

Lactate Albumin Ratio in Comparison with Lactate to Predict Outcomes in Sepsis and Septic Shock

Albee¹, Anurag Prasad², Tapas Tripathi³, Mohd Junaid Khan⁴

¹Corresponding Author, Third Year Post Graduate Resident, Department of Medicine, SMS&R, Sharda University, Greater Noida, Uttar Pradesh, India

²Professor and Head of Unit, Department of Medicine SMS&R, Sharda University, Greater Noida, Uttar Pradesh, India

³Second Year Post Graduate Resident, Department of Medicine, SMS&R, Sharda University, Greater Noida, Uttar Pradesh, India

⁴Second Year Post Graduate Resident, Department of Medicine, SMS&R, Sharda University, Greater Noida, Uttar Pradesh, India

Abstract: ***Background:** It is important to have sensitive markers for predicting morbidity and mortality in patients with sepsis to improve the outcomes of such patients. The aim of this study was to assess the prognostic value of Lactate to Albumin (L/A) ratio with lactate alone. **Methods:** This was a single-center retrospective cohort study. Patients that had a suspicion of sepsis. The primary outcome was prolonged ventilatory days and in-hospital stay, with a secondary outcome of in-hospital mortality. **Results:** A total of 350 patients were included, of which most of the patients belonged to 40-50 years, and 56% were female. 60% of patients were admitted to ICU, and of this 22.5% had ventilatory support for more than 7 days. The average in-hospital stay was 21±5.6 days. The overall in-hospital mortality rate was 34.5%, with that being related to septic shock being as high as 72%. The area under the curve value for lactate was 0.68 (at 95% confidence interval, it is 0.61–0.70, $p < 0.05$) and for the L/A ratio was 0.72 (at 95% confidence interval, it is 0.65–0.73, $p < 0.05$). The cutoff generated was 1.22 (sensitivity 62%, specificity 68%) for the L/A ratio in all septic patients. The L/A ratio was a predictor of prolonged ventilatory days and in-hospital stay, as well as in-hospital mortality (OR 1.47, $p < 0.05$). **Conclusion:** The L/A ratio is a better prognostic indicator than lactate alone in patients with sepsis and septic shock for prolonged ventilatory stay, in-hospital stay, and in-hospital mortality.*

Keywords: sepsis, lactate/albumin ratio, prognostic, in-hospital stay, prolonged ventilation

1. Introduction

According to global estimates, there are 31.5 million cases of sepsis worldwide each year, with over 5 million deaths (1). With overall mortality rates between 20 to 30%, it is to blame for around 30% of all hospital deaths (2, 3). Early diagnosis and prompt use of broad-spectrum antibiotics have been found to be the most important sepsis management factors (4–7). Delays in management have been linked to higher rates of mortality and morbidity (8, 9).

It is still difficult to identify high-risk patients quickly, hence numerous efforts are being done to find conveniently available and affordable biomarkers that can be used to prognosticate and risk-strategize septic patients. Serum lactate, a proxy for tissue perfusion, and mortality in critically ill patients have a substantial independent connection, according to a wealth of literature (10, 11). In all patients with suspected sepsis, it is currently advised to get a serum lactate level during the first hour of presentation, and if the initial lactate is greater than 2 mmol/L, to repeat the measurement within 2-4 hours (12). But patients using metformin and albuterol (13), those with diabetic ketoacidosis (14), cancer (15), those who are intoxicated (16), those who have a hepatic or renal impairment (17, 18), and lastly, those who have received epinephrine (18) have all been reported to experience lactic acidosis (13). It is difficult to predict in these situations purely based on lactate levels. The lactate to albumin (L/A) ratio is one newly discovered sepsis indicator. A flaw in current main scoring systems, such as the SOFA score, could be fixed by including albumin and considering nutritional status in septic patients (19). There is evidence that in people with serious illnesses, serum albumin levels are correlated with morbidity and mortality (20). This ratio has been proven to be predictive of mortality and multiple organ failure in

critically sick patients with sepsis, according to a growing body of literature. This is because lactate has limitations, and there is a need for a substitute marker of illness severity (7, 21, 22).

