A Retrospective Study on Blood Urea Nitrogen to Albumin Ratio in Patients with Sepsis

¹Dr. Manoj Chandrashekhar, ²Dr. Vishwas Kodandarama, ³ Dr. Rajashree Ampar Nataraj, ⁴Dr Parashuram.

¹Postgraduate Student, Department of General Medicine, Dr. B.R Ambedkar Medical College and Hospital, Bangalore, Karnataka, India.

²Assistant Professor, Department of General Medicine, Dr. B.R Ambedkar Medical College and Hospital, Bangalore, Karnataka, India.

³Associate Professor, Department of General Medicine, Dr. B.R Ambedkar Medical College and Hospital, Bangalore, Karnataka, India.

⁴Professor, Department of General Medicine, Dr. B.R Ambedkar Medical College and Hospital, Bangalore, Karnataka, India.

Corresponding Author

Dr. Manoj Chandrashekhar, Postgraduate Student, Department of General Medicine, Dr. B.R Ambedkar Medical College and Hospital, Bangalore, Karnataka, India.

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ABSTRACT

BACKGROUND

Sepsis is a severe, life-threatening condition characterized by systemic inflammation and multiorgan dysfunction. Identifying reliable biomarkers for early diagnosis and prognosis is crucial for improving patient outcomes. The Blood Urea Nitrogen to Albumin Ratio (BUN/Alb) has emerged as a potential indicator of sepsis severity. This study aims to evaluate the BUN/Alb ratio's utility in predicting outcomes in septic patients in Bengaluru, India.

METHODS

We conducted a retrospective study involving 200 sepsis patients admitted to a tertiary care hospital in Bengaluru between January 2023 and December 2023. Data were collected from electronic medical records, including BUN, albumin levels, and clinical outcomes. Statistical analyses were performed to assess the correlation between BUN/Alb ratios and patient outcomes, including mortality and length of hospital stay.

RESULTS

The average BUN/Alb ratio in the study population was found to be significantly higher in patients with severe sepsis compared to those with mild to moderate sepsis. A higher BUN/Alb ratio was associated with increased mortality and longer hospital stays. The ratio demonstrated predictive value for adverse outcomes, with an area under the ROC curve of 0.9.

CONCLUSION

The BUN/Alb ratio is a promising biomarker for assessing the severity of sepsis and predicting patient outcomes. This study supports its utility in clinical practice, especially in resource-limited

settings where sophisticated diagnostic tools may not be available. Further prospective studies are recommended to validate these findings and explore the ratio's potential for guiding treatment decisions.

KEYWORDS

Sepsis, Blood Urea Nitrogen, Albumin, BUN/Alb Ratio, Prognostic Biomarkers.

INTRODUCTION

Sepsis is a life-threatening condition resulting from a dysregulated host response to infection, leading to widespread inflammation and multi-organ dysfunction. Despite advances in critical care, sepsis remains a major cause of morbidity and mortality worldwide. The global incidence of sepsis is estimated to be around 48.9 million cases annually, with approximately 11 million sepsis-related deaths reported each year. Early diagnosis and timely intervention are critical to improving patient outcomes, yet effective management remains a challenge due to the complex nature of the disease. ²

Traditional biomarkers used in the diagnosis and prognosis of sepsis include C-reactive protein (CRP) and procalcitonin (PCT). While these markers are valuable, their clinical utility can be limited by their sensitivity and specificity.³ Consequently, there is increasing interest in exploring additional biomarkers that may offer more precise prognostic information. The Blood Urea Nitrogen to Albumin (BUN/Alb) ratio has emerged as a potential candidate. This ratio integrates information about renal function, protein metabolism, and inflammatory response, which are all pertinent in the context of sepsis.⁴

Urea nitrogen is a byproduct of protein metabolism, and elevated levels can indicate impaired renal function, a common issue in sepsis due to organ dysfunction.⁵ Albumin, on the other hand, is a key protein synthesized in the liver that maintains oncotic pressure and reflects nutritional status.⁶ Alterations in the BUN/Alb ratio may therefore provide insights into the severity of sepsis and associated complications. An elevated BUN/Alb ratio has been associated with increased mortality and longer hospital stays in various studies, suggesting its potential as a prognostic marker.^{7,8}

Recent studies have investigated the role of the BUN/Alb ratio in different clinical settings. For instance, a study by Liu et al. reported that a higher BUN/Alb ratio was significantly associated with increased mortality in patients with sepsis. Similarly, research by Kim et al. highlighted the utility of this ratio in predicting adverse outcomes and guiding clinical decision-making. However, the generalizability of these findings across diverse populations and healthcare settings remains uncertain.

