Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/2bw9v769

IMPACT OF HYPONATREMIA ON CLINICAL OUTCOMES, RECOVERY, AND MORTALITY IN STROKE PATIENTS

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ABSTRACT

Background: Low sodium levels in the blood, known as Hyponatremia is a usual electrolyte ailment in stroke patients and may contribute to adverse clinical outcomes.

Objective: This study evaluates the impact of hyponatremia on functional recovery, hospital mortality, and hospital stay in stroke patients.

Methods: This multicentre prospective study was carried out at three medical universities from July to December 2024. A total of 300 stroke patients were registered using consecutive sampling. Hyponatremia was defined as serum sodium <135 mEq/L at admission. Clinical outcomes, including hospital stay, GCS, mRS, complications, and mortality, were compared between hyponatremic and normonatremic patients. Multivariate logistic regression identified independent mortality predictors.

Results: Hyponatremia was observed in 90 (30%) patients. Hyponatremic patients had significantly longer hospital stays (9.2 ± 3.1 vs. 6.8 ± 2.4 days, p<0.001), lower GCS at admission (10.9 ± 3.0 vs. 12.8 ± 2.6, p<0.001), and altered rates of ICU admission (26.7% vs. 14.3%, p=0.006). They also had increased in-hospital complications, including aspiration pneumonia (22.2% vs. 11.9%, p=0.02) and seizures (15.6% vs. 8.6%, p=0.05). In-hospital mortality was significantly increased in hyponatremic patients (15.6% vs. 5.7%, p=0.005). Hyponatremia independently predicted mortality (OR 2.98, p=0.01).

Conclusion: Hyponatremia in stroke patients is associated to prolonged hospitalization, increased ICU admissions, worse neurological outcomes, and higher mortality. Early identification and management of hyponatremia may improve clinical outcomes.

KEYWORDS: Hyponatremia, Stroke, Clinical Outcomes, Mortality, Recovery

INTRODUCTION

Stroke is the second foremost reason of mortality and the third most known cause of death and disability globally, despite recent medical advancements [1]. Approximately 65% of strokes are ischemic, characterized by episodes of neurological impairment resulting from focal cerebral, spinal, or retinal infarction [2]. Electrolyte imbalances frequently occur due to stroke-related comorbidities such as diabetes mellitus, hypertension, and congestive heart failure.

Hyponatremia (serum sodium <135 mmol/L) is one of the most prevalent electrolyte abnormalities observed in ischemic stroke patients [3,4]. It is commonly reported in cases of intracerebral hemorrhage, ischemic stroke, and subarachnoid hemorrhage [5,6]. In the context of acute stroke, hyponatremia may negatively impact disease progression by exacerbating brain edema and worsening neurological deficits [6]. While stroke-related comorbidities are often implicated in hyponatremia, mechanisms such as cerebral salt wasting (CSW), the syndrome of inappropriate antidiuretic hormone secretion (SIADH), and pituitary ischemia have also been proposed as underlying causes of stroke-induced hyponatremia [6,7].

Hyponatremia has been linked to an increased risk of mortality in both the short term (hazard ratio = 1.78, 95% CI = 1.19–2.75) and long term (hazard ratio = 2.23, 95% CI = 1.30–3.82), according to a meta-analysis of 21,973 stroke cases [8]. A study by Rodrigues et al. found that patients who are having hyponatremia had lower National Institutes of Health Stroke Scale (NIHSS) scores. These scores are lower both at admission and discharge compared to patients with normal levels of sodium [9]. Early identification and correction of hyponatremia in stroke patients may help reduce adverse outcomes and mortality. This study aims to determine the occurrence of hyponatremia in stroke patients. It also assess the connection of hyponatremia with clinical outcomes, recovery, and in-hospital mortality.

Methodology

The present study is a multicenter prospective observational study. This has been carried out at Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, Isra University, Hyderabad, and Peoples University of Medical and Health Sciences (PUMHS), Nawabshah. The study spans six months, from July 2024 to December 2024. The study aims to assess the effect of hyponatremia on clinical outcomes, mortality and recovery in stroke patients. The study protocol was permitted by the respective Institutional Review Boards. An informed consent, in writing, was attained from all participants or their legal guardians beforehand.

A total of 300 stroke patients were participated in the study. The sample size was calculated using OpenEpi software. An expected prevalence of hyponatremia was considered in stroke patients of 20%, a confidence level of 95%, and a margin of error of 5%. A non-probability method of consecutive sampling technique was used to select the participants.

