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Original Article

Lactate/ Albumin Ratio as Compared to Serum Lactate Levels as Mortality Indicator in Sepsis Patients

Hassan Javed, Abdul Rehman Arshad, Muhammad Iqbal, Irfan Najam, Muhammad Uzair, Elleyyeen Avais

Department of Medicine, Pak Emirates Military Hospital, Rawalpindi/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To compare lactate/ albumin ratio versus serum lactate levels as predictors of morbidity and mortality in sepsis patients.

Study Design: Analytical cross-sectional study.

Place and Duration of Study: Department of Medicine, Pak Emirates Military Hospital, Rawalpindi, Pakistan, from Sep 2023 to Apr 2024.

Methodology: This study was done on patients with a diagnosis of sepsis, while individuals with protein losing enteropathy, nephrotic syndrome, severe skin burns, recent history of albumin, and blood product transfusions were excluded. Demographic characteristics and investigations including serum lactate and albumin levels were recorded, and the primary outcome was the patient's status post-hospital admission (remained alive and shifted toward or discharged) or died. Statistical significance was analyzed using receiver operating curve (ROC) analysis.

Results: One hundred eight (n=108) patients with a median age of 55.33(38.25-70.00) years with male 62.00(57.41%) predominance were enrolled in this study. The median serum lactate and serum albumin levels at admission were 4.160 (2.95-6.40) mmol/L and 32.00 (27.00-37.75) g/L at the time of primary outcome. Lactate albumin ratio was 0.14(0.08-0.21). The receiver operating curve analysis for lactate showed area under curve 0.669 (95% confidence interval 0.563-0.776, *p*=0.003) while for lactate albumin ratio area under curve was 0.696 (95% confidence Interval 0.586-0.805, *p*=0.001).

Conclusion: Serum lactate levels and lactate to albumin ratio both were significant and had a comparable profile in the prediction of morbidity and mortality of sepsis.

Keywords: Prognostic markers, Receiver operating curve analysis, Sepsis, Serum albumin.

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INTRODUCTION

Sepsis is caused by dysregulated host immune response system which can lead from simple organ dysfunction to multiple organs failing and ultimately leading to death.[1] There were 11 million deaths worldwide due to sepsis in 2017.[2] Scoring systems like Sepsis Related Organ Failure Assessment (SOFA), quick Sepsis Related Organ Failure Assessment (qSOFA), and National Early Warning Score (NEWS), provide useful insight regarding the severity of sepsis and patient outcomes.[3,4] Inflammatory cytokines like TNF alpha, Interleukins (IL-1, IL-12, IL-18), and interferons are released resulting in activation of complement and coagulation cascade leading to a cytokine syndrome,[5] leading to oxygen supply and demand mismatch causing single to multiple organ dysfunction and biochemical markers like lactate, C reactive protein, ESR, procalcitonin, and platelets are raised.[5,6] Serum lactate levels are routinely used as a septic marker as raised serum lactate levels >2mmol/L have been associated with worse outcomes in sepsis patients.[7] In sepsis, patients' serum albumin levels also fluctuate during disease activity,[8] but the role of serum albumin levels during sepsis is limited because the nutritional status of the patients is also compromised.[6] In this study, we explored the role of lactate/ albumin ratio (LAR) as compared to serum lactate levels alone as predictors of mortality and morbidity in sepsis patients. In the ongoing era of scientific research, diverse septic markers have surfaced in the scientific literature but in a resource-poor country with financial restraints along with a lack of availability of specialized equipment existing markers have been studied to understand a better relation and to explore the utility of these in clinical settings to predict better or worse outcomes.

Correspondence: Dr Hassan Javed, Department of Medicine, Pak Emirates Military Hospital, Rawalpindi Pakistan

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METHODOLOGY

This analytical cross-sectional study was carried out at the Medical Intensive Care Unit (ICU-M) and Acute Medical Unit (AMU) of Pak Emirates Military Hospital (PEMH), Rawalpindi, Pakistan, for a period

of 8 months from September 2023 to April 2024 after Institutional Ethics Review Board approval vide ethical certificate no A/28/ERC/623/23. Sample size calculation was done using EasyROC: a web tool for ROC curve analysis (ver. 1.3.1). For this purpose, we assumed that area under the ROC curve of 0.7 for LAR.[9] Considering a mortality rate of 15%, allocation ratio was set at 6. The power of statistical analysis was set at 80% and considering a 5% chance of Type I error, we calculated a need for 98 patients to be a part of this study (including a minimum of 14 patients dying in the hospital) and the rest of the survivors.

