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"Association of Lactate to Albumin Ratio Level with Organ Failure and Mortality in Severe Sepsis and Septic Shock Patients"

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Abstract: Introduction : The prognostic role of lactate to albumin (L/A) ratio has hardly been explored in severe sepsis patients. This study examines the utility of L/A ratio as a clinical & prognostic marker in severe sepsis patients. **Objectives :** To investigate the potential utility of the lactate to albumin ratio as a prognostic marker for Multiple Organ Dysfunction Syndrome (MODS) and mortality in patients with severe sepsis and septic shock. **Methodology:** This prospective follow-up study was conducted with non-trauma adult (>18 years) ICU patients with severe sepsis for 4 months at R.L. Jalappa Hospital and Research Centre. Clinical and laboratory data for day 1 (D1) and 2 (D2) were collected. **Results:** We recruited 28 patients with a mean age 57.7 years (Standard deviation or SD 15.0 years), majority being female (n=17, 60.7%). The median L/A was 1.96 (SD 0.54) and 1.74 (SD 0.51) on D1 & D2, respectively. The D1 L/A was positively correlated with APACHE II score (Pearson's correlation co-efficient or r=0.61, p<0.001) (figure 1), heart rate on D1 (r=0.52, p=0.004) and D2 (r=0.51, p=0.005), respiratory rate on D1 (r=0.77, p<0.001) and D2 (r=0.76, p<0.001), serum creatinine on D1 (r=0.8, p<0.001) and D2 (r=0.81, p<0.001); and negatively correlated with D1 mean arteriolar pressure (r=-0.43, p=0.02), platelets on D1 (r=-0.64, p<0.001) and D2 (r=-0.71, p<0.001). Three (10.7%) hospital deaths were reported and the median Lactate/albumin ratio for these patients (2.72, IQR 2.67 to 2.98) were high compared to those who survived (1.78, IQR 1.44 to 2.29) (p<0.05, Wilcoxon signed rank test).

Keywords: Albumin, Sepsis, Lactate, Multiple Organ Dysfunction Syndrome, Prognosis

Background (Introduction)

Sepsis leads to a significant number of admissions to intensive care units (ICUs) and is linked with high rates of morbidity and mortality. Severe cases of sepsis, including septic shock, often result in multiple-organ dysfunction syndrome (MODS), which can be fatal in a majority of cases where three or more organs are affected[1]. The severity of organ dysfunction plays a crucial role in determining the prognosis of sepsis[2,3]. In critical illness, inadequate oxygen delivery to tissues leads to oxygen debt, tissue hypoxia, anaerobic metabolism, and lactate accumulation[4]. Numerous studies have identified lactate levels as a valuable marker for diagnosing, treating, and predicting outcomes in circulatory shock. Elevated lactate levels, particularly above 4mmol/L in patients meeting systemic inflammatory response syndrome (SIRS) criteria, are associated with increased mortality rates in normotensive patients[5]. Besides lactate, serum albumin levels may also serve as a significant prognostic marker[6]. As an acute-phase protein, serum albumin decreases during acute inflammation, correlating with the severity of the inflammatory response in critically ill patients[7]. Therefore, lactate and serum albumin levels may exhibit different trends during sepsis. While lactate is vital in severe sepsis and septic shock, combining lactate and albumin levels could provide a variable that captures the relationship between MODS and mortality more comprehensively. With this background, the objective of the present study was to investigate the potential utility of the lactate to albumin ratio as a prognostic marker for Multiple Organ Dysfunction Syndrome (MODS) and mortality in patients with severe sepsis and septic shock.

Lacuna in Knowledge

In patients with severe sepsis and multiorgan dysfunction syndrome, lactate and albumin levels are closely monitored to assess anaerobic metabolism and to analyse acid base abnormality respectively.

There are not many studies found in the literature investigating lactate to albumin ratio as a prognostic marker in patients with severe sepsis and MODS.

Hence, we intended to conduct this study.

Objectives

To investigate the potential utility of the lactate to albumin ratio as a prognostic marker for Multiple Organ Dysfunction Syndrome (MODS) and mortality in patients with severe sepsis and septic shock

Materials & Methods:

Study Design: Prospective observational study

Duration of study: 4 months(2nd February 2024 –2nd May 2024)

Study Participants: This study was conducted on patients of age more than 18 years admitted in the ICU at R.L. Jalappa Hospital and Research Centre, Tamaka, Kolar. Adult patients (>18 years of age) admitted with severe sepsis and multiorgan dysfunction syndrome in the ICU were eligible to take part in the study. We excluded patients admitted due to trauma.

Sample size: The sample size was calculated based on the following formula:

$N= (Z_{\alpha/2}+Z_{\beta})^2 (\sigma_1^2+ \sigma_2^2) / (\mu_1- \mu_2)^2$ where N=sample size per group, $Z_{\alpha/2}$=Z-score corresponding to the desired significance level, Z_{β}=Z-score corresponding to the desired power (1-β), σ_1 and σ_2= standard deviations of the two groups, and μ_1 and μ_2 are means of the two groups. Assuming the mean difference in L/A between the two groups as 0.8, SD as 0.3, (1-β) or power=80%, and α=0.05, we get a sample size of 28.

