Section: General Medicine

Original Research Article

A STUDY TO ANALYSE THE PROGNOSTIC VALUE OF LACTATE-ALBUMIN RATIO IN COMPARISON TO ISOLATED LACTATE LEVELS AS A BIOMARKER OF IN HOSPITAL MORTALITY AMONG SEPSIS PATIENTS IN A TERTIARY CARE CENTRE IN KERALA

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Abstract

Lactate and Albumin are individual markers defining the severity of sepsis. Combining the two parameters as Lactate-Albumin ratio could increase the accuracy in enabling early identification of high-risk groups and for timely intervention. This study was done to determine the prognostic value of Lactate-Albumin ratio as a marker of in hospital mortality, compared to isolated lactate level among sepsis patients in a tertiary care hospital. A cross-sectional study was conducted on 173 patients diagnosed with sepsis. The primary endpoints were the requirement for mechanical ventilation, dialysis and in-hospital mortality. Lactate levels were measured at admission and 24 hours postadmission, Lactate -albumin ratio and lactate clearance calculated, ROC curve was used to identify a cutoff value with best sensitivity and specificity. The Lactate-Albumin ratio demonstrated superior prognostic accuracy when compared to lactate, with a cut off value of 1.42 to predict in hospital mortality. Lactate-Albumin ratio was also found to be superior in predicting need for mechanical ventilation and dialysis, compared to lactate clearance among sepsis patients. The study concludes that the L/A ratio is a more reliable prognostic marker than lactate levels for predicting in-hospital mortality among sepsis patients. Its incorporation into clinical practice could enable more accurate risk stratification and timely interventions, potentially improving patient outcomes.

INTRODUCTION

The definition of sepsis states that it is a potentially fatal dysfunction of organs brought on by an uncontrolled immune response to infection. An increase in the total score on the Sequential Organ Failure Assessment (SOFA) by 2 or more points, secondary to an infection indicates organ dysfunction. In individuals without a documented history of organ dysfunction, the SOFA score at baseline should be 0.[1]
Septic shock is when sepsis occurs without hypovolemia but requires vasopressors to maintain 65 mmHg or higher mean arterial pressure and a lactate level above 2mmol/l (18 mg/dl). Sepsis is one of the deadliest and most disabling diseases worldwide causing around 30% mortality. Septic shock can cause 40% or more deaths.[2]
It is advocated that antibiotics be administered promptly, even prior to identification of organism, in order to manage sepsis effectively.2 Therefore patients with sepsis or septic shock can benefit greatly from antibiotics, if there is a suitable lab parameter which can diagnose sepsis in the initial stage.[3,4]
Lactic acid is the tissue product of anaerobic metabolism of glucose. A blood lactate concentration of 0.5-1 mmol/L is normal. Lactate above 2 mmol/L indicates that the patient is critically ill.[5-7]
Albumin being a negative acute-phase protein, can predict the degree of inflammation. A fall in Albumin level following an infection indicated unfavourable outcome.[8]
A conjunction of the two variables could be used for better prediction of mortality. Critical care and sepsis management have come a long way, but sepsis still ranks high in terms of patient deaths. Early detection

of high-risk cases is the most important part of sepsis care since it allows for the categorization of sepsis patients based on risk and the prompt administration of broad-spectrum antibiotics and inotropic support, if necessary.[9,10]

The lactate/albumin ratio is a novel and useful biomarker, and this study focused on its predictive utility in reducing mortality in sepsis patients, given the significance of early diagnosis and aggressive treatment.

