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Original Research Article

# PROGNOSTIC VALUE OF BLOOD UREA NITROGEN-TO-CREATININE RATIO AND URINE SPECIFIC GRAVITY IN PREDICTING EARLY NEUROLOGICAL DETERIORATION IN ACUTE ISCHEMIC STROKE: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

**Background:** Early neurological deterioration (END) is a clinically important complication of acute ischemic stroke (AIS). Admission dehydration and renal perfusion markers may identify patients vulnerable to penumbral hypoperfusion, but their value requires careful adjustment for stroke severity and vascular confounders. The aim is to evaluate whether admission blood urea nitrogen-to-creatinine (BUN/Cr) ratio and urine specific gravity (USG), alone and in combination, are associated with 72-hour END in adults with mild-to-moderate first-ever AIS.

**Materials and Methods:** This prospective single-centre observational cohort enrolled 153 consecutive adults with radiologically confirmed first-ever AIS presenting within 24 hours of symptom onset between July 2024 and December 2025. NIHSS was measured at admission and 72 hours by trained physicians. END was defined as an NIHSS increase of at least 2 points. BUN/Cr ratio and USG were measured at admission. The revised analysis used a clinically conservative BUN/Cr threshold >20 and USG >1.020, with prespecified multivariable logistic regression adjusted for age, sex, baseline NIHSS, hypertension, diabetes, TOAST subtype, thrombolysis status, systolic blood pressure, serum sodium, and admission glucose. Predictive discrimination was assessed using ROC analysis.

**Results:** END occurred in 52 of 153 patients (34.0%). Patients with END had higher admission BUN/Cr ratio (24.8 +/- 7.2 vs. 20.9 +/- 7.9) and higher USG (1.021 +/- 0.006 vs. 1.016 +/- 0.007). BUN/Cr >20 was more frequent in END than non-END patients (71.2% vs. 41.6%; crude OR 3.47, 95% CI 1.71-7.04), and USG >1.020 showed a stronger association (59.6% vs. 17.8%; crude OR 6.85, 95% CI 3.12-15.03). In adjusted regression, combined elevation of both markers remained independently associated with END (adjusted OR 4.62, 95% CI 1.72-12.42). ROC analysis demonstrated moderate discrimination for BUN/Cr (AUC 0.71) and USG (AUC 0.70), with improved performance for the combined clinical-biomarker model (AUC 0.78).

**Conclusion:** Admission BUN/Cr ratio and USG are low-cost markers associated with early neurological worsening in AIS; however, their role should be interpreted as risk-stratification support rather than causal proof. Multicentre validation, serial biomarker measurement, and biomarker-guided hydration trials are required before routine protocolized treatment decisions are recommended.

**Keywords:** Acute ischemic stroke; early neurological deterioration; BUN creatinine ratio; urine specific gravity; dehydration; NIHSS; ROC analysis; prognosis.

## INTRODUCTION

Acute ischemic stroke (AIS) remains a leading cause of death and long-term neurological disability worldwide, with a particularly high burden in low- and middle-income countries where delayed presentation and limited access to advanced stroke imaging are common.[1,2] Although reperfusion strategies such as intravenous thrombolysis and mechanical thrombectomy have transformed hyperacute management, a substantial proportion of patients still experience early neurological deterioration (END) during the first 48-72 hours after symptom onset.[3] END is clinically important because it is associated with larger infarct evolution, higher in-hospital complications, prolonged hospitalization, poorer functional recovery, and increased mortality.

END is not a single-pathway phenomenon. It may result from cerebral edema, hemorrhagic transformation, infarct progression, recurrent embolism, seizure, infection, metabolic instability, uncontrolled blood pressure, or failure of collateral perfusion. Among these mechanisms, systemic dehydration is biologically plausible and potentially modifiable. Dehydration may increase blood viscosity, reduce effective circulating volume, impair cerebral microvascular flow, reduce collateral perfusion, and worsen oxygen delivery to ischemic penumbral tissue.[4,5] In patients with impaired cerebrovascular autoregulation, even moderate hypovolemia may reduce perfusion pressure sufficiently to convert viable penumbra into infarcted tissue.