Inclusion criteria:

- Patients more than 18 years of age admitted with severe sepsis and multiorgan dysfunction syndrome in the ICU.

Exclusion criteria:

- Patients more than 18 years of age admitted with severe sepsis and multiorgan dysfunction syndrome in the ICU.

Methodology:

Patient baselines include age, sex, vital signs, severity of illness such as APACHE II score, blood gas analysis, hematologic, biochemical tests for day 1 and day 2 analyse the relevance to mortality in ICU patients on the day 1 and day 2 of admission. Vital signs include Heart rate (HR), temperature(C), mean arterial pressure (MAP), Respiratory rate (RR) was recorded on day 1 and day 2 of admission into ICU. Investigations such as white blood cells count (WBC), platelets, serum creatinine, serum albumin, arterial lactate from blood gas analysis were sent on day 1 and day 2 of admission into ICU. Lactate/ serum albumin ratio is calculated on day 1 and day 2 of ICU admission.

Statistical analysis: Data was entered in Microsoft Excel and data analysis was done in Stata version 18.0. Descriptive statistics was applied including frequency (%) for categorical variables. Mean and standard deviation (SD) or median and interquartile range (IQR) if variables are normally distributed depending upon the distribution of the

variables. Correlation between two variables was calculated by Pearson corelation coefficient (r) and the variability explained was expressed with R^2. The difference between two groups were checked using non-parametric Wilcoxon signed ranked test. A p-value <0.05 was considered as statistically significant for all statistical tests.

Conflict Of Interest- Nil

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Results:

A total of 28 participants were recruited for the study. There were 17 (60.7%) females and 11 (40.7%) males. The mean age of the participants was 57.7 years (SD 15 years) and mean duration of ICU admission was 5.6 days (SD 2.4 days). The median Apache II score was 21 (IQR 18 to 24). Twenty-three (82.1%) participants had at least one comorbidity including hypertension (n=12, 42.9%), diabetes (n=9, 32.1%), hypothyroidism (n=3, 10.7%), and bronchial asthma (n=2, 7.1%). The mean BMI of the participants was 24.3 (SD 5.0).

Clinical features on day 1 and day 2

The clinical features of the participants on day 1 and day 2 are presented in table 1. Fever was present for 7 (25%) patients on day 1 and 2 (7.1%) patients on day 2.

Table 1: Distribution of the clinical parameters on Day 1 and day 2

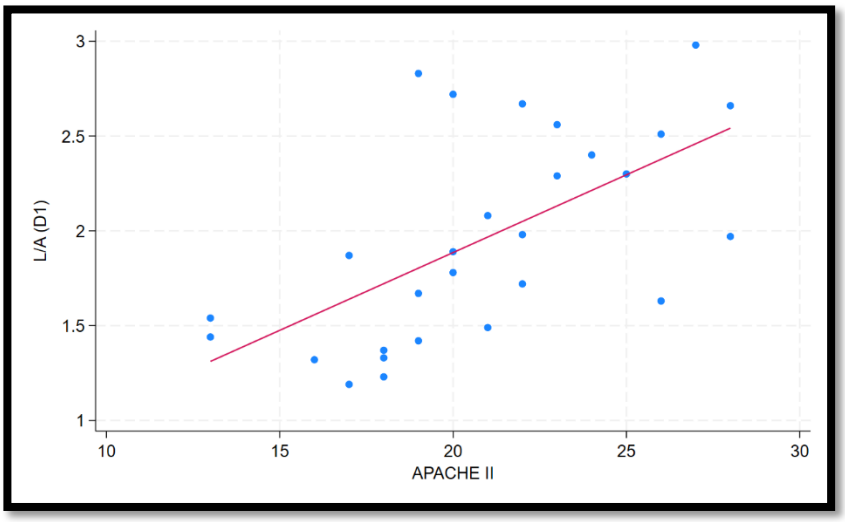
		MEAN (SD)	
SNo	CLINICAL PARAMETER	DAY 1	DAY 2
1	APACHE II	21 (IQR: 18 to 24)	
2	MAP	54 (7.0)	60 (7.0)
3	Heart rate/min	102 (12)	98 (12)
4	Respiratory rate/min	24 (IQR: 22 to 28)	20 (19 to 25)
5	WBC, n (%)		
	<4,000 (n=22)	13 (46.4)	12 (42.9)
	4000 to 10,000	0	1 (3.6)
	>10,000 (n=6)	15 (53.6)	15 (53.6)
6	Platelets (In lakhs)	1.47 (IQR: 1.18 t 2.07)	1.8 (1.4 to 2.04)
7	Creatinine	1.58 (0.58)	1.44 (0.54)
8	Serum Albumin	2.88 (0.57)	3.12 (0.65)
9	Lactate	2.76 (0.26)	2.56 (0.26)
10	Lactate/ Albumin (L/A)	1.0 (0.27)	0.87 (0.3)

