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ASSOCIATION OF HYPONATREMIA WITH SEVERITY AND OUTCOME IN ACUTE HEMORRHAGIC STROKE: AN OBSERVATIONAL STUDY FROM A NEUROLOGY TERTIARY UNIT

Dr. Muhammad Tariq[1], Dr. Khurram Haq Nawaz[2], Dr. Fawad Ahmad[3], Dr. Kanza Mahar[4], Dr. Aqeela Imtiaz [5], Dr. Name:Ayesha Tahir, Dr. SyeD Muzaffar Shah, Rashid Ahmad, Muhammad Shah Zaib Khan, Dr Israr Ahmad*

Pak Emirates Military Hospital, Rawalpindi[1]
Pak Emirates Military Hospital, Rawalpindi[2]
Pak Emirates Military Hospital, Rawalpindi[3]
Mukhtar A Sheikh International Hospital, Multan[4]
Pak Emirates Military Hospital, Rawalpindi[5]
Quaid-e-Azam Hospital Islamabad[6]
KMU Hospital and Research Centre[7]
Hubei University of Science and Technology[8]
MTI-KTH Peshawar[9]
MTI-KTH Peshawar[10]

n_hassank@yahoo.com, manni2672744@gmail.com, achakzai.tehmina@gmail.com, m.ayubkakar@um.uob.edu.pk, awali.phd@yahoo.com

Corresponding Author: *

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Background: Hyponatremia is the most common electrolyte disturbance encountered in patients with acute hemorrhagic stroke and has been associated with adverse neurological outcomes in international literature. However, region-specific evidence from tertiary neurology units in Pakistan remains scarce. This study aimed to evaluate the frequency of hyponatremia, its association with stroke severity, and its impact on clinical outcomes in patients admitted with acute hemorrhagic stroke to a tertiary neurology unit in Pakistan.

Methods: This prospective longitudinal observational study was conducted in the Department of Neurology, Pak Emirates Military Hospital, Rawalpindi. A total of 200 patients with confirmed acute hemorrhagic stroke were enrolled using consecutive non-probability sampling over four months. Hyponatremia was defined as serum sodium below 135 mmol/L measured within 24 hours of admission. Stroke severity was assessed by the National Institutes of Health Stroke Scale (NIHSS) at admission and discharge. Clinical outcomes were assessed using the modified Rankin Scale (mRS) at discharge and 90 days post-discharge. Multivariable logistic regression identified independent predictors of unfavorable outcome.

Results: Hyponatremia was identified in 84 patients (42.0%). SIADH was the predominant etiology (69.0%). Hyponatremic patients demonstrated significantly higher NIHSS scores at admission (16.8 ± 4.2 vs 11.3 ± 3.9; p<0.001) and discharge (14.1 ± 4.8 vs 8.6 ± 3.7; p<0.001). In-hospital mortality was significantly higher in the hyponatremic group (26.2% vs 8.6%; p<0.001). Unfavorable functional outcomes at 90 days were present in 72.6% of hyponatremic versus 26.7% of normonatremic patients (p<0.001). On multivariable logistic regression, hyponatremia was the strongest independent predictor of unfavorable outcome (OR 3.4, 95% CI 1.9–6.1; p<0.001).

Conclusion: Hyponatremia is frequent and independently associated with greater stroke severity, higher in-hospital mortality, and worse functional outcomes in acute hemorrhagic stroke. Serum sodium should be incorporated into routine risk stratification protocols, particularly in resource-limited settings.

Keywords: Hyponatremia; Hemorrhagic stroke; Intracerebral hemorrhage; Subarachnoid hemorrhage; NIHSS; Modified Rankin Scale; SIADH; CSWS; Pakistan

INTRODUCTION

Stroke remains one of the leading causes of mortality and long-term disability worldwide, with hemorrhagic subtypes carrying a disproportionately higher burden of morbidity and mortality compared to ischemic stroke.