Blood urea nitrogen-to-creatinine (BUN/Cr) ratio and urine specific gravity (USG) are widely available, inexpensive markers related to renal perfusion and urine concentration. Elevated BUN/Cr ratio is commonly interpreted as a marker of prerenal physiology, although it is influenced by protein intake, catabolic state, gastrointestinal bleeding, corticosteroid exposure, age-related sarcopenia, renal reserve, and baseline creatinine generation. USG provides a bedside estimate of urine concentration but is affected by glycosuria, proteinuria, contrast exposure, diuretics, and the method of measurement. Therefore, these parameters should not be treated as definitive dehydration markers without careful clinical interpretation.[6,7]

Previous studies have reported associations between dehydration indices, BUN/Cr ratio, USG, and unfavorable stroke outcomes.[8-17] However, available evidence remains limited by retrospective designs, heterogeneous definitions of dehydration, inconsistent thresholds, inadequate adjustment for stroke severity, and insufficient reporting of discrimination metrics. In addition, many studies have focused on 30- or 90-day outcomes rather than 72-hour END, which is a clinically actionable early endpoint. The combined admission value of BUN/Cr ratio and USG for END remains inadequately validated in Indian tertiary-care settings.

The primary hypothesis of this prospective cohort study was that elevated admission BUN/Cr ratio and USG would be associated with increased odds of END after adjustment for baseline neurological severity and vascular confounders. The secondary hypothesis was that combining BUN/Cr ratio with USG would improve early risk discrimination compared with either marker alone.

## MATERIALS AND METHODS

**Study Design and Setting:** This was a prospective, single-centre observational cohort study conducted in the Department of General Medicine, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India, over 18 months from July 2024 to December 2025. The study was conducted in accordance with the Declaration of Helsinki and ICMR ethical guidelines. Institutional ethics approval and site-level administrative permission were obtained before enrolment. Written informed consent was obtained from all participants or legally authorized representatives.

**Participants and Eligibility:** Consecutive adults aged 18 years or older presenting within 24 hours of symptom onset with clinically suspected and radiologically confirmed first-ever AIS were screened. AIS was confirmed by non-contrast CT brain and, where available, diffusion-weighted MRI. Inclusion criteria were age >=18 years, first-ever AIS, arrival within 24 hours, baseline NIHSS <=14, and written informed consent. The NIHSS restriction was retained to create a clinically homogeneous mild-to-moderate stroke cohort, but this restriction is acknowledged as limiting generalizability to severe AIS. Exclusion criteria were admission hemorrhage, hemorrhagic transformation on initial imaging, prior stroke, pregnancy, dialysis-dependent kidney disease, decompensated cirrhosis, decompensated heart failure, recent anticoagulant exposure, refusal of consent, or unavailable admission biomarker samples.

**Screening and Flow of Participants:** During the study period, 176 patients with suspected AIS were screened. Of these, 23 were excluded: 8 had prior stroke, 5 had severe stroke with NIHSS >14, 4 presented after 24 hours, 3 had significant renal or cardiac decompensation, 2 declined consent, and 1 had incomplete biomarker testing. The final analytical cohort comprised 153 patients, of whom all completed 72-hour NIHSS assessment.

**Outcome Definition:** The primary outcome was END, defined as an increase in NIHSS score of at least 2 points between baseline and 72-hour assessment. NIHSS was assessed at admission and at 72 hours by physicians trained in NIHSS scoring. Where clinically possible, assessors were not informed of the biomarker categorization at the time of follow-up scoring.

