tools in critical care, offering insights into the physiological and pathological states of patients [5, 6]. Additionally, it aids in early

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identification of high-risk patients, monitoring disease progression, guiding therapeutic decisions, and predicting clinical outcomes [7, 8]. Lactate is produced during anaerobic metabolism, which occurs when oxygen delivery to tissues is insufficient, a common scenario in critically ill patients experiencing shock, sepsis, or severe hypoxia [9]. Elevated lactate levels are significant indicator of metabolic stress and tissue hypoxia and have been consistently linked with higher mortality and worse clinical outcomes. Lactate profiles are routinely used in the ICU to assess the severity of illness, guide resuscitation efforts, and monitor the effectiveness of therapeutic interventions [10, 11]. CRP is an acute-phase reactant synthesized by the liver in response to pro-inflammatory cytokines, particularly interleukin-6 (IL-6) and is considered as a sensitive marker of systemic inflammation, rising rapidly in response to infection, trauma, and other inflammatory stimuli [12]. Upsurge in CRP levels are linked with adverse effects in various clinical settings, including sepsis, trauma, and postoperative complications, and it is frequently used in the ICU to evaluate the inflammatory status of patients and guide anti-inflammatory and antimicrobial therapies [13]. Albumin is the most abundant plasma protein, synthesized by the liver, and plays a critical role in maintaining oncotic pressure, transporting various substances (such as hormones, drugs, and electrolytes), and modulating inflammatory responses [14]. Hypoalbuminemia is common in critically ill patients and is often indicative of poor nutritional status, systemic inflammation, and increased capillary permeability. Low albumin levels are linked with higher mortality, extended hospital stays, and increased risk of complications. Albumin investigation provides a valuable tool for assessing the nutritional and inflammatory status of patients [15]. The integration of these biomarkers into composite indices, such as lactate-to-albumin ratio (LAR) and CRP to Albumin Ratio (CAR), has been proposed to enhance their prognostic utility. These ratios combine the prognostic information provided by each biomarker, offering a more comprehensive assessment of the patient's condition [16]. LAR is calculated by dividing the serum lactate level by the serum albumin level. This ratio integrates the effects of tissue hypoxia and metabolic stress (indicated by lactate) with the patient's nutritional and inflammatory status (indicated by albumin). Previous studies have shown that an elevated LAR is associated with worse outcomes, including higher mortality in critically ill patients. By combining lactate and albumin, the LAR provides a more nuanced view of the patient's physiological state, potentially offering better prognostic information than either marker alone [16]. CRP to Albumin ratio (CAR) is calculated by dividing the serum CRP by serum albumin level. This ratio reflects the balance between systemic inflammation (indicated by CRP) and nutritional status (indicated by albumin). Higher CAR values have been linked to adverse outcomes in conditions like sepsis and other critical illnesses. By integrating the inflammatory response with nutritional status, the CAR provides a composite measure that may be more predictive of outcomes than either marker alone [17]. Despite the numerous potential benefits of these composite indices, there is limited data on their comparative utility in mechanically ventilated patients. Understanding which ratio provides superior prognostic information could help clinicians prioritize and tailor interventions more effectively [18]. Henceforth, this study focused on comparing the prognostic value of LAR and CAR in mechanically ventilated patients and to determine whether one ratio offers superior prognostic information than the other, thereby informing clinical practice and potentially guiding therapeutic strategies.

Materials and methods

This cross-sectional study was conducted at Vinayaka Missions Medical College, Karaikal involving mechanically ventilated patients admitted to the intensive care unit (ICU) between the timeline of 12/8/22 to 12/2/24. Informed consent was taken from the patient's attender due to the retrospective nature of the study. All the procedures performed in the study were based on the principles of Helsinki 1964 and institutional guidelines. The study was initiated after obtaining clearance from the Institutional Ethical Committee with the reference number (VMCC/GENMED/2022/July/02) dated 25/7/2022. Around fifty adult patients (age ≥18 years old) who were admitted to the ICU and mechanically ventilated were included and the data were collected from their medical profiles. Patients with incomplete medical records or missing key variables (e.g., lactate, CRP, albumin levels), protein-losing diseases, chronic kidney disease and decompensated liver disease were excluded from the study.

