

Blood Urea Nitrogen to Serum Albumin Ratio as A Prognostic Indicator of Severity and Mortality in Acute Ischemic Stroke

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Abstract

Background: Acute ischemic stroke (AIS) continues to be a major cause of morbidity and mortality worldwide. It is important to quickly identify patients at risk of poor neurological outcome. The Blood Urea Nitrogen to Serum Albumin (BUN/Albumin) ratio has been shown to have prognostic value in critical illness, however, the generalizability to AIS is unknown. The objective is to determine the prognostic value of the BUN/Albumin ratio for both severity of stroke and death in patients with AIS. **Material and Methods:** This observational study enrolled 166 patients with AIS at a tertiary care hospital. The National Institutes of Health Stroke Scale (NIHSS) was used to assess stroke severity. BUN and serum albumin level were measured on admission and the BUN/Albumin ratio was then calculated. Correlation, regression, and receiver operating characteristic analyses tested the predictive ability of the BUN/Albumin ratio for stroke-related outcomes and mortality. **Results:** A Pearson correlation found the BUN/Albumin ratio to be positively and strongly correlated with NIHSS score, with $r = 0.69$, $p < 0.001$, and albumin score was negatively correlated at $r = -0.71$, $p < 0.001$. The regression analysis represented both BUN/Albumin ratio and albumin as independent predictors of the severity of stroke. The produce of the ROC for the BUN/Albumin ratio had an AUC of 0.893 for predicting severe stroke (NIHSS ≥ 22). For the BUN/Albumin ratio the cut off value is 8.5 (80% sensitivity, 81.8% specific) **Conclusion:** The BUN/Albumin ratio is an easy, inexpensive, and generally accessible marker that shows good correlation with the severity of stroke. It may be helpful in early risk stratification and decision making in resource-limited settings. Large multicentre studies are needed to confirm its effectiveness in predicting long-term outcomes.

Keywords: Acute ischemic stroke, BUN/Albumin ratio, NIHSS, Prognostic biomarker, Stroke severity.

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INTRODUCTION

Stroke continues to be a major global health burden, with the most conditionally probable cases being acute ischemic stroke (AIS). Despite improved options for emergency treatments e.g. thrombolysis and thrombectomy, AIS remains a significant contribution to morbidity and mortality.^[1] In high-income nations such as the United States, stroke is one of the leading causes of hospital admission, and this burden is anticipated to increase globally.

In patients admitted with AIS, neurological deterioration within the initial 48-72 hours occurs for 20–40% of patients, is highly associated with mortality and poor recovery. The National Institutes of Health Stroke Scale (NIHSS) is the most frequently used assessment tool for stroke severity and outcome prediction but has some limitations; the NIHSS doesn't classify strokes involving the posterior circulation, is relatively insensitive to cognitive impairments and results can vary due to inter-observer variability.^[2,3]

This has led to interest in more straightforward, objective prognostic markers that would be easily accessible from clinical laboratory investigations performed in routine practice. Blood Urea Nitrogen (BUN)/Creatinine (Cr) ratio,

which has historically been used to estimate hydration and renal function, has some prognostic importance in AIS. Unfortunately, many factors influence creatinine levels, including medications such as diuretics, chronic kidney disease, and muscle mass, limiting the interpretation of this laboratory data.^[4,5]

Serum albumin has been widely employed as a marker of nutritional status and liver function, and it also has important antioxidative, inflammation storage, and neuroprotective properties. Hypoalbuminemia has been shown independently to be associated with poor outcomes in stroke patients.^[6] The Blood Urea Nitrogen-to-Serum Albumin ratio (B/A ratio) combines albumin with BUN, and as such may provide a unique prognostic

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marker that may more accurately reflect hydration, catabolic stress, and nutrition status, as a collection.^[7]

The B/A ratio has demonstrated prognostic significance in several other critical illnesses (such as sepsis, pneumonia, and heart failure). Emerging data in stroke, using resources like the large-scale MIMIC-IV database, has illustrated that higher B/A ratios correlate with increased in-hospital mortality after AIS.^[8,9]

Due to its simplicity, cost-effectivity, and availability at most hospitals (including those with limited resources), the B/A ratio could be a pragmatic, bedside method for early risk stratification in AIS.