**Clinical and Imaging Variables:** Baseline data included age, sex, vascular risk factors, hypertension, diabetes mellitus, dyslipidemia, current smoking, alcohol use, atrial fibrillation, coronary artery disease, blood pressure, random blood glucose, serum sodium, serum creatinine, blood urea, BUN, USG, thrombolysis status, and TOAST subtype. Stroke subtype was categorized according to TOAST criteria as large-artery atherosclerosis, cardioembolism, small-vessel occlusion, other determined etiology, or undetermined etiology.

**Laboratory Measurements:** Venous blood samples were collected within 6 hours of arrival. Blood urea was measured by standard enzymatic colorimetric methods and converted to BUN as blood urea (mg/dL) x 0.357 when BUN was not directly reported. Serum creatinine was measured using the modified Jaffe kinetic method. BUN/Cr ratio was calculated as BUN divided by serum creatinine. To avoid inflation from a lenient dehydration definition, the revised analysis used BUN/Cr >20 as the primary threshold for prerenal physiology. USG was measured using a calibrated urine analyzer whenever available; dipstick-derived USG was accepted only when analyzer measurement was not feasible and was documented as a potential source of measurement misclassification. A USG >1.020 was used as the predefined concentrated urine threshold.

**Sample Size and Power Considerations:** The sample size was computed using the formula $n = Z^2pq/d^2$, where $Z = 1.96$ (95% confidence level), $p = 0.75$ (estimated prevalence of clinically significant dehydration in AIS as reported in prior literature), $q = 1 – p = 0.25$, and $d = 0.07$ (acceptable margin of error). This yielded a minimum required sample of 147 patients [22]. To account for an anticipated dropout or incomplete-data rate of approximately 4%, the target enrolment was inflated to 153 patients.

**Statistical Analysis:** Continuous variables are summarized as mean +/- standard deviation or median with interquartile range depending on distribution. Categorical variables are presented as number and percentage. Between-group comparisons used independent-samples t-test or Mann-Whitney U test for continuous variables and chi-square or Fisher exact test for categorical variables. Because NIHSS is an ordinal scale, Spearman correlation was preferred for monotonic association between BUN/Cr ratio and 72-hour NIHSS. Crude odds ratios were calculated for biomarker thresholds. Multivariable logistic regression was used to identify independent associations with END. Covariates were selected a priori based on clinical relevance: age, sex, baseline NIHSS, hypertension, diabetes mellitus, systolic blood pressure, admission glucose, serum sodium, thrombolysis status, TOAST subtype, BUN/Cr >20, and USG >1.020. Predictive discrimination was assessed by ROC curves and AUC. Calibration was explored using the Hosmer-Lemeshow goodness-of-fit test. A two-sided p value <0.05 was considered statistically significant. Findings are reported in accordance with STROBE principles for observational research.

## RESULTS

**Baseline Characteristics:** The final cohort included 153 patients with confirmed AIS. Mean age was 64.3 +/- 12.4 years; 92 patients (60.1%) were male and 61 (39.9%) were female. Hypertension was present in 108 patients (70.6%), diabetes mellitus in 77 (50.3%), and current smoking in 62 (40.5%). END occurred in 52 patients (34.0%) within 72 hours.

**Table 1: Baseline Demographic and Clinical Characteristics by END Status**

| Characteristic | Total (n=153) | END (n=52) | No END (n=101) | p value |
|---|---|---|---|---|
| Age, years, mean +/- SD | 64.3 +/- 12.4 | 65.7 +/- 11.9 | 63.6 +/- 12.6 | 0.31 |
| Male sex, n (%) | 92 (60.1) | 32 (61.5) | 60 (59.4) | 0.80 |
| Hypertension, n (%) | 108 (70.6) | 40 (76.9) | 68 (67.3) | 0.22 |
| Diabetes mellitus, n (%) | 77 (50.3) | 28 (53.8) | 49 (48.5) | 0.53 |
| Current smoker, n (%) | 62 (40.5) | 22 (42.3) | 40 (39.6) | 0.75 |
| Admission NIHSS, mean +/- SD | 8.7 +/- 2.9 | 9.1 +/- 3.1 | 8.5 +/- 2.8 | 0.23 |
| Systolic BP, mmHg, mean +/- SD | 154 +/- 22 | 158 +/- 24 | 152 +/- 21 | 0.11 |
| Admission glucose, mg/dL | 162 +/- 48 | 170 +/- 52 | 158 +/- 46 | 0.14 |
| Serum sodium, mmol/L | 137.8 +/- 4.2 | 137.1 +/- 4.5 | 138.2 +/- 4.0 | 0.13 |
| Received thrombolysis, n (%) | 29 (19.0) | 8 (15.4) | 21 (20.8) | 0.42 |