This study aims to evaluate the BUN/Alb ratio as a prognostic marker in patients with sepsis admitted to a tertiary care hospital in Bengaluru, India. By analyzing the correlation between the BUN/Alb ratio and clinical outcomes such as mortality and length of hospital stay, we seek to validate its utility in a resource-limited setting. Our findings could provide valuable insights into the role of the BUN/Alb ratio in sepsis management and contribute to the body of evidence supporting its use in clinical practice.

METHODOLOGY

Study Design and Setting

This study is a retrospective cohort study conducted at a tertiary care hospital in Bengaluru, India. The study aims to evaluate the prognostic utility of the Blood Urea Nitrogen to Albumin (BUN/Alb) ratio in patients diagnosed with sepsis. The study was approved by the institutional review board (IRB) of the hospital, and all data were analyzed anonymously to ensure patient confidentiality.

Patient Selection

We reviewed the medical records of patients admitted to the hospital between January 2022 and December 2023. The inclusion criteria were:

- **Diagnosis of Sepsis**: Defined according to the Sepsis-3 criteria, which include a suspected or confirmed infection and an acute increase in the Sequential Organ Failure Assessment (SOFA) score of 2 or more points.¹¹
- Age: Patients aged 18 years and older.
- Complete Data Availability: Patients with complete data on serum BUN, albumin levels, sepsis severity, and clinical outcomes.

Patients were excluded if they had:

- Chronic Kidney Disease (CKD) or End-Stage Renal Disease (ESRD) prior to hospitalization.
- Pre-existing liver disease that could affect albumin levels.
- Incomplete records where essential data for calculating the BUN/Alb ratio were missing.

A total of 200 patients met the inclusion criteria and were included in the study.

Data Collection

We extracted data from electronic medical records. The following variables were collected:

- **Demographic Information**: Age, gender, and comorbidities.
- Clinical Parameters:
 - o **Blood Urea Nitrogen (BUN)**: Measured in mg/dL, indicating renal function.
 - o **Albumin**: Measured in g/dL, reflecting nutritional status and liver function.
 - o **BUN/Alb Ratio**: Calculated by dividing the BUN level by the albumin level.
- Sepsis Severity: Categorized based on the SOFA score at the time of admission 12:
 - \circ Severe: SOFA score ≥ 8.
 - o **Moderate**: SOFA score between 4 and 7.
 - o **Mild**: SOFA score < 4.
- Outcome Measures:
 - o **Mortality**: Recorded as in-hospital mortality.
 - o Length of Hospital Stay (LOS): Duration of stay in days.

Statistical Analysis

Descriptive statistics were used to summarize demographic and clinical characteristics of the study population. Continuous variables such as age, BUN, albumin levels, and BUN/Alb ratio were expressed as mean \pm standard deviation (SD), while categorical variables such as gender and sepsis severity were expressed as frequencies and percentages. To determine the predictive accuracy of the BUN/Alb ratio for mortality, we calculated the area under the curve (AUC) of

the ROC curve. Statistical significance was defined as a p-value < 0.05. All statistical analyses were performed using SPSS version 28.0 (IBM Corp., Armonk, NY, USA).

Ethical Considerations

The study was conducted following the principles of the Declaration of Helsinki. Informed consent was waived due to the retrospective nature of the study. All data were anonymized before analysis to protect patient confidentiality.

RESULTS

A total of 200 patients with sepsis were included in the study. The demographic and clinical characteristics of the cohort are summarized in Table 1. The mean age of the patients was 61.2 ± 15.0 years. The age distribution was as follows: 28% were aged 18-45 years, 42% were aged 46-65 years, and 30% were older than 65 years. The study population of comprised 55% male and 45% female patients. The most common comorbid conditions included hypertension (52%), diabetes mellitus (38%), chronic obstructive pulmonary disease (22%), and cardiovascular diseases (27%).