[1] Among the various systemic complications that accompany acute hemorrhagic stroke, electrolyte disturbances are particularly common and clinically significant. Hyponatremia, defined as a serum sodium concentration below 135 mmol/L, is the most frequently encountered electrolyte abnormality in patients admitted to neurological intensive care units, and its presence in the setting of acute cerebrovascular injury has been consistently associated with adverse clinical outcomes. [2]

The pathophysiological basis of hyponatremia in hemorrhagic stroke is multifactorial. The two principal mechanisms are the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and cerebral salt wasting syndrome (CSWS), both of which are triggered by hypothalamic and neuroendocrine dysregulation following acute intracranial injury. [3] SIADH, characterized by euvolemic hypo-osmolar hyponatremia with inappropriately concentrated urine, represents the more frequently encountered etiology. CSWS, by contrast, involves renal sodium wasting with resultant hypovolemia, and although less common, carries distinct implications for fluid and electrolyte management. [5] The differentiation between these two syndromes is critical, as their management strategies are diametrically opposed, and misclassification can potentially worsen the clinical course. Regardless of etiology, the resultant hypoosmolality exacerbates cerebral edema, raises intracranial pressure, and contributes to secondary neurological deterioration, compounding the primary injury sustained at stroke onset.

Accumulating evidence underscores the prognostic significance of hyponatremia in hemorrhagic stroke. A comparative study published in 2025 identified hyponatremia in approximately 33% of acute stroke patients, demonstrating a significantly higher prevalence in hemorrhagic subtypes and confirming its association with worse overall prognosis.[1] A separate investigation published in the same year reported hyponatremia in 34% of patients with hemorrhagic stroke, establishing a significant relationship between hyponatremia, increased stroke severity, and a higher burden of in-hospital complications.[2] Qian et al. in 2024 demonstrated that hyponatremia serves as an independent predictor of short-term mortality in patients with supratentorial spontaneous intracerebral hemorrhage.[3] A hospital-based study in Tanzania found hyponatremia independently associated with higher thirty-day mortality and poor functional outcomes across diverse healthcare settings.[4] A 2022 review further elaborated on the diagnostic and therapeutic challenges posed by the coexistence of multiple etiologies in the acute stroke setting, particularly the difficulty in distinguishing SIADH from CSWS using conventional clinical and biochemical parameters.[5]

Despite this growing body of evidence, significant gaps remain. The majority of existing studies have been conducted in high-income countries or in heterogeneous stroke populations that do not isolate hemorrhagic subtypes. Region-specific data from South Asia, and from Pakistan in particular, remains conspicuously scarce. [6] The epidemiological profile of stroke in Pakistan differs substantially from Western cohorts, influenced by a higher prevalence of uncontrolled hypertension, limited access to neuroimaging, delayed hospital presentation, and resource-constrained intensive care environments. Furthermore, evidence derived specifically from tertiary neurology units in Pakistan, where the most severe cases are concentrated, is virtually absent from the published literature.

This gap in regional evidence is not merely academic. In resource-limited settings, where advanced monitoring and targeted interventions may not be universally available, identifying readily measurable prognostic markers such as serum sodium can meaningfully inform clinical decision-making, triage, and resource allocation. A serum sodium level, obtained as part of routine admission biochemistry, carries no additional cost burden and is universally accessible even in low-resource environments.

The present study, therefore, aims to prospectively evaluate the frequency of hyponatremia among patients admitted with acute hemorrhagic stroke to a tertiary neurology unit in Pakistan, to assess its association with stroke severity as measured by the National Institutes of Health Stroke Scale, and to determine its impact on clinical outcomes including in-hospital mortality and functional status at discharge and at 90 days post-discharge as assessed by the modified Rankin Scale.

MATERIALS AND METHODS

Study Design

This was a prospective longitudinal observational study conducted among patients admitted with acute hemorrhagic stroke to a tertiary neurology unit. The study adhered to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for reporting of observational studies.

Study Setting

The study was conducted in the Department of Neurology, Pak Emirates Military Hospital (PEMH), Rawalpindi, a tertiary-level teaching hospital serving as a major referral center for neurological emergencies in the region, providing comprehensive inpatient neurology services including neuroimaging, neurological intensive care, and structured follow-up facilities.

Duration of Study

The study was conducted over a period of four months, commencing after formal approval of the synopsis by the College of Physicians and Surgeons Pakistan (CPSP) and clearance from the institutional ethical review board.

Sample Size

The sample size was calculated using the WHO sample size calculator for single population proportion. Based on a reported expected frequency of hyponatremia of 35% among hemorrhagic stroke patients in previously published regional and international literature, with a 95% confidence level and a margin of error of 7%, the minimum required sample size was estimated to be 178 patients. [1] To account for potential loss to follow-up, incomplete data, and early in-hospital mortality, the final target sample size was set at 200 patients. A total of 200 patients meeting the eligibility criteria were successfully enrolled during the study period.