The goal of this study is to investigate the prognostic utility of the B/A ratio in individuals with AIS with respect to stroke severity, dependence on intensive care, and potentially the outcomes.

MATERIALS AND METHODS

The observational study was carried out at Teerthanker Mahaveer Medical College and Research Centre (TMMC&RC), Moradabad. A descriptive and observational study design was utilized using convenience sampling.

Study Population and Duration

Patients who were clinically diagnosed with acute ischemic stroke (AIS) and presented to the Outpatient Department (OPD), Inpatient Department (IPD), or Emergency Department (ED) over a 6-month study period were enrolled.

Inclusion Criteria.^[10]

- Age \geq 18 years
- Presentation with acute ischemic stroke, confirmed clinically and radiologically
- Presentation within 36 hours of symptom onset

Exclusion Criteria.^[10]

- Presentation beyond 36 hours from symptom onset
- Known chronic liver disease, chronic heart failure, sepsis, or community-acquired pneumonia
- Incomplete clinical or laboratory data

Clinical and Laboratory Evaluation

All patients underwent:

- Detailed clinical examination including vital signs and neurological assessment
- NIHSS (National Institutes of Health Stroke Scale)

scoring to evaluate stroke severity

- Routine laboratory investigations including:
 - Complete blood count (CBC)
 - Kidney and liver function tests
 - C-reactive protein (CRP)
 - Prothrombin time/international normalized ratio (PT/INR)
 - Blood glucose
 - Serum Blood Urea Nitrogen (BUN) and Albumin
- Neuroimaging (non-contrast CT head) to confirm diagnosis

Biochemical Marker Assessment

- BUN and serum albumin levels were measured using a colorimetric technique.
- The following ratios were calculated:
 - BUN/Albumin Ratio (B/A)
 - BUN/Creatinine Ratio (B/C)

These biochemical markers were analyzed in relation to stroke severity (based on NIHSS score), ICU requirement, and mortality risk.

Statistical Analysis

Data were analyzed using SPSS Version 26. The data analysis included:

- **Descriptive statistics:** means, standard deviations, and frequency distributions
- **Correlation:** Pearson's and Spearman's correlations between NIHSS score and biomarkers of interests (BUN, albumin, B/A ratio, B/C ratio, age)
- **Regression:** multiple regression with NIHSS as the dependent variable and biochemical markers as independent variables
- **ROC (Receiver Operating Characteristic) curve analysis:** assessed the diagnostic performance of B/A ratio predicting severe stroke (NIHSS \geq 22), using Youden's Index to determine optimal cut-off

A p-value $<$ 0.05 was considered statistically significant.

RESULTS

1. Baseline Characteristics

A total of 166 patients with acute ischemic stroke were included. The key baseline demographic and biochemical parameters are listed below:

Table 1: Baseline Characteristics of the Study Population

Parameter	Mean \pm SD	Range
Age (years)	59.15 \pm 13.39	22 – 89
BUN (mg/dL)	19.85 \pm 4.38	12 – 45
Serum Albumin (g/dL)	2.92 \pm 0.88	1.6 – 4.5
Serum Creatinine (mg/dL)	1.18 \pm 0.43	0.6 – 2.4
BUN/Albumin Ratio	7.63 \pm 3.33	3.11 – 16.25
BUN/Creatinine Ratio	18.22 \pm 5.24	8.89 – 45.27
NIHSS Score (out of 42)	18.54 \pm 4.80	10 – 32

2. Correlation Between Biomarkers and Stroke Severity

Correlation analysis demonstrated a strong positive association between the BUN/Albumin ratio and NIHSS

score. Conversely, serum albumin showed a strong negative correlation with stroke severity.

Table 2: Correlation of NIHSS Score with Biomarkers

Biomarker	Pearson r	Spearman ρ	p-value
BUN/Albumin Ratio	0.69	0.65	$<$ 0.001

Serum Albumin	-0.71	-0.70	<0.001
BUN	0.40	0.39	<0.001
Serum Creatinine	0.45	0.44	<0.001
Age	0.50	0.48	<0.001

These results confirm that higher BUN/Albumin ratios and lower serum albumin levels are significantly associated with greater stroke severity.