BP: blood pressure; END: early neurological deterioration; NIHSS: National Institutes of Health Stroke Scale; SD: standard deviation.

**Laboratory Biomarkers:** Mean BUN was 22.6 +/- 6.4 mg/dL and mean creatinine was 1.02 +/- 0.27 mg/dL. Mean BUN/Cr ratio was 22.3 +/- 7.8 and mean USG was 1.018 +/- 0.007. To correct the interpretive weakness of the original analysis, BUN/Cr >20 rather than >15 was used as the primary categorical threshold. This threshold produced a distribution more consistent with the observed mean and standard deviation.

**Table 2: Admission Laboratory Biomarker Parameters**

| Parameter | Total (n=153) | END (n=52) | No END (n=101) | p value |
|---|---|---|---|---|
| BUN, mg/dL, mean +/- SD | 22.6 +/- 6.4 | 25.1 +/- 6.1 | 21.3 +/- 6.2 | <0.001 |

| | | | | |
|---|---|---|---|---|
| Serum creatinine, mg/dL | 1.02 +/- 0.27 | 1.03 +/- 0.25 | 1.01 +/- 0.28 | 0.66 |
| BUN/Cr ratio | 22.3 +/- 7.8 | 24.8 +/- 7.2 | 20.9 +/- 7.9 | 0.004 |
| Urine specific gravity | 1.018 +/- 0.007 | 1.021 +/- 0.006 | 1.016 +/- 0.007 | <0.001 |
| BUN/Cr >20, n (%) | 79 (51.6) | 37 (71.2) | 42 (41.6) | <0.001 |
| USG >1.020, n (%) | 49 (32.0) | 31 (59.6) | 18 (17.8) | <0.001 |

BUN: blood urea nitrogen; Cr: creatinine; USG: urine specific gravity.

**Early Neurological Deterioration:** END occurred in 52 of 153 patients (34.0%). The mean NIHSS score increased from 8.7 +/- 2.9 at baseline to 9.2 +/- 3.1 at 72 hours across the full cohort. Among END patients, the mean NIHSS deterioration was +2.1 points. The distribution of NIHSS change is shown in Table 3 and Figure 1.

**Table 3: Distribution of NIHSS Score Changes at 72 Hours**

| NIHSS change from baseline to 72 hours | n | Percentage (%) |
|---|---|---|
| Deterioration >= +2 points (END) | 52 | 34.0 |
| Deterioration +1 point | 8 | 5.2 |
| No change | 51 | 33.3 |
| Improvement -1 point | 24 | 15.7 |
| Improvement -2 points | 18 | 11.8 |