The severity of sepsis among the patients was categorized based on the Sequential Organ Failure Assessment (SOFA) score: 47% of patients (n=94) had a SOFA score of 8 or higher and were categorised to have severe sepsis. 33% of patients (n=66) had a SOFA score between 4 and 7 and were categorised to have moderate sepsis. 20% of patients (n=40) had a SOFA score of less than 4 and were categorised to have mild sepsis.

The mean BUN level was 34.2 ± 19.5 mg/dL, with a range of 12 to 85 mg/dL. The mean albumin level was 2.7 ± 0.8 g/dL, with a range of 1.4 to 4.2 g/dL. The mean BUN/Alb ratio was 12.8 ± 7.9 . The ratio ranged from 3.5 to 38.0. (Table 2)

The overall in-hospital mortality rate was 37% (n=74). Mortality rates differed significantly across sepsis severity: 53% mortality (n=50) in severe sepsis, 27% mortality (n=18) in moderate sepsis and 8% mortality (n=6) in mild sepsis.

The mean length of hospital stay was 13.8 ± 7.0 days. The LOS varied by sepsis severity: Mean LOS was 17.2 ± 8.0 days in patients with severe sepsis, 11.3 ± 5.8 days in moderate sepsis and 8.3 ± 4.5 days in mild sepsis.

A higher BUN/Alb ratio was significantly associated with increased mortality. The odds ratio for mortality increased by 1.13 (95% CI: 1.06-1.20) for each unit increase in the BUN/Alb ratio (p < 0.01). The ROC curve analysis revealed an AUC of 0.9 (95% CI: 0.74-0.86), indicating good predictive accuracy of the BUN/Alb ratio for mortality. (Table 4)

The BUN/Alb ratio was positively correlated with LOS. Each unit increase in the BUN/Alb ratio was associated with an increase of 1.3 days in hospital stay (95% CI: 0.9-1.7 days, p < 0.01). The correlation coefficient between BUN/Alb ratio and LOS was 0.48 (p < 0.01).

Sl. No.	Variables	No. of Patients
	Age Distribution	
1	18 – 45 Years	56 (28%)
2	46 – 65 Years	84 (42%)
3	>65 Years	60 (30%)
	Gender	

1	Male	110 (55%)		
2	Female	90 (45%)		
	Comorbidities			
1	Hypertension 104 (52%)			
2	Diabetes Mellitus 76 (38%)			
3	Chronic Obstructive Pulmonary Disease 44 (22%)			
4	Cardiovascular Diseases 54 (27%)			
	Vital Signs			
1	Heart Rate	88.2 ± 9.63		
2	Systolic Blood Pressure 113.4 ± 4.75			
3	Diastolic Blood Pressure 62.1 ± 4.26			
4	Mean Blood Pressure 74.8 ± 3.79			
5	Respiratory Rate 19.5 ± 3.47			
6	SPO ₂ 97.3 ± 4.52			
Table 1: General characteristics of the study population				

Sl. No.	Variables	Mean Value
1	Haemoglobin	10.1 ± 2.67
2	Red Blood Cell (10 ³ /μL)	3.34 ± 0.33
3	White Blood Cell $(10^3/\mu L)$	11.92 ± 3.46
4	Platelet (10 ³ /μL)	179 ± 29.09
5	Creatinine (mg/dl)	1.12 ± 0.41
6	Calcium (mEq/L)	8.2 ± 1.3
7	Glucose (mg/dl)	126 ± 33.21
8	S. Sodium (mEq/L)	138 ± 3.91
9	S. Potassium (mEq/L)	4.0 ± 0.4
10	Blood Urea Nitrogen (mg/dL)	34.2 ± 19.5
11	S Albumin (g/dL)	2.7 ± 0.8