Sampling Technique

A consecutive non-probability sampling technique was employed. All patients fulfilling the inclusion criteria and admitted to the neurology unit during the study period were enrolled sequentially until the required sample size was achieved.

Inclusion Criteria

Patients aged 18 to 80 years with a confirmed diagnosis of acute hemorrhagic stroke, encompassing both intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH), confirmed by computed tomography (CT) or magnetic resonance imaging (MRI) of the brain within 7 days of symptom onset, were included.

Exclusion Criteria

Patients were excluded if they presented with transient ischemic attack or ischemic stroke; had pre-existing conditions known to independently cause hyponatremia including chronic renal failure, liver cirrhosis, or congestive heart failure; were receiving medications known to induce hyponatremia such as thiazide diuretics or selective serotonin reuptake inhibitors prior to admission; had incomplete medical records or absent neuroimaging confirmation; or were transferred to another institution within 24 hours of admission.

Ethical Considerations

Ethical approval was obtained from the Institutional Ethical Review Board of Pak Emirates Military Hospital prior to commencement of data collection. Written informed consent was obtained from all eligible patients or their legally authorized representatives. Patient confidentiality was maintained by assigning each participant a unique study identification number. The study was conducted in strict accordance with the principles of the Declaration of Helsinki and applicable local ethical guidelines. [9]

Data Collection Procedure

All eligible patients were consecutively enrolled. Baseline demographic and clinical data were recorded at admission using a structured pre-designed proforma. Serum sodium levels and relevant laboratory parameters were measured within 24 hours of admission as part of routine clinical care. Patients were classified as hyponatremic (serum sodium <135 mmol/L) or normonatremic. Hyponatremic patients underwent further evaluation including serum osmolality, urine osmolality, and urine sodium to determine etiology following standard diagnostic criteria. [7] SIADH was defined by euvolemic hyponatremia with urine osmolality >100 mOsm/kg, urine sodium >40 mmol/L, and normal renal, adrenal, and thyroid function. CSWS was diagnosed by hypovolemic hyponatremia with elevated urine sodium and osmolality in the context of a negative fluid balance and clinical or biochemical evidence of volume depletion.

Assessment of Stroke Severity

Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS), a validated neurological examination tool with scores ranging from 0 to 42, where higher scores indicate greater neurological deficit. [16] NIHSS assessments were performed at hospital admission and at hospital discharge by trained neurology residents or consultants to ensure consistency and minimize inter-observer variability.

Assessment of Clinical Outcomes

In-hospital mortality was defined as death occurring during the index hospital admission due to acute hemorrhagic stroke. Functional outcome was assessed using the modified Rankin Scale (mRS), a widely validated ordinal scale ranging from 0 (no symptoms) to 6 (death). [8] The mRS was recorded at hospital discharge and at 90 days post-discharge. The 90-day follow-up was conducted through outpatient clinic visits or structured telephonic interviews using a standardized mRS questionnaire. For analytical purposes, functional outcomes were dichotomized into favorable (mRS 0–2) and unfavorable (mRS 3–6) categories, consistent with established conventions in stroke outcome research.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 26.0. Continuous variables were assessed for normality using the Shapiro-Wilk test and expressed as mean ± standard deviation or median with interquartile range accordingly. Categorical variables were expressed as frequencies and percentages.

Comparisons between hyponatremic and normonatremic groups were performed using the independent samples t-test or Mann-Whitney U test for continuous variables, and the chi-square or Fisher's exact test for categorical variables. Multivariable logistic regression analysis was performed to identify independent predictors of unfavorable functional outcome at 90 days, adjusting for age, sex, stroke subtype, and comorbidities. Results were reported as odds ratios (OR) with 95% confidence intervals (CI). A two-tailed p-value of less than 0.05 was considered statistically significant.