MATERIALS AND METHODS

A total of 173 patients admitted to the Medical ICU for a duration of eighteen months following the date of ethical approval of the Jubilee Mission Medical College and Research Institute, Thrissur, with sepsis or septic shock and who satisfied all inclusion criteria were included in this cross-sectional study. All patients diagnosed with Sepsis based on SOFA score >/= 2, associated with infection, Septic shock – Sepsis with 1) Vasopressor for MAP >/= 65mmHg, Serum lactate > 2mmol/L, Age >/ =18 years, Patients diagnosed with sepsis elsewhere and referred and Patients giving written informed consent were included in the study. While Patients who do not meet sepsis-3 criteria, Patients who developed sepsis as a secondary diagnosis during their hospital stay, Patients less than the age of 18, chronic kidney disease, chronic liver disease patients, Patients on Metformin with nephropathy, Muscle disorders, Patients having cardiac arrest at presentation, Trauma patients, Pregnant patients and Patients or relatives not giving consent for the study were excluded from the study.

The study was started upon approval by the institutional ethics committee. Patients diagnosed as sepsis or septic shock and satisfying inclusion criteria, admitted in the ICU of the Medicine Department were selected. Detailed history taken especially to rule out comorbidities included in exclusion criteria. Vitals at the time of presentation were noted. Necessary blood investigations like complete hemogram, urine routine, liver function test, renal function test, electrolytes, blood culture were done. Serum lactate level and albumin level at the time of admission tested. Lactate levels after 24hours of admission repeated for calculating clearance. Patients are followed throughout their hospital stay to determine the development of organ failure – need for dialysis or mechanical intubation and in hospital mortality. Serum lactate to albumin ratio and 24hour lactate clearance calculated.

Data will be entered into MS Excel and coded, further analysed using SPSS software. Categorical variables are presented as frequency with percentages and continuous variables are presented as mean +/- SD. Categorical data analysed by Chi square test or Fischer's exact test. A p-value of 0.05 or less will be considered statistically significant. ROC curve will be generated for lactate and lactate /albumin ratio. Patient stratified into 2 groups – survivors and non survivors. Receiver operating characteristic curve (ROC), will be used to obtain the Lactate/albumin ratio cutoff with the best sensitivity and specificity to discriminate between survivors and non survivors among sepsis patients. Sub group analysis will be done to look at the area under ROC curve of both lactate clearance and L/A ratio in patients requiring dialysis and mechanical intubation.

RESULTS

The mean age among Group A(survivors) was 45.92 ± 14.67 years and among Group B(non-survivors) was 59.56 ± 16.75 years, which was statistically significant. ($p < 0.05$). In our study mortality was higher in the aged population. The numbers of males and females among Group A(survivors) were 54.87% and 55.13% respectively and in Group B(non-survivors) were 56.67% and 43.33% respectively. There were a greater number of male patients (56.67%) among Nonsurvivors in our study. The mean Lactate level at admission and L/A ratio was significantly high among those who expired in our study. ($p = 0.0001$).

Table 1: Basic characteristics.

	Group A (Survivors) (n = 113)	Group B (Non-Survivors) (n = 60)	P-value
MEAN AGE (years)	45.92 ± 14.67 years	59.56 ± 16.75 years	<0.001
GENDER Male Female	 62 (54.87%) 51(55.13%)	 34(56.67%) 26(43.33%)	0.892
Lactate level on admission (mmol/L)	2.59 ± 0.95	5.42 ± 1.39	<0.001
Albumin level (gm/dL)	3.41 ± 0.48	2.78 ± 0.48	<0.001
Lactate/Albumin ratio	0.78 ± 0.34	1.99 ± 0.62	<0.001

The mean Lactate level at admission and L/A ratio was significantly high among those who expired in our study. ($p = 0.0001$). In our study, the cut off value for predicting mortality, for L/A ratio was 1.42 with a sensitivity of 100% and specificity of 96.4%, and the cut-off value for lactate at admission was 4 with a relatively lesser accuracy.

The need for mechanical ventilation and dialysis was more in GROUP B(Nonsurvivors). i.e. 80% and 75% respectively in our study. While among Group A (survivors) it is 19% and 14% respectively.