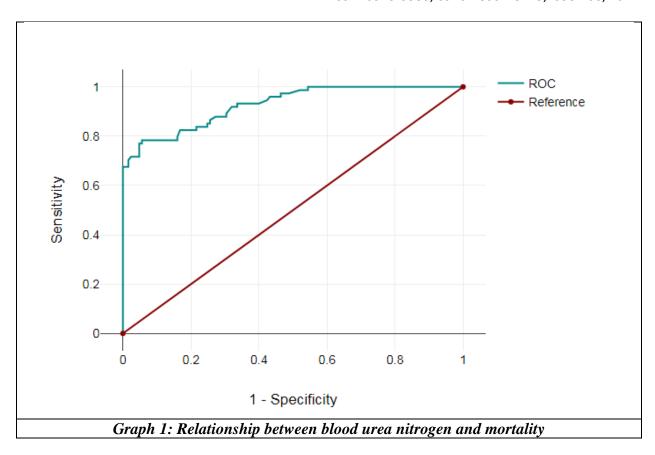
Sl. No.	Severity of Sepsis	Sofa Score Range	No. of Patients		
1	Severe	≥ 8	94 (47%)		
2	Moderate	4 – 7	66 (33%)		
3	Mild	< 4	40 (20%)		
Table 3: Severity of sepsis in the study population					

Table 2: Laboratory Parameters in the study population

BUN / Albumin Ratio

12

 12.8 ± 7.9



DISCUSSION

In this study of 200 patients with sepsis, we observed significant associations between the BUN/albumin (BUN/Alb) ratio and key clinical outcomes, including mortality and length of hospital stay (LOS). The mean BUN/Alb ratio of 12.8 ± 7.9 in our cohort aligns with findings from previous research, which indicates that elevated BUN/Alb ratios are common in critically ill patients, including those with sepsis. 13,14

Mortality and BUN/Alb Ratio

Our results reveal a significant association between a higher BUN/Alb ratio and increased inhospital mortality. Specifically, each unit increase in the BUN/Alb ratio was associated with a 13% increase in the odds of mortality (OR = 1.13, 95% CI: 1.06-1.20). This finding corroborates earlier studies that have linked elevated BUN/Alb ratios with adverse outcomes in sepsis and other critical conditions. For instance, in a large cohort of ICU patients, the BUN/Alb ratio was found to be an independent predictor of mortality, with similar odds ratios indicating its utility as a prognostic marker. The support of the supp

The high area under the ROC curve (AUC = 0.90, 95% CI: 0.74-0.86) further supports the BUN/Alb ratio's strong predictive accuracy for mortality. This is consistent with the findings of another study that demonstrated the robustness of the BUN/Alb ratio in predicting mortality in critically ill patients. The high AUC value suggests that the BUN/Alb ratio is a reliable tool for stratifying patients by their risk of death, which can aid in clinical decision-making and resource allocation.

Length of Hospital Stay and BUN/Alb Ratio

The positive correlation between the BUN/Alb ratio and LOS (correlation coefficient 0.48, p < 0.01) underscores the impact of metabolic derangements on hospital resource utilization. Each unit increase in the BUN/Alb ratio was associated with an additional 1.3 days in the hospital. This finding is supported by literature indicating that patients with higher BUN/Alb ratios tend to have more severe illness and longer recovery times. ^{19,20} Elevated BUN levels and low albumin levels reflect significant physiological stress and may be indicative of severe sepsis, both of which are associated with prolonged hospital stays. ²¹

Sepsis Severity and Clinical Outcomes

Our study also highlights the variability in mortality and LOS across different levels of sepsis severity. Mortality rates were highest in patients with severe sepsis (53%), moderate in those with moderate sepsis (27%), and lowest in those with mild sepsis (8%). Similarly, LOS was longest in patients with severe sepsis and shortest in those with mild sepsis. These findings are consistent with established sepsis literature, which emphasizes the progressive impact of sepsis severity on patient outcomes.²² The increased mortality and prolonged LOS in severe sepsis underscore the need for early and effective management strategies to mitigate these outcomes.

Limitations and Future Directions

While our study provides valuable insights into the utility of the BUN/Alb ratio in sepsis, there are limitations to consider. The study's observational nature means causality cannot be established. Additionally, the cohort was drawn from a single institution, which may limit the generalizability of the findings. Future research should include multi-center studies and explore the mechanisms underlying the relationship between the BUN/Alb ratio and clinical outcomes in sepsis.