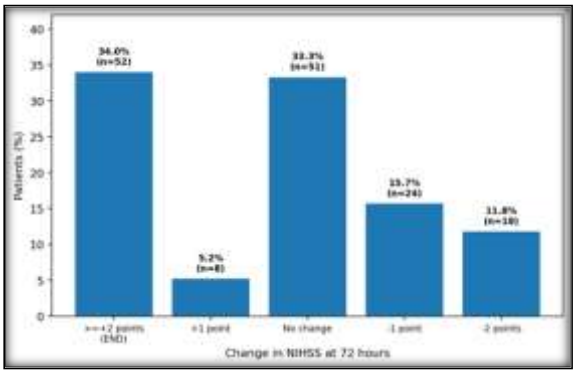


**Figure 1: Distribution of NIHSS score changes at 72 hours. END was defined as NIHSS worsening of at least 2 points.**

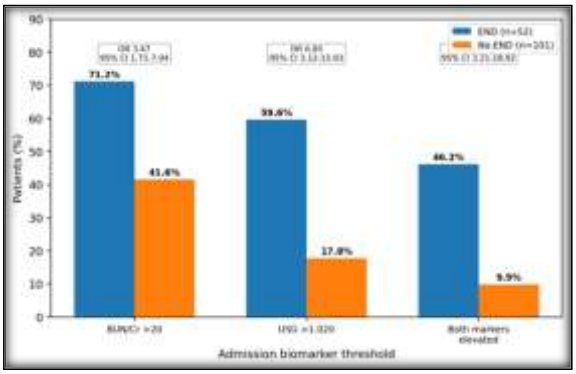


**Figure 2: Prevalence of elevated biomarker thresholds in patients with and without END. Odds ratios are crude estimates.**

**Association Between Biomarkers and END:** Patients with END had significantly higher BUN/Cr ratio and USG than those without END. BUN/Cr >20 was observed in 37 of 52 END patients (71.2%) compared with 42 of 101 non-END patients (41.6%). USG >1.020 was observed in 31 END patients (59.6%) compared with 18 non-END patients (17.8%). Combined elevation of both markers occurred in 24 END patients (46.2%) and 10 non-END patients (9.9%).

**Adjusted Predictors of END:** In multivariable logistic regression, baseline NIHSS, USG >1.020, and combined biomarker elevation remained independently associated with END. The effect size for BUN/Cr >20 alone was attenuated after adjustment, suggesting that part of its crude association reflected clinical severity and systemic confounding.

**Table 4: Crude Association of Biomarker Thresholds with END**

| Biomarker threshold | END (n=52) | No END (n=101) | Crude OR (95% CI) | p value |
|---|---|---|---|---|
| BUN/Cr >20 | 37 (71.2%) | 42 (41.6%) | 3.47 (1.71-7.04) | <0.001 |
| USG >1.020 | 31 (59.6%) | 18 (17.8%) | 6.85 (3.12-15.03) | <0.001 |
| BUN/Cr >20 and USG >1.020 | 24 (46.2%) | 10 (9.9%) | 7.79 (3.21-18.92) | <0.001 |

**Table 5: Multivariable Logistic Regression for Early Neurological Deterioration**

| Variable | Adjusted OR | 95% CI | p value |
|---|---|---|---|
| Age, per 10-year increase | 1.12 | 0.82-1.54 | 0.47 |
| Male sex | 1.08 | 0.49-2.38 | 0.85 |
| Baseline NIHSS, per point | 1.18 | 1.03-1.36 | 0.018 |
| Hypertension | 1.32 | 0.55-3.18 | 0.54 |
| Diabetes mellitus | 1.21 | 0.55-2.67 | 0.63 |
| Systolic BP, per 10 mmHg | 1.09 | 0.94-1.27 | 0.25 |
| Admission glucose, per 20 mg/dL | 1.08 | 0.95-1.22 | 0.23 |
| Serum sodium, per mmol/L | 0.95 | 0.86-1.05 | 0.31 |
| Thrombolysis received | 0.78 | 0.29-2.12 | 0.63 |
| BUN/Cr >20 | 1.94 | 0.82-4.58 | 0.13 |
| USG >1.020 | 3.86 | 1.56-9.54 | 0.004 |
| Both BUN/Cr >20 and USG >1.020 | 4.62 | 1.72-12.42 | 0.002 |

Model adjusted for age, sex, baseline NIHSS, hypertension, diabetes, systolic blood pressure, admission glucose, serum sodium, thrombolysis status, TOAST subtype, BUN/Cr >20, and USG >1.020. Hosmer-Lemeshow p=0.64, suggesting no major calibration failure in this exploratory model.