The cut-off value of the L/A ratio was 1.33 and Lactate clearance was 14 for predicting the need for mechanical ventilation, in our study. In our study, the L/A ratio had excellent predictive validity in predicting the need for mechanical ventilation i.e. secondary outcome, compared to Lactate clearance as specified by the AUC of 0.904 (95% CI: 0.8482 -

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0.9402; p-value 0.0001) In our study, the L/A ratio had excellent predictive validity in predicting the need for Dialysis i.e. secondary outcome, compared to Lactate clearance as specified by the AUC of 0.9087 (95% CI: 0.854 -0.943; p=0.0001). The cut-off value of the L/A ratio was 1.27 and Lactate clearance was 14 for predicting the need for Dialysis, in our study.

Table 2: Overview of cutoff values for predicting outcome

	Mortality i.e. Nonsurvivors			Need for mechanical ventilation			Need for Dialysis		
Parameter	**Cutoff value**	**AUC**	**P**	**Cutoff value**	**AUC**	**p**	**Cutoff value**	**AUC**	**p**
SOFA	10	0.9113	0.0001	-	-	-	-	-	-
L/A ratio	1.42	0.997	0.0001	1.33	0.904	0.0001	1.27	0.908	0.0001
Lactate at admission	4	0.96	0.0001	-	-	-	-	-	-
Lactate at 24hrs	2.9	0.941	0.0001	-	-	-	-	-	-
Lactate clearance	-	-	-	14	0.778	0.0001	14	0.7398	0.0001

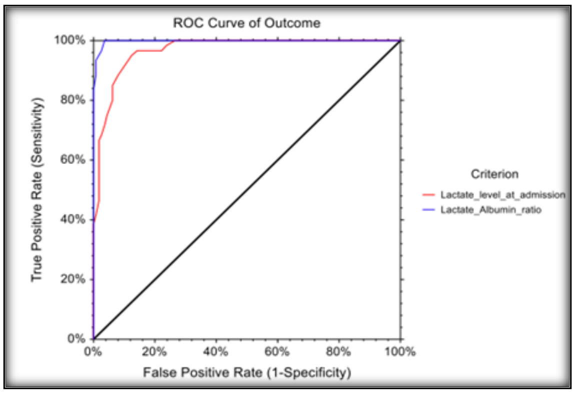

Figure 1: ROC curve for Lactate level and Lactate/Albumin ratio at admission with mortality

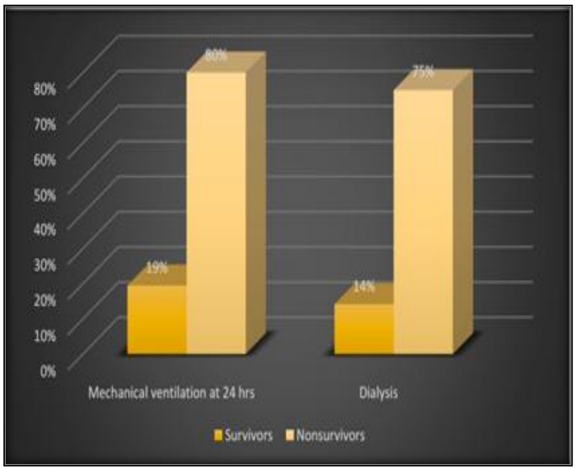

Figure 2: Need for mechanical ventilation at 24hrs and Dialysis

DISCUSSION

Anaerobic glycolysis caused by insufficient oxygen delivery has been attributed as the pathophysiology for lactic acidosis in sepsis. But it's now evident that hypoxic tissue injury is not the only cause of hyperlactatemia in sepsis; other factors also play a role.[11]

Endogenous adrenaline stimulates beta 2 receptors, especially in skeletal muscles, which results in a lactate rise in sepsis. Increased glycolysis is produced as a result of this stimulation, producing more pyruvate than the cell mitochondria can utilize via the TCA cycle. Lactate is produced from excess pyruvate.[12]

Rise in lactate levels indicated endogenous catecholamine release. Hence lactate can be used to identify patients who are experiencing occult shock but are nevertheless maintaining their vital signs because of a strong endogenous catecholamine response. Elevated lactate levels, therefore, aid in the identification of individuals who need more intensive care since they are more likely to experience decompensation.[13]