Inclusion Criteria: The patients included in the study had to be older than 18 years, fulfilling the 3rd International Consensus Definition of Sepsis (Sepsis-3) criteria, and have a NEWS2 score >7.

Exclusion Criteria: Individuals with conditions like protein losing enteropathy and/or nephropathy and severe skin burns were excluded. Moreover, patients with a recent history of albumin and blood products like red cell concentrate, platelets, and fresh frozen plasma transfusions were excluded. After obtaining consent, patient's demographic details, clinical history, reason for admission, and co-morbid conditions were considered. Baseline investigations including serum ALT, serum creatinine, C-reactive protein, serum albumin, and serum lactate levels were noted. A sample of serum lactate and albumin was collected, if it was not already done. Serum lactate levels were done once every 48 hours, and serum albumin was also repeated after 48 hours side by side. Moreover, serum lactate and albumin levels were repeated before stepping down/ discharge of the patient to quantify and compare with initial readings. NEWS2 score was calculated at the time of admission, was evaluated on 12 12-hourly basis and at the time of off-stepping the patient/ discharge from the hospital. In case of death of the patient, the last recorded values of serum Lactate, albumin and NEWS2 score were considered.. The interquartile range (IQR) and median were computed for a skewed distribution. Qualitative data was represented using frequency and percentage. Statistical Package for Social Sciences Version 20.0 (IBM SPSS ver. 20.0) was used. The ROC Curve and independent sample Mann-Whitney U test were used for statistical analysis where a *p*-value <0.05 was taken as statistically significant.

RESULTS

A total of one hundred and eight (n=108) individuals were studied with a median age of 55.33(38.25-70.00) years with males being more (62,57.41%). A total of 61(56.48%) patients had hypertension, 79(73.15%) had ischemic heart disease (IHD), 90(90.33%) had a history of smoking, 81(75.00%) had chronic kidney disease (CKD), and 20(18.52) were on ionotropic support. In our study, 40.00(57.34%) patients died during the hospital stay while the rest were stepped down to high dependency units or discharged. The median levels of serum lactate were 4.160(2.95-6.40) mmol/L and median LAR was 0.14(0.08-0.21). Further demographic details are shown in Table-I.

Table-I: Demographic and Clinical Features of Participants (n=108)

Characteristics	Value
Median Age (years)	55.33 (38.25-70.00)
Gender	
Male	62(57.41%)
Female	46(42.59%)
Comorbid Conditions	
Diabetes	61(56.48%)
IHD	90(90.33%)
HTN	91(46.43%)
CKD	20(18.52%
Smokers	81(75.00%)
Median Hospital stay (days)	10.42(7.00-12.00)
Median Serum Lactate (mmol/L)	4.160(2.95-6.40)
Median Serum Albumin (g/L)	32.00(27.00-37.75)
Median Serum Lactate/Albumin Ratio	0.14(0.08-0.21)

Serum lactate (p=0.001) as well as serum lactate to albumin ratio (p=0.003) at the time of primary outcome was able to predict the morbidity and mortality independently while none of the other variables were able to do so, which is shown in Table-II.

Table-II: Comparison of Different Clinical Features with Primary Outcome (n=108)

Clinical Characteristics	Alive (n=68) Median (IQR)	Dead (n=40) Median (IQR)	p-value (≤0.05)
Age (years)	68.00 (38.25-69.75)	40.00 (38.75-70.00)	0.881
CRP Admission (mg/L)	99.25 (42.17-161.87)	83.85 (53.90-158.37)	0.663
Albumin Admission (g/L)	32.00 (26.00-37.75)	31.50 (28.25-37.75)	0.866
Serum Lactate (mmol/L)	4.00 (2.15-5.17)	6.00 (3.02-7.05)	0.001
Serum ALT (mg/L)	28.00 (21.00-36.00)	26.00 (21.00-43.00)	0.836
Serum Creatinine (mmol/L)	112.00 (89.00-237.00)	108.00 (61.00-357)	0.656
Albumin Outcome (g/L)	28.00 (25.0-30.0)	28.00 (25.0-30.0)	0.713
Hospital stay (days)	9.00 (7.00-12.00)	9.00 (6.00-12.00)	0.313
LAR Outcome	0.128 (0.609-0.200)	0.163 (0.137-0.309)	0.003

When it was tested statistically, area under curve for LAR was 0.669(95% Confidence Interval 0.563-0.776, p=0.003) while that for lactate was 0.696(95%

Confidence Interval 0.586-0.805, p=0.001) as shown in Figure-1.