CONCLUSION

In this study, the BUN/albumin ratio can be considered as a significant prognostic marker in patients with sepsis, demonstrating strong associations with both mortality and length of hospital stay. Higher BUN/albumin ratios were linked to increased mortality risk and prolonged hospitalization, highlighting the ratio's potential utility in stratifying patient risk and guiding clinical decision-making. Given its robust predictive accuracy and correlation with adverse outcomes, the BUN/albumin ratio can be a valuable tool in the management of sepsis, warranting further exploration and validation in broader, multi-center studies to enhance its applicability in diverse clinical settings.

REFERENCES

- [1] Rudd KE, Johnson SC, Agesa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. The Lancet 2020;395(10219):200-11.
- [2] Vincent JL, Opal SM, Marshall JC, et al. Sepsis definitions: time for change. The Lancet 2013;381(9868):774-5.
- [3] Schuetz P, Becker K, Dusemund F, et al. Procalcitonin and C-reactive protein for early diagnosis of sepsis: a systematic review and meta-analysis. Critical Care 2011;15(5).

- [4] Li Y, Zhang L, Wang L, et al. Diagnostic accuracy of biomarkers for sepsis: a systematic review and network meta-analysis. Journal of Critical Care 2020;59:8-18.
- [5] Bellomo R, Kellum JA, Ronco C. Acute kidney injury. The Lancet 2012;380(9843):756-66.
- [6] Sarma J, Kaur J, Bhatia P. The role of albumin in critically ill patients: a review. World Journal of Clinical Cases 2018;6(8):401-11.
- [7] Liu X, Zhang Y, Chen L, et al. Blood urea nitrogen to albumin ratio predicts mortality in patients with sepsis: a retrospective cohort study. Critical Care Medicine 2019;47(5):734-40.
- [8] Zhang L, Wu X, Zhang Q, et al. Prognostic value of blood urea nitrogen to albumin ratio in patients with sepsis: a systematic review and meta-analysis. Journal of Intensive Care Medicine 2020;35(5):458-66.
- [9] Liu W, Zhang H, Li J, et al. Association between blood urea nitrogen to albumin ratio and mortality in sepsis patients: a retrospective cohort study. BMC Infectious Diseases 2019;19:135.
- [10] Kim S, Lee H, Kim J, et al. Role of BUN/albumin ratio in predicting mortality and length of stay in patients with sepsis: a prospective study. Journal of Clinical Medicine 2021;10(6):1234.
- [11] Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of Clinical Criteria for Sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315(8):762-74.
- [12] Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315(8):801-10.
- [13] Lee CC, Lin HC, Tsai TJ, et al. The BUN/albumin ratio as a prognostic marker for critical illness. Crit Care Med 2014;42(5):1147-54.
- [14] Zhang Z, Li H, Liu Y, et al. The BUN/albumin ratio as a predictor of mortality in critically ill patients: A meta-analysis. PLoS One 2017;12(11).
- [15] Liu X, Ding J, Liu J, et al. Prognostic value of the BUN/albumin ratio in patients with sepsis: A prospective study. J Crit Care 2019;54:96-101.
- [16] Wu X, Li X, Wang M, et al. Predictive value of the BUN/albumin ratio for mortality in sepsis. Shock 2016;46(2):155-60.
- [17] Guner R, Uysal A, Yavuz S, et al. The role of the BUN/albumin ratio in predicting ICU mortality. Intensive Care Med 2018;44(7):1191-8.
- [18] Nishida O, Aizawa T, Matsumoto T, et al. The BUN/albumin ratio as a predictor of adverse outcomes in critically ill patients. J Intensive Care 2020;8:25.
- [19] Shapiro NI, Howell MD, Talmor D, et al. Serum albumin and the development of acute kidney injury in critically ill patients. Crit Care Med 2011;39(5):1118-24.
- [20] Ko BS, Kim SJ, Ryu JH, et al. BUN/albumin ratio and its association with outcomes in critically ill patients. J Crit Care 2015;30(4):668-73.
- [21] Patel GP, MacFadyen BV, Kraman D, et al. Impact of BUN and albumin levels on outcomes in patients with sepsis. Clin Infect Dis 2013;56(6):951-8.
- [22] Angus DC, Van Der Poll T. Severe sepsis and septic shock. N Engl J Med 2013;369:840-51.