Liver is the primary organ involved in metabolism of lactate, followed by the kidney. Liver dysfunction and acute renal injury contribute to lactate elevation in sepsis, especially septic shock, by decreased clearance of lactate.[14]

One of the main cytokines released during sepsis, TNF alpha, has the ability to directly block albumin synthesis at the transcriptional level, which leads to hypoalbuminemia.[15] The half-life of intracellular newborn Fc receptors is increased by albumin binding.[16]

However, the Fc receptor is downregulated in sepsis, which reduces the half-life and further contributes to hypoalbuminemia.[17] One class of negative acute-phase reactants is albumin. Serum albumin escapes into the interstitial space and capillary permeability increases as a result of cytokines generated during sepsis, particularly TNF-alpha.[18] Albumin serves as the primary extracellular scavenger in the interstitium. The redox activity is made possible by a free thiol group produced from cysteine. Serum albumin is present in a reduced form in the body, which contributes to its antioxidant properties. Serum albumin that has been oxidized degrades more quickly than albumin that has been reduced.[19]

Combining serum lactate and albumin measurements to create the lactate albumin ratio may help predict prognosis of critically ill patients more accurately, especially among sepsis patients. In order to evaluate the prognostic value of the L/A ratio as a biomarker of hospital mortality in sepsis patients relative to lactate, as well as its prognostic value in need of mechanical ventilation and dialysis, this research had been performed among 173 patients who had sepsis.

While comparing the demographic details of the study population it was noted that the mortality was

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higher in the elderly population. There was a greater number of male patients (56.67%) among non survivors in our study. Among non survivors, the mean values of L/A ratio were significantly high. A high L/A ratio is related to high mortality rates, similarly, a low level of albumin also leads to increased mortality according to this study.

According to the AUC of 0.997, the L/A ratio had superior predictive validity in predicting mortality when compared to the lactate level at admission individually

When it came to predicting the need for mechanical ventilation, the L/A ratio outperformed lactate clearance. In this study, the threshold values for predicting the need for mechanical ventilation were 14 for lactate clearance and 1.33 for L/A ratio.

Compared to lactate clearance, the L/A ratio had superior predictive validity in predicting the need for dialysis, as indicated by the AUC of 0.9087 (95percent CI: 0.854 -0.943; p-value 0.0001). For predicting the need for dialysis, the cut-off values for the L/A ratio and lactate clearance were 1.27 and 14, respectively.

Overall, the L/A ratio was found to be statistically significantly more accurate in predicting mortality, the need for mechanical ventilation, and the need for dialysis in our study.

According to an investigation by Chebl et al., the L/A ratio is a more accurate predictor of mortality.[20]

Additionally, a study by Makram et al. discovered that the L/A ratio has a strong positive predictive value for predicting mortality in patients with sepsis.[21]

In their research, Lichtenauer et al. demonstrated that in sepsis patients, a high L/A ratio is associated with a higher risk of organ failure.[22]

Similarly, Biao Wang et al. proposed that in patients with sepsis, a high L/A ratio is linked to multiorgan failure.[23]

To optimize clinical decision-making and to identify individuals at high risk of death, the LAR may be useful as advised by Yoon et al. (0.680 cut-off value).[24]

E Cakir et al observed that the L/A ratio was a more robust indicator of mortality among ICU sepsis patients than either lactate or albumin alone.[25] A simple but potentially useful metric for severely sick individuals is the lactate/albumin ratio.