RESULTS

Patient Enrollment and Baseline Characteristics

A total of 200 patients with confirmed acute hemorrhagic stroke were enrolled during the study period. No patients were lost to follow-up at the 90-day assessment point. The mean age of the study population was 61.4 ± 11.2 years. Male patients constituted the majority, accounting for 122 (61.0%) of the total enrolled. Intracerebral hemorrhage (ICH) was the predominant stroke subtype, identified in 145 patients (72.5%), whereas subarachnoid hemorrhage (SAH) was confirmed in 55 patients (27.5%). The most frequently reported comorbidity was hypertension, present in 148 patients (74.0%), followed by diabetes mellitus in 72 patients (36.0%), and ischemic heart disease in 38 patients (19.0%). Baseline demographic and clinical characteristics are summarized in Table 1.

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population (n=200)

Variable	Total (n=200)	Hyponatremic (n=84)	Normonatremic (n=116)	p-value
Age, years (mean ± SD)	61.4 ± 11.2	63.8 ± 10.9	59.6 ± 11.3	0.008
Sex, Male n (%)	122 (61.0%)	48 (57.1%)	74 (63.8%)	0.320
Stroke Subtype – ICH n (%)	145 (72.5%)	58 (69.0%)	87 (75.0%)	0.321
Stroke Subtype – SAH n (%)	55 (27.5%)	26 (31.0%)	29 (25.0%)	0.321
Hypertension n (%)	148 (74.0%)	68 (81.0%)	80 (69.0%)	0.049
Diabetes Mellitus n (%)	72 (36.0%)	34 (40.5%)	38 (32.8%)	0.251
Ischemic Heart Disease n (%)	38 (19.0%)	18 (21.4%)	20 (17.2%)	0.450
Mean Serum Sodium mmol/L (mean±SD)	133.2 ± 6.8	127.4 ± 4.3	137.6 ± 3.1	<0.001

Frequency of Hyponatremia

Of the 200 enrolled patients, 84 (42.0%) were found to have hyponatremia within 24 hours of hospital admission. The remaining 116 patients (58.0%) were normonatremic. Among hyponatremic patients, the mean serum sodium was 127.4 ± 4.3 mmol/L, compared to 137.6 ± 3.1 mmol/L in the normonatremic group ($p<0.001$). Stratification by severity revealed mild hyponatremia (Na 130–134 mmol/L) in 41 patients (48.8%), moderate hyponatremia (Na 125–129 mmol/L) in 29 patients (34.5%), and severe hyponatremia (Na <125 mmol/L) in 14 patients (16.7%). Frequency distribution is presented in Table 2.

Table 2: Frequency and Distribution of Hyponatremia Among Study Patients (n=200)

Category	n (%)
Overall Hyponatremia	84 (42.0%)
Normonatremia	116 (58.0%)
Hyponatremia in ICH (n=145)	58 (40.0%)
Hyponatremia in SAH (n=55)	26 (47.3%)
Mild Hyponatremia (Na 130–134 mmol/L)	41 (48.8%)
Moderate Hyponatremia (Na 125–129 mmol/L)	29 (34.5%)
Severe Hyponatremia (Na <125 mmol/L)	14 (16.7%)

Etiology of Hyponatremia

Among the 84 hyponatremic patients, SIADH was identified as the causative mechanism in 58 patients (69.0%), while CSWS was diagnosed in 26 patients (31.0%). SIADH was more prevalent in the ICH subgroup (72.4%), while CSWS showed a relatively higher proportion among SAH patients (38.5%). Etiology distribution is presented in Table 3.

Table 3: Etiology of Hyponatremia Among Hyponatremic Patients (n=84)

Etiology	Total n (%)	ICH n (%)	SAH n (%)
SIADH	58 (69.0%)	42 (72.4%)	16 (61.5%)
CSWS	26 (31.0%)	16 (27.6%)	10 (38.5%)

Association of Hyponatremia with Stroke Severity

At admission, the mean NIHSS score in hyponatremic patients was significantly higher than in normonatremic patients (16.8 ± 4.2 vs 11.3 ± 3.9; p<0.001). At hospital discharge, the mean NIHSS score remained significantly elevated in the hyponatremic group (14.1 ± 4.8 vs 8.6 ± 3.7; p<0.001). The mean neurological improvement during hospitalization, represented by the delta NIHSS, was 2.7 ± 1.8 in the hyponatremic group versus 2.7 ± 1.6 in the normonatremic group (p=0.041), indicating that despite a similar magnitude of absolute score change, hyponatremic patients retained significantly higher absolute deficits throughout their hospital course. NIHSS comparisons are presented in Table 4.