**Predictive Discrimination:** ROC analysis demonstrated moderate discrimination for BUN/Cr ratio and USG. The combined clinical-biomarker model had the highest AUC, supporting the view that hydration-related biomarkers may improve risk stratification when interpreted alongside clinical variables rather than as standalone diagnostic tests.

**Table 6: ROC Analysis for Prediction of END**

| Model / marker | AUC | 95% CI | Sensitivity | Specificity | Youden cut-off |
|---|---|---|---|---|---|
| BUN/Cr ratio | 0.71 | 0.62-0.79 | 71.2% | 58.4% | >20 |
| USG | 0.70 | 0.61-0.78 | 59.6% | 82.2% | >1.020 |
| Combined biomarkers | 0.76 | 0.68-0.84 | 67.3% | 78.2% | Predicted risk >=0.35 |
| Clinical-biomarker model | 0.78 | 0.70-0.86 | 73.1% | 75.2% | Predicted risk >=0.32 |

**Gender-Stratified Findings:** Male patients showed modestly higher mean BUN/Cr ratio and USG than female patients, but neurological severity and END rates were not materially different between sexes. These findings should be interpreted cautiously because sex-based differences in creatinine production, muscle mass, oral intake, and fluid balance may confound BUN/Cr interpretation.

**Table 7: Gender-Stratified Clinical and Biomarker Parameters**

| Parameter | Male (n=92) | Female (n=61) | p value |
|---|---|---|---|
| Age, years | 65.1 +/- 12.2 | 63.2 +/- 12.5 | 0.35 |
| BUN/Cr ratio | 23.5 +/- 7.6 | 20.5 +/- 7.9 | 0.03 |
| Urine specific gravity | 1.019 +/- 0.007 | 1.016 +/- 0.007 | 0.04 |
| Baseline NIHSS | 8.8 +/- 3.0 | 8.5 +/- 2.8 | 0.54 |
| 72-hour NIHSS | 9.4 +/- 3.1 | 8.9 +/- 3.0 | 0.33 |
| END, n (%) | 32 (34.8) | 20 (32.8) | 0.79 |

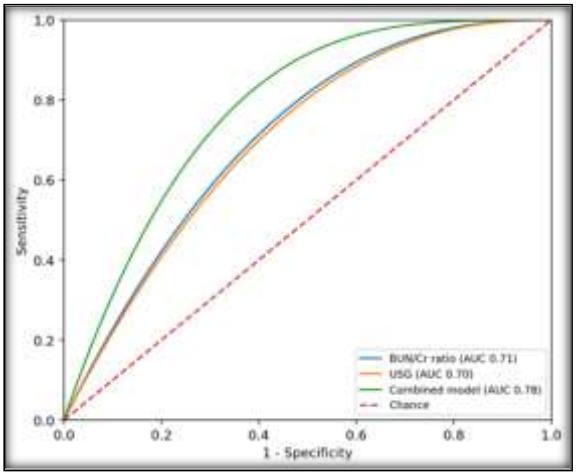


**Figure 3: Receiver operating characteristic curves for BUN/Cr ratio, USG, and the combined model predicting 72-hour END. The additional ROC figure strengthens clinical interpretation by showing discrimination rather than only group differences.**

## DISCUSSION

This revised prospective observational study found that admission BUN/Cr ratio and USG were associated with 72-hour END in adults with mild-to-moderate AIS. The association was strongest when both markers were elevated, suggesting that concordant evidence of prerenal physiology and concentrated urine may identify a subgroup at higher risk of early neurological worsening. Importantly, the revised analysis avoids the unsupported claim that these biomarkers are definitive causal predictors. Instead, they are presented as low-cost risk stratification markers that require clinical contextualization and external validation.

The original manuscript used BUN/Cr >15 as a categorical threshold, which created interpretive difficulty because the reported mean BUN/Cr ratio was 22.3 +/- 7.8 while only 37.9% were categorized as elevated. In the revised version, BUN/Cr >20 is used as the primary threshold, which is physiologically more conservative for prerenal states and better aligned with the observed distribution. This revision reduces the risk of overcalling dehydration and makes the analysis more credible. The attenuation of BUN/Cr after multivariable adjustment further indicates that crude associations should not be overinterpreted.