Although encouraging, there are currently insufficient data, and before the L/A ratio can be used in clinical practice, it needs to be further validated. Hence, the aim of our study was to assess the prognostic value of Lactate to Albumin (L/A) ratio with lactate alone.

2. Methods

Between January 2022 and June 2022, this retrospective cohort study was carried out in the Department of Medicine in Sharda Hospital, Greater Noida. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) guidelines describe sepsis as the presence of an infection along with indications of organ dysfunction, as measured by a Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score of two points or higher (7). To maintain a mean arterial pressure of 65 mm Hg or higher and a serum lactate level of more than 2 mmol/L (>18 mg/dL) in the absence of hypovolemia, septic shock was considered (7).

The study included all adult patients over the age of 18 who had the ICD-9 diagnoses of sepsis and septic shock, 350 participants were identified. Participants in the study had to meet the sepsis-3 criteria. Patients who were admitted to the hospital and later got sepsis as a secondary diagnosis during their hospital stay, as well as patients who were diagnosed as septic patients but did not meet sepsis-3 criteria, were all excluded from the study. A semi-structured pro forma was collected data that had been taken from the patient's electronic medical record and anonymized. The lead investigator designed a standardized protocol for the data

Volume 12 Issue 3, March 2023

www.ijsr.net

Licensed Under Creative Commons Attribution CC BY

extraction procedure prior to the data collection. The study team met with each other several times to standardize the data extraction process. Patient characteristics, vital signs at the time of ED presentation, laboratory results, disposition, duration of stay, mortality outcome, and interventions such as the use of antibiotics, mechanical ventilation, vasopressors, and steroids were among the variables gathered. According to the most recent Sepsis-3 guidelines, lactate levels were assessed at initial presentation (7). An albumin level was included in the study whether it was tested on admission or during the hospital stay because albumin has a half-life of approximately 20 days. In-hospital mortality was the main result. Statistical analysis was done with SPSS v21.

3. Results

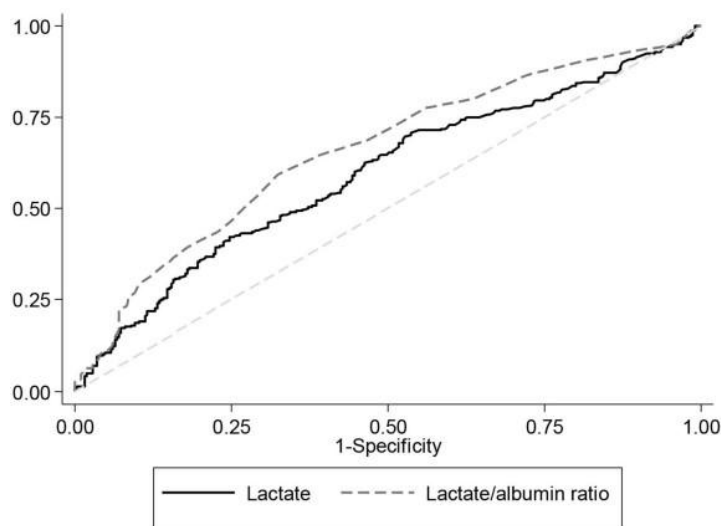
Of the 350 patients included in the study, the most common age group was 40-50 years, 34.2%. Amongst the 350 participants, 56% were female, 32.6% were smokers and their mean age was 44.2 ± 10.3 years. There was a total of 59.4% of patients with septic shock. The most common patient comorbidities were diabetes mellitus (64.2%), hypertension (45.6%) dyslipidemia (42.3%), and coronary artery disease (23.4%). The average in-hospital stay was 21 ± 5.6 days for the patients that survived.

Overall ICU admission was 60%, and it was found that the patients admitted to ICU that succumbed to the disease were found to have a higher rate of admission to ICU than those patients that recovered from the sepsis (72.3% vs 45.6%). The overall population that had ventilation for more than 7 days was 22.5%. The overall in-hospital mortality rate was 34.5%, with that being related to septic shock being as high as 72%.