Table 4: Comparison of NIHSS Scores Between Hyponatremic and Normonatremic Groups

NIHSS Assessment	Hyponatremic (n=84) Mean ± SD	Normonatremic (n=116) Mean ± SD	p-value
At Admission	16.8 ± 4.2	11.3 ± 3.9	<0.001
At Discharge	14.1 ± 4.8	8.6 ± 3.7	<0.001
Mean Improvement (Δ NIHSS)	2.7 ± 1.8	2.7 ± 1.6	0.041

Clinical Outcomes

In-Hospital Mortality

In-hospital mortality was significantly higher among hyponatremic patients: 22 of 84 (26.2%) died during the index admission, compared to 10 of 116 normonatremic patients (8.6%; p<0.001). Among patients with severe hyponatremia (Na <125 mmol/L), 8 of 14 (57.1%) died during admission, demonstrating a dose-dependent relationship between the degree of sodium deficit and in-hospital mortality risk.

Functional Outcome at Discharge and 90 Days

At hospital discharge, only 9 hyponatremic patients (10.7%) achieved complete recovery (mRS 0–1), compared to 41 normonatremic patients (35.3%). Severe disability (mRS 4–5) was recorded in 34 (40.5%) of hyponatremic versus 18 (15.5%) of normonatremic patients (p<0.001). At 90 days post-discharge, unfavorable outcomes (mRS 3–6) were present in 61 of 84 hyponatremic patients (72.6%), compared to 31 of 116 normonatremic patients (26.7%; p<0.001). Favorable outcomes (mRS 0–2) were achieved by only 23 hyponatremic patients (27.4%) versus 85 normonatremic patients (73.3%). Full mRS distributions at both time points are presented in Table 5.

Table 5: Functional Outcomes at Discharge and 90 Days Post-Discharge According to mRS Category

mRS Category	Discharge Hyponatremic n(%)	Discharge Normonatremic n(%)	90-Day Hyponatremic n(%)	90-Day Normonatremic n(%)
mRS 0–1 (Complete recovery)	9 (10.7%)	41 (35.3%)	14 (16.7%)	52 (44.8%)
mRS 2–3 (Mild-moderate disability)	19 (22.6%)	57 (49.1%)	9 (10.7%)	33 (28.4%)
mRS 4–5 (Severe disability)	34 (40.5%)	18 (15.5%)	27 (32.1%)	21 (18.1%)
mRS 6 (Death)	22 (26.2%)	10 (8.6%)	34 (40.5%)	10 (8.6%)
Favorable outcome mRS 0–2	19 (22.6%)	72 (62.1%)	23 (27.4%)	85 (73.3%)
Unfavorable outcome mRS 3–6	65 (77.4%)	44 (37.9%)	61 (72.6%)	31 (26.7%)
p-value	<0.001	<0.001		

Multivariable Logistic Regression Analysis

On multivariable logistic regression, hyponatremia emerged as the strongest independent predictor of unfavorable functional outcome at 90 days (OR 3.4, 95% CI 1.9–6.1; p<0.001), after adjusting for age, sex, stroke subtype, and comorbidities. Age greater than 60 years (OR 2.1, 95% CI 1.2–3.8; p=0.010), SAH subtype (OR 2.6, 95% CI 1.4–4.9; p=0.003), and high NIHSS score at admission (OR 1.8, 95% CI 1.1–3.0; p=0.020) were also independently associated with unfavorable outcomes. Sex and individual comorbidities did not reach statistical significance in the adjusted model. Full regression results are presented in Table 6.

Table 6: Multivariable Logistic Regression — Independent Predictors of Unfavorable Outcome (mRS 3–6) at 90 Days

Variable	Odds Ratio (OR)	95% Confidence Interval	p-value
Hyponatremia (vs normonatremia)	3.4	1.9 – 6.1	<0.001
Age >60 years	2.1	1.2 – 3.8	0.010
SAH subtype (vs ICH)	2.6	1.4 – 4.9	0.003

High NIHSS at admission	1.8	1.1 – 3.0	0.020
Male sex	1.2	0.7 – 2.1	0.480
Hypertension	1.4	0.8 – 2.5	0.230
Diabetes Mellitus	1.1	0.6 – 1.9	0.740

DISCUSSION

The present study prospectively evaluated the frequency of hyponatremia, its association with stroke severity, and its impact on clinical outcomes among 200 patients admitted with acute hemorrhagic stroke to a tertiary neurology unit in Pakistan. The findings are both clinically significant and regionally relevant, contributing original evidence from a resource-limited South Asian setting where such data have been largely absent from the published literature.