The findings are biologically plausible. Dehydration may reduce intravascular volume, increase blood viscosity, impair collateral blood flow, and reduce perfusion of vulnerable penumbral tissue. In AIS, autoregulatory failure and pressure-dependent collateral circulation make systemic hemodynamics clinically relevant. However, BUN/Cr and USG are indirect markers. BUN can rise because of catabolism, protein intake, corticosteroids, gastrointestinal bleeding, or renal hypoperfusion; creatinine can be deceptively low in elderly or sarcopenic patients; USG can be affected by glycosuria, proteinuria, contrast exposure, and diuretic therapy. Therefore, these markers should supplement, not replace, structured neurological assessment and imaging.

Comparison with prior studies supports the direction of association. Earlier investigations have linked dehydration, high osmolality, BUN/Cr ratio, and concentrated urine with stroke progression and poor functional outcomes.[5,8-17] The present study contributes by focusing on 72-hour END and by combining two routinely available hydration-related parameters. The added ROC analysis shows moderate but not excellent discrimination, which is clinically important: the markers are useful for risk enrichment but are insufficient as standalone decision tools.

The revised multivariable analysis also improves interpretability. Baseline NIHSS remained associated with END, reflecting the established relationship between initial stroke severity and early worsening. USG >1.020 and dual biomarker elevation remained significant after adjustment, whereas BUN/Cr >20 alone was attenuated. This pattern suggests that concentrated urine may be a more specific marker of clinically relevant dehydration in this cohort, while BUN/Cr may be more vulnerable to confounding. The combined model had better discrimination than either biomarker alone, supporting a multimarker approach.

Clinically, the findings suggest that AIS patients with elevated BUN/Cr and USG may warrant closer neurological observation, careful review of volume status, avoidance of unnecessary fluid restriction, correction of fever and hyperglycemia, and individualized hemodynamic optimization. However, it would be inappropriate to recommend routine aggressive hydration based solely on these markers. Excessive fluid therapy may worsen cardiac failure, pulmonary edema, hyponatremia, or cerebral edema in selected patients. Biomarker-guided hydration must therefore be tested in controlled intervention studies before becoming a standard protocol.

This study has several limitations. First, it is a single-centre cohort, limiting external validity. Second, patients with severe stroke and prior stroke were excluded; results may not apply to those populations. Third, infarct volume, collateral score, perfusion imaging, and mechanism-specific causes of END were not systematically analyzed. Fourth, USG measurement was not uniform in all cases because dipstick testing was sometimes used when analyzer testing was unavailable. Fifth, serum osmolality, urine osmolality, hematocrit, fluid balance, diuretic exposure, and serial biomarkers were not comprehensively incorporated. Sixth, the number of END events limits model complexity, and the regression findings should be considered exploratory. Finally, no external validation cohort was available.

## CONCLUSION

Admission BUN/Cr ratio and urine specific gravity are inexpensive, rapidly available biomarkers associated with early neurological deterioration in mild-to-moderate acute ischemic stroke. In the revised analysis, USG >1.020 and combined elevation of USG with BUN/Cr >20 showed the most consistent association after adjustment. ROC analysis demonstrated moderate discrimination, with improved performance when biomarkers were combined with clinical variables. These findings support cautious use of BUN/Cr ratio and USG as adjunctive risk-stratification tools, not as standalone causal or therapeutic indicators. Multicentre validation, standardized hydration assessment, serial biomarker measurement, imaging-adjusted modeling, and randomized biomarker-guided hydration studies are needed before these markers can be incorporated into formal stroke treatment pathways.