Table 2: Correlation of L/A with different parameters

SNo	Parameter (L/A versus)	R^2
1	APACHE II	0.62
2	MAP day 1	0.77
3	MAP day 2	0.7217
4	Creatinine day 1	0.5363
5	Creatinine day 2	0.5081

Total 3 (10.7%) death reported. L/A ratio on day 1 is significantly high among those who died (median 1.63) vs who survived (median 0.91) (p=0.001, Wilcoxon signed rank test). L/A ratio on day 2 is significantly high among those who died (median 1.61) vs who survived (median 0.75) (p<0.001, Wilcoxon signed rank test). However, there was no significant difference in duration in hospital stay between those who died (median 7 days) vs who survived (median 5 days) (p=0.24, Wilcoxon signed rank test).

Figure: 1



Discussion:

In this study, we aimed to evaluate the utility of the L/A ratio as a clinical and prognostic indicator in severe sepsis patients admitted to the intensive care unit (ICU). Our findings indicate a significant association between the L/A ratio and multiple markers of disease severity and organ dysfunction, including APACHE II score, heart rate, respiratory rate, serum creatinine, mean arteriolar pressure, and platelet count. Importantly, we observed a strong correlation between higher L/A ratios and increased mortality, with non-survivors exhibiting significantly higher L/A ratios compared to survivors. These results suggest that the L/A ratio may serve as a valuable tool for risk stratification and prognostication in severe sepsis and septic shock patients, potentially aiding clinicians in optimizing management strategies and improving outcomes in this high-risk population.

In our study of severe sepsis and septic shock patients, we observed a predominance of females, consistent with previous literature suggesting a higher susceptibility to severe sepsis among females. The mean age of our participants was 57.7 years, reflecting the vulnerability of the elderly population to sepsis-related complications[8]. Furthermore, the majority of our participants had at least one comorbidity, with hypertension and diabetes being the most common, highlighting the impact of underlying medical conditions on sepsis outcomes.

It is widely recognized in the literature that a solitary arterial lactate level from blood gas analysis serves as a dependable biomarker for risk stratification in patients presenting to theICUwith suspected sepsis, and it serves as a valuable prognostic indicator for mortality and organ failure in critically ill patients. However, various patient-related factors can influence serum lactate levels[9–12]. Commonly prescribed medications such as albuterol and metformin can induce lactic acidosis or hyperlactatemia. Liver disease can also impede lactate clearance, resulting in elevated blood levels[13,14]. Moreover, certain critically ill patients may exhibit normal arterial lactate levels, potentially leading to inaccurate prognostic assessments[15]. Consequently, the standalone use of lactate may be limited in high-acuity settings like the Emergency Department[7,16].

Compared to solitary lactate, the L/A ratio serves as a better predictor of sepsis outcomes including mortality[9,17].Our study also investigated the relationship between lactate to albumin ratio and mortality in severe sepsis and septic shock patients. Consistent with previous research, we found a significant association between higher L/A ratios and mortality, suggesting the potential of L/A ratio as a prognostic marker in this population. Analysis of clinical features on day 1 and day 2 revealed fever as a common presenting symptom, although its prevalence decreased on day 2[7]. This observation underscores the dynamic nature of sepsis presentation and the importance of serial assessments in monitoring disease progression. Notably, the L/A ratio

outperformed lactate alone in predicting mortality, highlighting its superiority as a prognostic indicator in severe sepsis and septic shock.

Our findings align with previous studies demonstrating the prognostic value of the L/A ratio across various critical illnesses, including sepsis, heart failure, and traumatic brain injury. The robust predictive ability of the L/A ratio underscores its clinical relevance and potential utility in guiding therapeutic interventions and risk stratification in critically ill patients.

Overall, our study contributes to the growing body of evidence supporting the use of the L/A ratio as a prognostic marker in severe sepsis and septic shock patients. Further research is warranted to validate these findings in larger cohorts and explore the mechanistic underpinnings of the relationship between L/A ratio and sepsis outcomes.

Conclusion:

In conclusion, this study sheds light on the potential utility of the lactate to albumin ratio as a prognostic marker for multiple organ dysfunction syndrome (MODS) and mortality in patients with severe sepsis and septic shock. Our findings underscore the importance of considering this ratio alongside traditional markers in the clinical management of critically ill patients. However, further research in the Indian setting is warranted to validate these findings and elucidate the underlying mechanisms driving the observed associations. Ultimately, integrating the lactate to albumin ratio into routine clinical practice may enhance risk stratification and inform more targeted therapeutic interventions for patients with severe sepsis and septic shock.

Limitations:

Notable limitations of the study include its small sample size and single-center setting. With only 28 participants recruited from a single tertiary care hospital, the study's findings should be judiciously used.