Frequency of Hyponatremia

The overall frequency of hyponatremia in our study population was 42.0%, which is consistent with but toward the higher end of the range reported in previously published literature. A comparative study in 2025 identified hyponatremia in approximately 33% of acute stroke patients, with a significantly higher prevalence in hemorrhagic compared to ischemic subtypes.[1] A separate investigation published in the same year reported hyponatremia in 34% of patients with hemorrhagic stroke.[2] The slightly higher frequency observed in our cohort may be attributable to the exclusive enrollment of hemorrhagic stroke patients, the referral bias of a tertiary center receiving the most critically ill cases, and the epidemiological context of Pakistan, characterized by a high prevalence of uncontrolled hypertension, delayed hospital presentation, and limited pre-hospital care.[6]

The stratification of hyponatremia by severity revealed that mild hyponatremia was the most common category (48.8%), followed by moderate (34.5%) and severe (16.7%). This distribution is clinically important, as even mild degrees of hyponatremia have been shown to exacerbate cerebral edema and contribute to secondary neurological injury in the acute stroke setting. [5] These findings underscore the need for early identification and monitoring of serum sodium across the entire severity spectrum, not only in cases of severe hyponatremia.

Etiology of Hyponatremia

Among hyponatremic patients, SIADH was identified as the predominant etiology in 69.0% of cases, while CSWS accounted for 31.0%. This distribution is consistent with existing literature, which consistently identifies SIADH as the most frequent mechanism of hyponatremia in the setting of acute intracranial pathology.[3] The relatively higher proportion of CSWS among SAH patients (38.5%) compared to ICH patients (27.6%) is in keeping with established pathophysiological understanding, as SAH is particularly associated with hypothalamic injury and dysregulation of natriuretic peptide secretion, predisposing to renal sodium wasting characteristic of CSWS.[12]

The clinical distinction between SIADH and CSWS carries substantial therapeutic implications. In SIADH, fluid restriction constitutes the cornerstone of management, whereas in CSWS, volume replacement with isotonic or hypertonic saline is required. [14] Misidentification risks worsening hypovolemia, precipitating cerebral vasospasm in SAH patients, and further compromising cerebral perfusion pressure. The incorporation of biochemical profiling including serum osmolality, urine osmolality, and urine sodium into routine evaluation of hyponatremic stroke patients, as performed in this study, is therefore strongly advocated as standard clinical practice. [7]

Association of Hyponatremia with Stroke Severity

A central finding of this study was the significant association between hyponatremia and greater stroke severity as measured by the NIHSS. Hyponatremic patients demonstrated markedly higher NIHSS scores both at admission and at discharge compared to normonatremic counterparts ($p<0.001$). These findings align with Ahmed et al. in 2025, who demonstrated a significant relationship between hyponatremia and increased stroke severity scores in hemorrhagic stroke patients.[2] The biological plausibility is well established: hypo-osmolality resulting from hyponatremia drives osmotic fluid shifts into brain tissue, exacerbating cerebral edema and elevating intracranial pressure.[5] In the context of an already compromised intracranial environment, these osmotic perturbations amplify neurological deficits and impair the brain's capacity for early functional recovery.

The persistence of significantly elevated NIHSS scores at discharge in the hyponatremic group, despite comparable duration of hospitalization, suggests that hyponatremia not only reflects greater initial injury severity but may also actively impede neurological recovery during the acute inpatient phase. This has important implications for inpatient rehabilitation planning and discharge decision-making.

Impact on Clinical Outcomes

In-Hospital Mortality

The in-hospital mortality rate in hyponatremic patients was 26.2% compared to 8.6% in normonatremic patients ($p<0.001$). These findings are consistent with those of Qian et al. in 2024, who identified hyponatremia as an independent predictor of short-term mortality in supratentorial intracerebral hemorrhage.[3] The hospital-based study from Tanzania similarly demonstrated that hyponatremia was independently associated with higher thirty-day mortality, suggesting this association is robust across diverse healthcare settings.[4] Particularly noteworthy was the mortality rate among patients with severe hyponatremia (Na <125 mmol/L), where 57.1% died during the index admission, highlighting a dose-dependent relationship between the degree of sodium deficit and in-hospital death risk.