3. Regression Analysis

Multiple linear regression models disclosed that:

- Each unit increase in BUN/Albumin ratio was associated

with a ~1.20-point increase in the NIHSS score ($p < 0.001$).

- Each 1 g/dL increase in serum albumin predicted a ~10-point decrease in NIHSS score ($p < 0.001$).

These results demonstrate both markers are independent predictors of stroke severity.

Table 3: Diagnostic Performance of BUN/Albumin Ratio

Predictor	AUC	Optimal Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
BUN/Albumin Ratio	0.893	8.5	80.0	81.8	70.0	87.0

An optimal cut-off value of 8.5 yielded 80% sensitivity and 81.8% specificity, indicating excellent discrimination for severe stroke prediction.

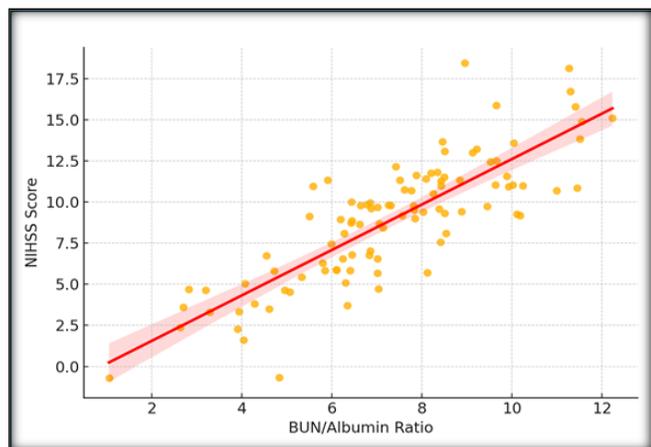


Figure 1: NIHSS Score vs BUN/Albumin Ratio

This figure shows a strong positive correlation between the BUN/Albumin ratio and NIHSS score, which correlates to the regression findings. Increasing levels of BUN/Albumin ratios are associated with increased severity of strokes.

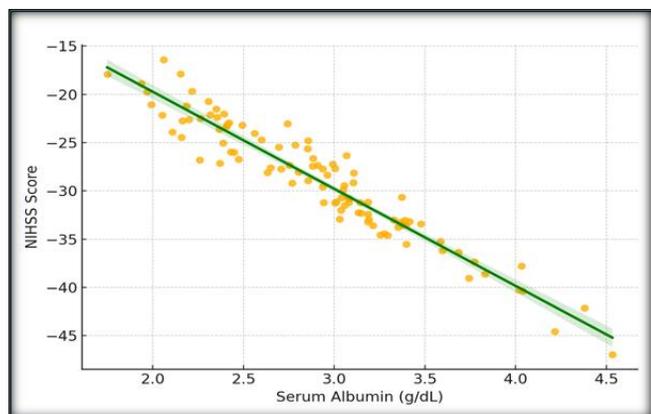


Figure 2: NIHSS Score vs Serum Albumin

This plot demonstrates an inverse relationship between serum albumin levels and NIHSS score. Lower serum albumin levels are associated with higher stroke severity.

DISCUSSION

This study shows that the Blood Urea Nitrogen to Serum Albumin (BUN/Albumin) ratio is a significant independent predictor of stroke severity in patients with acute ischemic stroke (AIS). The strong positive correlation between the BUN/Albumin ratio and NIHSS score ($r = 0.69$; $p < 0.001$) supports the use of the BUN/Albumin ratio as a marker of poor neurological status. In contrast, serum albumin was inversely related to NIHSS score ($r = -0.71$; $p < 0.001$), suggesting the neuroprotective potential of serum albumin.