A study by GT Altun et al also suggested that the lactate albumin ratio is a better predictor of in-hospital mortality compared to lactate alone.[26]

CONCLUSION

The findings from this study underscore the importance of the Lactate/Albumin (L/A) ratio as a more accurate and reliable biomarker compared to lactate levels alone for predicting hospital mortality, the need for mechanical ventilation, and dialysis in patients with sepsis. Our research shows that the L/A ratio has superior prognostic value, as evidenced by its significant correlation with poor outcomes among Nonsurvivors. The elevated L/A ratio, coupled with reduced albumin levels and lactate clearance, distinctly marked the Nonsurvivors group, highlighting the potential of this metric in clinical decision-making and patient stratification. The observed mortality trends in older populations, coupled with a higher incidence of severe outcomes such as the need for mechanical ventilation and dialysis, emphasize the vulnerability of these groups to septic complications. The statistically significant differences in mean lactate levels and the L/A ratio between survivors and non survivors affirm the critical role of early biochemical assessment in identifying at risk patients. Specifically, our cut-off values for lactate and the L/A ratio provide practical thresholds for anticipating patient needs and adjusting therapeutic approaches accordingly. Our results align with previous studies suggesting the L/A ratio's efficacy as a predictive tool. The high area under the curve (AUC) values for the L/A ratio indicate its robust sensitivity and specificity, making it a valuable addition to current sepsis management protocols. The data advocate for the routine incorporation of the L/A ratio in clinical assessments to improve patient outcomes, particularly in intensive care settings where timely interventions are crucial. In conclusion, the L/A ratio emerges as a vital prognostic marker that can enhance the prediction of severe outcomes in septic patients. Its implementation in routine clinical practice could lead to earlier and more precise interventions, potentially reducing mortality and morbidity rates. Continued investigation into this and other emerging biomarkers will be crucial for advancing sepsis care and improving patient prognosis. Compared to isolated lactate levels, we find that the L/A ratio is a more reliable indicator of hospital mortality, the need for mechanical ventilation, and the need for dialysis in septic patients.

Limitations

This study is single-centre design.

The sample size is small and can therefore affect the generalizability of the results.

REFERENCES

1. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM, Hotchkiss RS. The third international consensus definitions for sepsis and septic shock (Sepsis-3). Jama. 2016 Feb 23;315(8):801-10.
2. Yoon SH, Choi B, Eun S, Bae GE, Koo CM, Kim MK. Using the lactate-to-albumin ratio to predict mortality in patients with sepsis or septic shock: a systematic review and meta-analysis.
3. Lippi G, Montagnana M, Fiamma B, Andrea B, Ivo C, Mario C, Da Rin G, Daniele C, Giavarina D, Fabrizio G, Paola P. Academy of Emergency Medicine and Care-Society of Clinical Biochemistry and Clinical Molecular Biology consensus recommendations for clinical use of sepsis biomarkers in the emergency department. Emergency Care Journal. 2017;13(2):42-50.
4. Eymour CW, Gesten F, Prescott HC, Friedrich ME, Iwashyna TJ, Phillips GS, Lemeshow S, Osborn T, Terry KM, Levy