Data were collected from electronic medical records using a standardized data collection form. The following parameters like demographic information (age, sex), clinical characteristics (reason for ICU admission, comorbidities), and laboratory biomarkers (serum lactate, CRP, albumin levels) were collected upon ICU admission. Additional data on ICU outcomes (mortality, length of ICU stay, duration of mechanical ventilation) and incidence of sepsis during ICU stay were also recorded.

LAR was calculated by dividing the serum lactate level (mg/dL) by the serum albumin level (g/dL) obtained on ICU admission. Similarly, CAR was calculated by dividing the serum CRP level (mg/dL) by the serum albumin level (g/dL). These ratios were then categorized into tertiles or quartiles for statistical analysis. The collected data were transformed into variables, coded and entered in Microsoft Excel. Data were statistically analysed using the SPSS-PC-25 version.

The normal distribution of different parameters was tested by the Shapiro-Wilk normality test. Quantitative data was expressed in mean ± standard deviation and the difference between the mean of the two groups were compared by Mann Whiney U test. Qualitative data were expressed in frequency as a percentage. ROC curve was prepared using C RP/albumin ratio and Lactate/albumin ratio to predict different outcomes. Cut-off value was calculated using Youden Index and based on cut off value sensitivity, specificity, positive predictive value and negative predictive value were calculated. Spearman correlation coefficient was used to see the correlation between two quantitative variables. P' value less than 0.05 was considered statistically significant.

Results

Demographic Details

In this study 50 mechanically ventilated patients with a mean age of 55.64±16.52 years, inclusive of both males (56%) and females (44%). In this study 36% were above 75years, 28% were 60-74yrs, 24% were 35-59yrs and 12% were 20-34 yrs in (Figure 1).

Length of Hospital Stay and Mortality Rates of Ventilated Patients

Among the 50 patients, the average length of hospital stay by mechanically ventilated patients were6.36±4.74 days. 66% of patients stayed in the ICU for up to 7 days, while 24% of patients were in the ICU for 8-14 days and the remaining 10% of patients stayed for more than 14 days. However, 82% of ventilated patients were successfully discharged and the mortality rate was noticed in 8% of individuals (Figure 2).

Biomarkers

The findings of various biomarkers like HB, TC, urea and creatinine were analyzed in mechanically ventilated patients. The mean values are 10.954 ±2.4751, 11.724±6.0011, 45.910±33.8164, 1.536±1.7043 respectively. Additionally, liver markers were analyzed and the mean values of Total bilirubin (1.223±1.4939), Total protein (6.072±.5119), and S. Albumin (3.260±.5322) (Table 1).

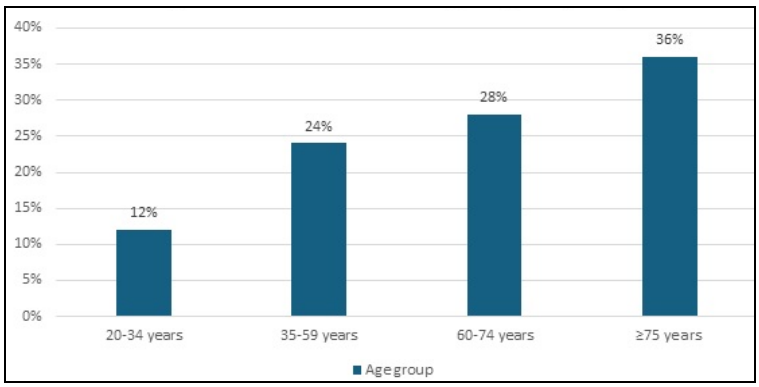

Figure 1. Age-wise Distribution of Study Participants

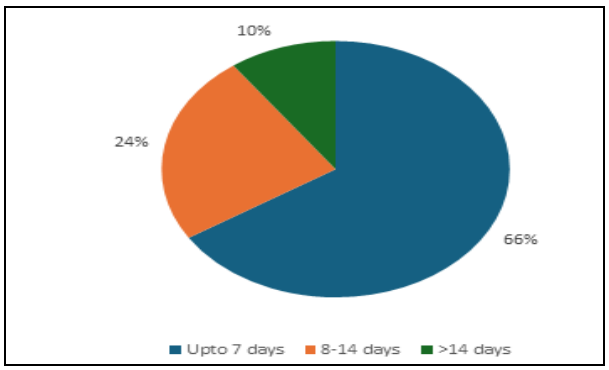

Figure 2. Hospital Stay in Study Subjects

Table 1. Biomarkers Analyzed in Mechanically Ventilated Patients

Parameters	Mean	SD
HB	10.954	2.4751
Total counts	11.724	6.0011
Urea	45.910	33.8164
Creatinine	1.536	1.7043
Total bilirubin	1.223	1.4939
Total protein	6.072	.5119
S. Albumin (g/dL)	3.260	.5322