The average lactate/albumin ratio was 1.45 ± 1.22 . The patients that survived had a lower mean lactate level (4.22 ± 0.99 mmol/L) vs those patients succumbed. The patients that were ventilated for longer than 7 days were also found to have lower albumin levels and higher L/A ratio (1.77 vs 1.23), which was found to be statistically significant ($p < 0.05$)

The area under the curve value for lactate was 0.68 (at 95% confidence interval, it is 0.61–0.70, $p < 0.05$) and for the L/A ratio was 0.72 (at 95% confidence interval, it is 0.65–0.73, $p < 0.05$).

The cutoff generated was 1.22 (sensitivity 62%, specificity 68%) for the L/A ratio in all septic patients. The L/A ratio was a predictor of prolonged ventilatory days and in-hospital stay, as well as in-hospital mortality (OR 1.47, $p < 0.05$).



ROC Curve for L/A Ratio VS Lactate

4. Discussion

Our study adds to the body of knowledge on the L/A ratio's potential utility as a prognostic indicator in sepsis patients. Despite being a well-researched prognostic indicator, the pathophysiology that can cause elevated serum lactate makes lactate interpretation difficult (13–18). Furthermore, in high-risk individuals, normal lactate levels could be mistakenly regarded as a favorable prognosis. As a result, the L/A ratio's value in predicting the prognosis of sepsis patients is increased by the inclusion of albumin as a reflection of the nutritional state.

When compared to lactate, several investigations have demonstrated that the L/A ratio has good discriminating power (24). Similar results were obtained when Lichtenauer

et al. (21) analyzed adult ICU patients ($n = 348$). They discovered that the L/A ratio had a decent discriminative capacity for in-hospital stay and prolonged ventilation and an AUC of 0.70, which is like the findings of our study

The largest study was carried out by Shin et al. (22) who, to the best of our knowledge, had the largest collective of patients analysed for the relevance of the L/A ratio prior to this study ($n = 946$). They obtained data from a multicenter registry of 10 emergency departments. These results are consistent with ours and support the conclusion that the L/A ratio is better than lactate alone as a prognostic marker in sepsis. Their AUC for the L/A ratio was 0.69 and was considerably higher than that of lactate (0.62) for predicting 28-day death.

5. Conclusion

The L/A ratio is a better prognostic indicator than lactate alone in patients with sepsis and septic shock for prolonged ventilatory stay, in-hospital stay, and in-hospital mortality.