ISSN (O): 2687-5365; ISSN (P): 2753-6556

MM. Time to treatment and mortality during mandated emergency care for sepsis. New England Journal of Medicine. 2017 Jun 8;376(23):2235-44.
5. Andersen LW, Mackenhauer J, Roberts JC, Berg KM, Cocchi MN, Donnino MW. Etiology and therapeutic approach to elevated lactate levels. InMayo Clinic Proceedings 2013 Oct 1 (Vol. 88, No. 10, pp. 1127-1140). Elsevier.
6. Shapiro NI, Howell MD, Talmor D, Nathanson LA, Lisbon A, Wolfe RE, Weiss JW. Serum lactate as a predictor of mortality in emergency department patients with infection. Annals of emergency medicine. 2005 May 1;45(5):524-8.
7. Dominguez de Villota E, Mosquera JM, Rubio JJ, Galdos P, Díez Balda V, de la Serna JL, Tomás MI. Association of a low serum albumin with infection and increased mortality in critically ill patients. Intensive care medicine. 1980 Jan;7:19-22.
8. Wu H, Li M, Shou C, Shi F, Song X, Hu Q, Wang Y, Chen Y, Tong X. Pathogenic spectrum and drug resistance of bloodstream infection in patients with acute myeloid leukaemia: a single centre retrospective study. Frontiers in Cellular and Infection Microbiology. 2024 Jun 7;14:1390053.
9. Meregalli A, Oliveira RP, Friedman G. Occult hypoperfusion is associated with increased mortality in hemodynamically stable, high-risk, surgical patients. Critical care. 2004 Apr;8:1-6.
10. Lee SM, An WS. New clinical criteria for septic shock: serum lactate level as new emerging vital sign. Journal of thoracic disease. 2016 Jul;8(7):1388.
11. Chertoff J, Chisum M, Garcia B, Lascano J. Lactate kinetics in sepsis and septic shock. J intensive care. 2015; 39(3):1-4
12. Nalos M , Robert R. Understanding Hyperlactatemia in Sepsis : Are we there yet?
13. 2019; 200(8): 1069-1070
14. Meregalli A, Olieveira RP, Friedman Gilberto. Occult hypoperfusion is associated with increased mortality in hemodynamically stable, high risk surgical patients.Crit Care.2004;8(2):R60-R65
15. Lee SM, An WS , Dong D , Gu S. New clinical criteria for septic shock: serum lactate level as new emerging vital sign. J Thorac Dis.2016; 8(7): 1388-1390
16. Brenner DA, Buck M , Feitelberg SP, Chojkier M. Tumor necrosis factor – alpha inhibits albumin gene expression in a murine model of cachexia. J Clin Invest. 1990; 85 (1):248-255
17. Pyzik M, Sand KMK, Hubbard JJ, Andersen JT, Sandlie I , Blumberg RS. The neonatal Fc receptor : A misnomer. Front Immunol.2019; 10:1540
18. Mkaddem SB, Benhamou M, Monteiro RC. Undestanding Fc receptor involvement in inflammatory disease: from mechanism to new therapeutic tools. Front Immunol.2019. 10: 811
19. Gill SE , Taneja R, Rohan M , Wang L , Mehta S. Pulmonary microvascular albumin leak is associated with endothelial cell death in murine sepsis induced lung injury in vivo.2014.9(2):e88501
20. Bonifazi M, Meessen J, Alba P, Francesco V, Mattia B, Vassalli F, et al. Albumin oxidation status in sepsis patients treated with albumin or crystalloids. Front Physiol.2021 .12.682877
21. Bou Chebl R, Jamali S, Sabra M, Safa R, Berbari I, Shami A, Makki M, Tamim H, Abou Dagher G. Lactate/albumin ratio as a predictor of in-hospital mortality in septic patients presenting to the emergency department. Frontiers in medicine. 2020 Sep 22;7:550182
22. Makram E, Ibrahim M, Abdel Rahman A. Serum lactate/albumin ratio as a predictor of morbidity and mortality in patients with severe sepsis and septic shock. Benha Medical Journal. 2020 May 1;37(1):220-8.
23. Lichtenauer M, Wernly B, Ohnewein B, Franz M et.al. The lactate/albumin ratio: a valuable tool for risk stratification in septic patients admitted to ICU. International journal of molecular sciences. 2017 Sep 2;18(9):1893.
24. 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. Journal of critical care. 2015 Apr 1;30(2):271-5.
25. Yoon SH, Choi B, Eun S, Bae GE et.al. Using the lactate-to-albumin ratio to predict mortality in patients with sepsis or septic shock: a systematic review and metaanalysis.
26. Cakir E, Turan IO. Lactate/albumin ratio is more effective than lactate or albumin alone in predicting clinical outcomes in intensive care patients with sepsis. Scandinavian journal of clinical and laboratory investigation. 2021 May 3;81(3):225-9.
27. Altun GT, Arslantas MK, Dıncer PC, Arslantas R, Kararmaz A. Prognostic value of the lactate–albumin difference for predicting in-hospital mortality in critically ill patients with sepsis. Marmara Medical Journal. 2022;35(1):61-6.

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