Lactate/Albumin Ratio vs CRP/Albumin Ratio

The ROC curve using CRP/albumin ratio and Lactate/albumin ratio to predict the need of invasive ventilation showed **Lactate/albumin ratio**: 0.70 (95% CI: 0.55-0.86), **CRP/albumin ratio**: 0.69 (95% CI: 0.53-0.84). Both ratios had a similar AUC value, indicating moderate discriminative ability (Graph 2). P value showed a **Lactate/albumin ratio**: of 0.03 and a **CRP/albumin ratio**: of 0.04. Both ratios have P values less than 0.05, indicating that their diagnostic ability is statistically significant (Table 2). Cut-off values showed a **Lactate/albumin ratio** of 3.83 and **CRP/albumin ratio** of 10.73. These cut-off values are thresholds above which patients are predicted to need invasive ventilation in our study (Table 2). Both ratios had high sensitivity (83.33 %). The specificity was moderate for the Lactate/albumin ratio (60.53%) and lower for the CRP/albumin ratio (50.00%), indicating varying ability to correctly identify patients who do not need invasive ventilation (Table 2). Both ratios showed low positive predictive values and high negative predictive values. The Lactate/albumin ratio (66.00%) had higher accuracy compared to the CRP/albumin ratio (58.00%), suggesting it is a better overall predictor of the need for invasive ventilation (Table 2).

Table 2. Lactate/Albumin Ratio vs CRP/Albumin Ratio in Mechanically Ventilated Patients

	S. LACTATE (mg/dl)	**CRP (mg/dl)**	**Lactate /albumin**	**CRP/Albumin**
Mean	20.629	51.7953	6.5715	16.7152
Std. Deviation	21.087	38.7931	6.503	13.017
Median	12.760	44.2200	3.8330	13.2800
IQR	8.9-24.02	10.33-95.83	2.57-8.07	3.91-29.31
Minimum	2.0	1.41	0.52	0.37
Maximum	115.9	112.96	28.98	41.91

Discussion

The ability to accurately predict outcomes in mechanically ventilated patients is critical for optimizing care, allocating resources, and improving patient outcomes. By comparing the prognostic utility of LAR and CAR, this study aims to enhance the prognostic toolkit available to clinicians, providing them with more robust and comprehensive measures to assess the severity of illness and guide clinical decisions. The integration of these biomarkers into routine clinical practice could help to identify high-risk patients early, tailor therapeutic interventions more effectively, and ultimately improve survival rates and reduce complications in mechanically ventilated patients.

The findings exhibited a higher prevalence of critical illness among the older individuals, with 64% of individuals being 60 years and above, highlighting the increased vulnerability. This is consistent with existing literature, which shows that older adults are more likely to suffer from comorbidities and age-related physiological decline, making them more susceptible to severe in critical care settings [19, 20].

The gender distribution, with a slightly higher proportion of males (56%) than females (44%), suggests a potential gender disparity in the risk of critical illness. This could be

attributed due to numerous biological variations like, lifestyle factors, and the prevalence of certain comorbidities in males, such as cardiovascular diseases. The findings were similar to Lat et al., 2021, who explored that males are more frequently admitted to the intensive care unit than females. It is also suggested that males have better outcomes compared to females. However, the short and long-term survival rates are similar. The sex hormones appear to influence the trajectory of critical illness, while outcomes vary depending on the hormone cycle and diseased condition [21].

Accurate prognostication in mechanically ventilated patients is essential for several reasons. Primarily, it allows for better allocation of resources in the ICU, ensuring that the most critical patients receive the necessary attention and interventions. Secondly, it helps in planning the course of treatment, including decisions regarding the escalation or de-escalation of care based on the patient's predicted outcome. Thirdly, accurate prognostication can improve communication with patients' families, providing them with realistic expectations regarding the patient's prognosis and potential outcomes.