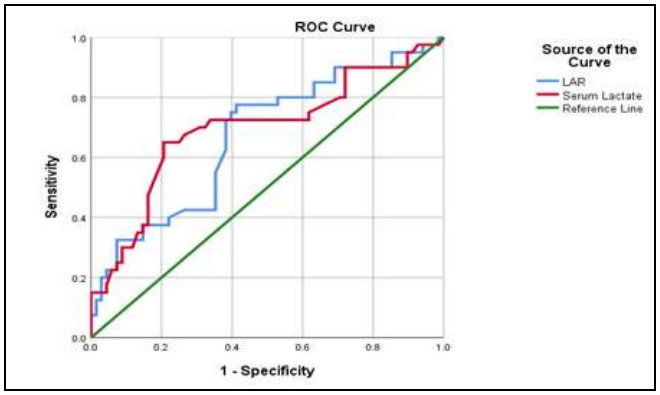

Figure-1: Receiver Operating Curve Analysis of Serum Lactate (Red) and Serum Lactate/Albumin Ratio (Blue)

DISCUSSION

Serum CRP, serum lactate, and LAR proved significant as diagnostic markers in the prediction of sepsis-related deaths.[6,10] Serum Lactate levels proved to be a better prognostic indicator in the outcome prediction with AUC 0.696(95% Confidence Interval 0.586-0.805, p=0.001) as compared to LAR 0.669(95% Confidence Interval 0.563-0.776, p=0.003). Other serum markers like C-reactive protein were also taken under account during the course of the study and been found that low levels of C-reactive proteins were found in patients who died of sepsis as compared to the survivors' group with insignificant p-values comparable to other studies.[11,12] Serum Lactate is a metabolic product of anaerobic glucose metabolism produced by the body during oxygen deficiency resulting multiple organ failure.[13] Ongoing studies have favored the significance of higher lactate levels in sepsis patients are associated with worse patient outcomes.[14,15] A study reported that patients having higher serum lactate levels had worse outcomes,[15] and serum albumin levels which depict the nutritional status of the patients can also help to indicate ongoing sepsis/septic shock.[15] Serum albumin levels correlate negatively with an ongoing septic shock state and low serum albumin levels at admission correlate with high 28-day in-hospital mortality.[16,17] Serum albumin levels get affected in different ways during systemic illnesses like sepsis, malnutrition, and chronic liver disease.[17] In our study, serum albumin levels were found to be low in the patients with worse outcomes but the p-value was not significant in our population group. Ongoing studies are in favor of LAR (Lactate albumin ratio) being a better predictor of mortality in sepsis patients.[18-20] Along with evaluating serum lactate levels and serum albumin levels, a combination of these factors provides another valuable marker in predicting sepsis morbidity and mortality as one study noted in intensive care settings during the course of sepsis and proved its correlation with the development of multiple-organ dysfunction syndrome (p<0.001) and mortality.[20] Another study conducted on the relevance of the lactate/ albumin ratio19 reported AUC for the lactate/albumin ratio as 0.69 and was significantly higher than that of lactate 0.62 for predicting 28-day mortality. These outcomes are similar to ours; however, serum lactate levels alone were found to be a better prognostic indicator in sepsis patients.

LIMITATIONS OF STUDY

It is a single-center study including only those patients who were admitted in the ICU-M and AMU, bringing an inherent bias of being critically ill and poorly managed in the outskirts of such a resource-limited country. A multicenter research approach is the need of the hour for further evaluation of this correlation. Moreover, the size of our sample was small; a larger sample size may provide a detailed insight into the effectiveness of LAR and serum lactate levels.

CONCLUSION

In our study, the predictive usefulness of the Lactate to albumin ratio in comparison of serum lactate levels in patients admitted with sepsis to a tertiary care hospital's medical intensive care unit and acute medical unit showed better results for serum lactate levels as a marker of clinical outcome while LAR results were comparable to those of serum lactate levels.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

HJ & ARA: Data acquisition, data analysis, critical review, approval of the final version to be published.

MI & IN: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MU & EA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity

of any part of the work are appropriately investigated and resolved.

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