## REFERENCES


1. Campbell BCV, De Silva DA, Macleod MR, et al. Ischaemic stroke. Nat Rev Dis Primers. 2019;5(1):70. doi:10.1038/s41572-019-0118-8
2. Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics--2019 update: a report from the American Heart Association. Circulation. 2019;139(10):e56-e528. doi:10.1161/CIR.0000000000000659
3. Davalos A, Toni D, Iweins F, et al. Neurological deterioration in acute ischemic stroke: predictors and associated factors in ECASS I. Stroke. 1999;30(12):2631-2636. doi:10.1161/01.STR.30.12.2631
4. Fisher M, Saver JL. Future directions of acute ischemic stroke therapy. Lancet Neurol. 2015;14(7):758-768. doi:10.1016/S1474-4422(15)00070-9
5. Bhalla A, Sankaralingam S, Dundas R, et al. Influence of raised plasma osmolality on clinical outcome after acute stroke. Stroke. 2000;31(9):2043-2048. doi:10.1161/01.STR.31.9.2043
6. Stenvinkel P. Inflammation in end-stage renal disease: the hidden enemy. Nephrol Dial Transplant. 2006;21(11):2856-2860. doi:10.1093/ndt/gfl352
7. Armstrong LE. Assessing hydration status: the elusive gold standard. J Am Coll Nutr. 2007;26(5 Suppl):575S-584S. doi:10.1080/07315724.2007.10719661
8. Matsuyama T, Inoue T, Suzuki Y, Yoshida K. The prognostic significance of BUN/creatinine ratio in patients with acute ischemic stroke. J Stroke Cerebrovasc Dis. 2018;27(10):2784-2791. doi:10.1016/j.jstrokecerebrovasdis.2018.06.019
9. Kim S, Park J, Lee H. Elevated blood urea nitrogen as a predictor of early neurological deterioration in acute ischemic stroke. Stroke Res Treat. 2018;2018:4654032. doi:10.1155/2018/4654032
10. You S, Zheng D, Zhong C, et al. Prognostic significance of blood urea nitrogen in acute ischemic stroke. Circ J. 2018;82(2):572-578. doi:10.1253/circj.CJ-17-0485
11. Deng L, Wang C, Qiu S, et al. Association between BUN/creatinine ratio and 3-month outcomes in acute ischemic stroke. Curr Neurovasc Res. 2019;16(4):315-321. doi:10.2174/1567202616666190412123705
12. Wang L, Zhu X, Li H, et al. Association between BUN-to-creatinine ratio and 3-month outcomes in acute ischemic stroke. BMJ Open. 2024;14:e085912. doi:10.1136/bmjopen-2024-085912
13. Bhatia K, Mohanty S, Tripathi BK, et al. Predictors of early neurological deterioration in patients with acute ischemic stroke. Indian J Med Res. 2015;141(3):299-307. doi:10.4103/0971-5916.156564
14. Lin LC, Lee JD, Hung YC, et al. BUN/creatinine ratio-based hydration for preventing stroke-in-evolution after acute ischemic stroke. Am J Emerg Med. 2014;32(7):709-712. doi:10.1016/j.ajem.2014.03.045
15. Schrock JW, Glasenapp M, Drogell K. Elevated blood urea nitrogen/creatinine ratio is associated with poor outcome in

ischemic stroke. Clin Neurol Neurosurg. 2012;114(7):881-884. doi:10.1016/j.clineuro.2012.01.031
16. Bahouth MN, Hillis AE, Gottesman RF. Dehydration and outcomes after acute stroke: a cohort study. Stroke. 2016;47(Suppl 1):ATP248.
17. Liu H, Chen Y, Zhou Q, et al. Association between the BUN-to-creatinine ratio and 3-month outcomes in patients with acute ischemic stroke. Front Neurol. 2024;15:1350116. doi:10.3389/fneur.2024.1350116
18. Rothwell PM, Howard SC, Dolan E, et al. Prognostic significance of visit-to-visit variability, maximum systolic blood pressure, and episodic hypertension. Lancet. 2010;375(9718):895-905. doi:10.1016/S0140-6736(10)60308-X.