References

- [1] Fleischmann C, Scherag A, Adhikari NK, Hartog CS, Tsaganos T, Schlattmann P, et al. Assessment of global incidence and mortality of hospital-treated sepsis. Current estimates and limitations. *Am J Respir Crit Care Med.* (2016) 193: 259–72. doi: 10.1164/rccm.201504-0781OC
- [2] Rhee C, Dantes R, Epstein L, Murphy DJ, Seymour CW, Iwashyna TJ, et al. Incidence and trends of sepsis in US hospitals using clinical vs claims data, 2009–2014. *JAMA.* (2017) 318: 1241–9. doi: 10.1001/jama.2017.13836
- [3] Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Crit Care Med.* (2001) 29: 1303–10. doi: 10.1097/00003246-200107000-00002
- [4] ARISE Investigators, ANZICS Clinical Trials Group, Peake SL, Delaney A, Bailey M, Bellomo R, et al. Goal-directed resuscitation for patients with early septic shock. *N Engl J Med.* (2014) 371: 1496–506. doi: 10.1056/NEJMoa1404380
- [5] Process Investigators, Yealy DM, Kellum JA, Huang DT, Barnato AE, Weissfeld LA, et al. A randomized trial of protocol-based care for early septic shock. *N Engl J Med.* (2014) 370: 1683–93. doi: 10.1056/NEJMoa1401602
- [6] Mouncey PR, Osborn TM, Power GS, Harrison DA, Sadique MZ, Grieve RD, et al. Trial of early, goal-directed resuscitation for septic shock. *N Engl J Med.* (2015) 372: 1301–11. doi: 10.1056/NEJMoa1500896
- [7] Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA.* (2016) 315: 801–10. doi: 10.1001/jama.2016.0287
- [8] Beck V, Chateau D, Bryson GL, Pisipati A, Zanotti S, Parrillo JE, et al. Timing of vasopressor initiation and mortality in septic shock: a cohort study. *Crit Care.* (2014) 18: R97. doi: 10.1186/cc13868
- [9] Gaieski DF, Mikkelsen ME, Band RA, Pines JM, Massone R, Furia FF, et al. Impact of time to antibiotics on survival in patients with severe sepsis or septic shock in whom early goal-directed therapy was initiated in the emergency department. *Crit Care Med.* (2010) 38: 1045–53. doi: 10.1097/CCM.0b013e3181cc4824
- [10] Villar J, Short JH, Lighthall G. Lactate predicts both short-and longterm mortality in patients with and without sepsis. *Infect Dis.* (2019) 12: 1178633719862776. doi: 10.1177/1178633719862776
- [11] Casserly B, Phillips GS, Schorr C, Dellinger RP, Townsend SR, Osborn TM, et al. Lactate measurements in sepsis-induced tissue hypoperfusion: results from the surviving sepsis campaign database. *Crit Care Med.* (2015) 43: 567–73. doi: 10.1097/CCM.0000000000000742
- [12] Levy MM, Evans LE, Rhodes A. The surviving sepsis campaign bundle: 2018 update. *Intensive Care Med.* (2018) 44: 925–8. doi: 10.1007/s00134-018-5085-0
- [13] Smith ZR, Horng M, Rech MA. Medication-induced hyperlactatemia and lactic acidosis: a systematic review of the literature. *Pharmacotherapy.* (2019) 39: 946–63. doi: 10.1002/phar.2316
- [14] Scale T, Harvey J. Diabetes, metformin and lactic acidosis. *Clin Endocrinol.* (2011) 74: 191–6. doi: 10.1111/j.1365-2265.2010.03891.x
- [15] Friedenberg AS, Brandoff DE, Schiffman FJ. Type B lactic acidosis as a severe metabolic complication in lymphoma and leukemia: a case series from a single institution and literature review. *Medicine.* (2007) 86: 225–32. doi: 10.1097/MD.0b013e318125759a
- [16] Gabow PA, Clay K, Sullivan JB, Lepoff R. Organic acids in ethylene glycol intoxication. *Ann Intern Med.* (1986) 105: 16–20. doi: 10.7326/0003-4819-105-1-16
- [17] Sterling SA, Puskarich MA, Jones AE. The effect of liver disease on lactate normalization in severe sepsis and septic shock: a cohort study. *Clin Exp Emerg Med.* (2015) 2: 197–202. doi: 10.15441/ceem.15.025
- [18] Shin TG, Jo IJ, Hwang SY, Jeon K, Suh GY, Choe E, et al. Comprehensive interpretation of central venous oxygen saturation and blood lactate levels during resuscitation of patients with severe sepsis and septic shock in the emergency department. *Shock.* (2016) 45: 4–9. doi: 10.1097/SHK.0000000000000466
- [19] Keller U. Nutritional laboratory markers in malnutrition. *J Clin Med.* (2019) 8: 775. doi: 10.3390/jcm8060775
- [20] Wang B, Chen G, Cao Y, Xue J, Li J, Wu Y. Correlation of lactate/albumin ratio level to organ failure and mortality in severe sepsis and septic shock. *J Crit Care.* (2015) 30: 271–5. doi: 10.1016/j.jcrc.2014.10.030
- [21] Lichtenauer M, Wernly B, Ohnewein B, Franz M, Kabisch B, Muessig J, et al. The lactate/albumin ratio: a valuable tool for risk stratification in septic patients admitted to ICU. *Int J Mol Sci.* (2017) 18: 1893. doi: 10.3390/ijms18091893
- [22] Shin J, Hwang SY, Jo IJ, Kim WY, Ryoo SM, Kang GH, et al. Prognostic value of the lactate/albumin ratio for predicting 28-day mortality in critically ill sepsis patients. *Shock.* (2018) 50: 545–50. doi: 10.1097/SHK.0000000000001128