Lactate is a well-known biomarker of tissue hypoxia and metabolic stress, and its upsurge often indicates severe illness and poor prognosis. Albumin, on the other hand, is a biomarker that indicates the nutritional status and systemic inflammation [22]. The LAR combines these two biomarkers to provide a comprehensive insightabout the functional status of the patients. In this study, the LAR showed a significant difference between intubated and non-intubated patients, with a higher ratio indicating a greater likelihood of requiring invasive ventilation. The cut-off value of 3.83 provided a sensitivity of 83.33% and specificity of 60.53%, making it a useful tool for identifying patients at high risk. Similarly, Erdogan et al., 2021 noticed that an increase in LAR ratio is noticed in the invasive ventilated patients [23].

C - C-reactive protein (CRP) is an acute-phase protein that upsurges in response to inflammation. The CAR reflects the balance between systemic inflammation and the nutritional and inflammatory status of patients. [24] This study shows that CAR was significantly higher in intubated patients, with a cut-off value of 10.73 providing a sensitivity of 83.33% and specificity of 50.00%. These findings are consistent with previous studies that have shown elevated CRP levels to be predictive of respiratory failure requiring mechanical ventilation. Similarly, the findings were consistent with Tharavath et al., 2023 showed elevation of CAR in non-cardiac surgery patients in association with requiring ventilator support [25].

While both LAR and CAR are valuable and cost-effective prognostic tools, this study found that LAR had a slight edge over CAR in terms of overall predictive accuracy. The higher specificity and accuracy of LAR are better at correctly identifying patients who will not require invasive ventilation, thereby reducing the number of false positives. This is important in clinical practice, where overestimation of risk could lead to unnecessary interventions and resource use. The slightly higher AUC for LAR also indicates it is a more reliable predictor of outcomes in mechanically ventilated patients.

Integrating LAR and CAR into routine assessments in the ICU could refine the clinical decision-making process. Patients with elevated LAR or CAR could be flagged for closer monitoring and more aggressive interventions. This proactive approach could help prevent the progression to more severe states that require invasive ventilation, potentially improving patient outcomes. Additionally, using these ratios could aid in resource allocation, ensuring that ICU resources are directed towards the patients who need them the most.

The significant association of elevated CRP and lactate levels with the need for invasive ventilation underscores the role of systemic inflammation and metabolic stress in respiratory failure. High CRP levels indicate a state of heightened inflammation, which can exacerbate respiratory conditions and lead to the deterioration of lung function. Similarly, elevated lactate levels are indicative of metabolic distress and poor tissue oxygenation, necessitating mechanical ventilation to support respiratory function. Understanding these underlying mechanisms can help in developing targeted therapeutic interventions to manage inflammation and metabolic stress in critically ill patients.

The integration of LAR and CAR into clinical practice could revolutionize the management of mechanically ventilated patients. By providing a more accurate assessment of patient risk, these biomarkers could help clinicians prioritize interventions for those most in need, thereby optimizing patient outcomes. This approach could also facilitate more effective use of ICU resources, ensuring that high-risk patients receive the necessary support while avoiding unnecessary interventions for those with a lower risk profile.

Both LAR and CAR are valuable prognostic tools in mechanically ventilated patients, with LAR showing a slight advantage in overall predictive accuracy. Integrating these biomarkers into clinical practice can enhance patient care by providing early identification of high-risk patients and guiding therapeutic interventions. Further research with larger cohorts and diverse populations is necessary to confirm these findings and expand on their clinical applicability. The ultimate goal is to improve survival rates and reduce complications in mechanically ventilated patients, thereby optimizing patient care and resource allocation in the ICU.

Limitations

The sample size of fifty patients is relatively small, which may limit the generalizability of the findings. Larger studies are needed to validate these results in different populations. Additionally, this study is observational and, therefore, cannot establish causality. The associations observed do not imply that the CRP/Albumin or Lactate/Albumin ratios cause the outcomes but rather that they are correlated. Additionally, investigating the integration of these ratios with other biomarkers and clinical parameters could provide a more comprehensive prognostic model.

Conclusion

Both CRP/albumin and Lactate/albumin ratios are significant predictors of the need for invasive ventilation, with high sensitivity and negative predictive values. The Lactate/albumin ratio performs better overall, with higher specificity, positive likelihood ratio, and accuracy compared to the CRP/albumin ratio. These findings can help healthcare providers make informed decisions about the need for invasive ventilation in patients, potentially improving patient outcomes by identifying those at risk more accurately.

Conflict of Interest

The authors declare that there are no conflicts of interest related to this study.

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