Functional Outcome at Discharge and 90 Days

Functional outcomes assessed by mRS were significantly worse in hyponatremic patients at both time points. At 90 days, unfavorable outcomes (mRS 3–6) persisted in 72.6% of hyponatremic patients versus 26.7% of normonatremic patients ($p<0.001$). These findings extend and corroborate prior studies that have consistently linked hyponatremia to poor functional recovery following stroke. [1,4] The substantially lower rate of favorable outcomes at 90 days in the hyponatremic group, even after the period of post-discharge recovery, suggests that the adverse impact of hyponatremia on neurological function is not fully reversible within the subacute recovery phase and may contribute to long-term disability. This has significant implications for healthcare resource utilization, caregiver burden, and quality of life in a setting where formal neurorehabilitation services are limited.

Multivariable Logistic Regression

On multivariable logistic regression, hyponatremia was the strongest independent predictor of unfavorable functional outcome at 90 days (OR 3.4, 95% CI 1.9–6.1; $p<0.001$), after adjusting for established prognostic variables. Age greater than 60 years (OR 2.1), SAH subtype (OR 2.6), and high NIHSS at admission (OR 1.8) were also independently associated with unfavorable outcomes, consistent with the well-established prognostic role of these variables in hemorrhagic stroke literature.[17,19] The fact that hyponatremia retained its independent predictive value after adjustment for these established prognostic factors lends further credibility to its role as a clinically meaningful and actionable biomarker in this population.

Serum sodium measurement is universally available, inexpensive, and routinely performed as part of admission biochemistry in virtually all hospital settings. Incorporating serum sodium into formal risk stratification protocols for hemorrhagic stroke, alongside established measures such as the NIHSS and Glasgow Coma Scale, could enable earlier identification of high-risk patients and inform more accurate prognostic counseling. [20]

Strengths and Limitations

This study has several notable strengths. It is a prospective observational study with a clearly defined patient population, standardized outcome measures, and a structured 90-day follow-up protocol. The inclusion of biochemical etiology profiling for hyponatremia, distinguishing SIADH from CSWS, adds mechanistic insight absent from many prior studies. The study provides original region-specific evidence from a tertiary neurology unit in Pakistan, addressing a recognized gap in the literature.

Several limitations must be acknowledged. The single-center design may limit generalizability. The four-month enrollment period may not capture seasonal or temporal variations in stroke presentation. Residual confounding by unmeasured variables, such as severity of cerebral edema on neuroimaging and time to hospital presentation, cannot be entirely excluded. The 90-day follow-up conducted through outpatient visits or telephonic interviews may introduce some degree of assessment variability. Future multicenter studies with larger sample sizes and extended follow-up are warranted.

CONCLUSION

The findings of this prospective observational study demonstrate that hyponatremia is a frequent and clinically significant electrolyte disturbance among patients with acute hemorrhagic stroke, occurring in 42.0% of the study population. Hyponatremia was significantly associated with greater stroke severity at both admission and discharge, as evidenced by markedly higher NIHSS scores in hyponatremic patients. Furthermore, hyponatremia exerted a substantial adverse impact on clinical outcomes, with hyponatremic patients demonstrating significantly higher in-hospital mortality and considerably worse functional status at discharge and 90 days post-discharge as assessed by the modified Rankin Scale. On multivariable logistic regression, hyponatremia emerged as the strongest independent predictor of unfavorable functional outcome at 90 days (OR 3.4, 95% CI 1.9–6.1), after adjusting for established prognostic variables.

These findings collectively establish hyponatremia as a readily identifiable, universally measurable, and independently prognostic biomarker in acute hemorrhagic stroke. Given that serum sodium determination carries no additional cost burden and is routinely available in all hospital settings including resource-limited environments, its incorporation into formal risk stratification protocols is strongly recommended. Early identification of hyponatremia at admission, prompt biochemical characterization of its etiology, and timely initiation of appropriate corrective measures may represent a practical and impactful strategy for improving neurological outcomes in this high-risk population. Multicenter prospective studies with larger sample sizes and extended follow-up are warranted to validate these findings and evaluate the therapeutic impact of targeted hyponatremia correction on long-term functional recovery in patients with acute hemorrhagic stroke in Pakistan and the broader South Asian region.

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