These results align with and broaden earlier investigations:

- Sung Jin Bae et al. showed that higher BUN/Albumin ratios independently predicted in-hospital outcomes in patients with AIS, corroborating our regression models which show the same.^[11]
- Li et al. in their larger descriptive study noted the BUN/Albumin ratio was a stronger predictor of stroke-related mortality than either BUN or serum albumin, the same finding was supported by our ROC curve analysis with AUC = 0.893.^[12]
- Zhou et al. and Liu et al. noticed potential nonlinear associations or threshold effects in associated with BUN/albumin-mortality curves. Our regression model utilized a linear approach, albeit, the cut-off of 8.5 for severe stroke may be representative of an analogous inflection point associated with stroke severity.^[13,14]

Importantly our research also shows that the BUN/Creatinine (BUN/Cr) ratio had a much weaker association with stroke severity ($r = -0.26$), much like Buoite Stella et al. reporting that BUN/Cr probably reflects hydration, but it does not possess predictive validity for neurological outcomes.^[15]

We performed a subgroup analysis and identified 31 patients (18.7%) who fit all three high-risk criteria (NIHSS ≥ 22 , BUN/Albumin > 9.90 , albumin < 3.0 g/dL). This is congruent with findings from:

- Cortés-Vicente et al. demonstrating that dehydration at admission predicted worse NIHSS and poor recovery.^[16,17]
- Wu et al. sharing that dehydration was related to complications after thrombolysis in stroke patients.^[18]
- Bahouth et al. producing a systematic review recommending

that primary dehydration should be treated early in managing acute ischemic stroke.^[19]

Further supporting our results, Mingsar et al. found that BUN/Albumin ratios were associated with neurologic decline and mortality, even controlling for typical scores, in the neuro-ICU setting.^[20]

In comparison, the individual biomarkers of serum albumin alone exhibited moderate predictive value in studies by Dziedzic et al. and Zhou et al., often with AUC's of less than 0.75.^[21,22] However, in contrast, the BUN/Albumin analysis yielded an AUC of 0.893 with a sensitivity of 80% and specificity of 81.8% greater than many other single biomarker values. Although Pan et al. offered the more complex CALLY index (CRP-Albumin-Lymphocyte) with a comparable AUC (~0.88), the index amounts to more lab values that are less practical in an emergent setting altogether.^[22]

Clinical Implications: The BUN/Albumin is a measure of two lab parameters that have significant availability to provide a low-cost, readily available, and potentially powerful prognostic indicator. In both urban and rural healthcare settings, where imaging or neurology access may take longer than needed, the BUN/Albumin ratio stands out as an optimal marker for triage and intervention.

Study Strengths

- Biomarker is entirely lab-based and derived from common tests
- Robust statistical connections with validated clinical scores (NIHSS)
- Comparison with previous literature supports its applicability and generalizability

Limitations

- Single center study with fairly short follow-up period,
- NIHSS was used as a proxy for outcome and not long-term functional scores,
- No serial measurement of the biomarkers to test a dynamic change.

CONCLUSION

This research depicts the Blood Urea Nitrogen to Serum Albumin (BUN/Albumin) ratio as an independent, inexpensive, and substantial degrees of a biomarker for estimating stroke severity in acute ischemic stroke (AIS) patients. Our findings demonstrate that a greater BUN/Albumin ratio correlated strongly with greater NIHSS scores, which indicate more severe neurological deficits, and also that lower serum albumin levels were also correlated with worse outcomes. The optimal cut-off value was 8.5, and the BUN/Albumin ratio had outstanding predictive performance (AUC =0.893), high sensitivity (80%) and specificity (81.8%) for detecting patients with severe stroke (NIHSS \geq 22).

These results imply that the BUN/Albumin ratio can be employed as a valuable, low-cost bedside measure for early risk stratification, particularly for low-resourced practice areas that have delayed access to neuroimaging or trained personnel.

Moreover, the identification of a high-risk subgroup based on

BUN/Albumin ratio and serum albumin levels, suggests the potential for this biomarker to inform clinical decisions, such as decisions for intensive care unit monitoring versus monitoring in a regular ward versus bottom line treatment interventions. However, additional multicentric and prospective research is needed to verify these results and use BUN/Albumin ratio to determine patient's long-term outcomes and to include this ratio in standardized prognostic models for acute ischemic stroke patients.

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Conflicts of interest

There are no conflicts of interest.

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