All the patients admitted within 48 hours of onset of the symptoms of low serum sodium levels with age ≥18 years, were scrutinized to include in the study. Among theese patients who were diagnosed with ischemic or hemorrhagic stroke based on clinical assessment and neuroimaging (CT or MRI) were selected. Stroke was defined according to the updated definition by the American Heart Association/American Stroke Association as "an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction" [10]. Hyponatremia was defined as serum sodium levels <135 mEq/L [11], measured at the time of admission. Patients who were with pre-existing electrolyte disorders, chronic kidney disease, uncontrolled diabetes mellitus, taking diuretics or hypertonic saline therapy and liver cirrhosis were excluded from the study to minimize confounding factors.

The primary outcome measures included in-hospital mortality, functional recovery assessed using the modified Rankin Scale (mRS) at discharge, and time duration of hospital stay. Secondary parameters involved the Glasgow Coma Scale (GCS) score at admission and discharge, incidence of in-hospital complications such as aspiration pneumonia, seizures, or deep vein thrombosis, and requirement for intensive care unit (ICU) admission. Laboratory parameters, including serum sodium levels, blood glucose, creatinine, and inflammatory markers (C-reactive protein), were documented at baseline and monitored during the hospital stay.

All data were recorded on a structured proforma and examined using SPSS version 26.0. Categorical variables were presented as percentages and frequencie. Comparisons among normonatremic and hyponatremic stroke patients were made using the chi-square test. Continuous variables were expressed as mean ± standard deviation (SD) and analyzed involving Mann-Whitney U test or an independent t-test based on data distribution. The association between hyponatremia and clinical outcomes was measured using multivariate logistic regression analysis, adjusting for potential confounders such as stroke type, age, comorbid conditions. A p-value of <0.05 was considered statistically significant.

Results

A total of 300 stroke patients were participated in the study, of which 90 (30%) had hyponatremia at the time of admission. The mean age of the study populace was 62.4 ± 11.8 years, with a male predominance (56.3%). Patients with hyponatremia were significantly older (65.1 ± 12.2 years) compared to normonatremic patients (61.2 ± 11.5 years, p = 0.02). Patients with hyponatremia were significantly older and had a advanced level of occurrence of hypertension compared to normonatremic patients. The distribution of ischemic and hemorrhagic stroke was similar in both groups (Table 1).

Table 1: Baseline Features of Participants

Variable	Normonatremia (n=210)	Hyponatremia (n=90)	p-value
Age in years (mean ± SD)	61.2 ± 11.5	65.1 ± 12.2	0.02
Male (%)	115 (54.8)	54 (60.0)	0.43
Hypertension (%)	120 (57.1)	65 (72.2)	0.01
Diabetes Mellitus (%)	85 (40.5)	42 (46.7)	0.35
Ischemic Stroke (%)	165 (78.6)	64 (71.1)	0.18
Hemorrhagic Stroke (%)	45 (21.4)	26 (28.9)	0.18

Patients with hyponatremia had significantly higher ICU admission rates, lengthier hospital stay, and lower GCS scores at both admission and discharge. A higher proportion of hyponatremic patients had poor functional recovery (mRS ≥3) and mortality compared to normonatremic patients (Table 2).

Table 2: Clinical Outcomes of Patients with and without Hyponatremia

Outcome	Normonatremia (n=210)	Hyponatremia (n=90)	p-value
Hospital Stay Duration (days, mean ± SD)	6.8 ± 2.4	9.2 ± 3.1	<0.001
ICU Admission (%)	30 (14.3)	24 (26.7)	0.006
Admission GCS (mean ± SD)	12.8 ± 2.6	10.9 ± 3.0	<0.001
Discharge GCS (mean ± SD)	14.1 ± 2.1	12.2 ± 2.8	<0.001
mRS Score (≥3 at Discharge, %)	80 (38.1)	50 (55.6)	0.004
In-Hospital Mortality (%)	12 (5.7)	14 (15.6)	0.005

Hyponatremic patients had significantly higher rates of aspiration pneumonia and seizures, while deep vein thrombosis incidence was not significantly dissimilar among the groups (Table 3).

Table 3: Association of Hyponatremia with In-Hospital Complications

Complication	Normonatremia (n=210)	Hyponatremia (n=90)	p-value
Aspiration Pneumonia (%)	25 (11.9)	20 (22.2)	0.02
Seizures (%)	18 (8.6)	14 (15.6)	0.05
Deep Vein Thrombosis (%)	10 (4.8)	8 (8.9)	0.19

Hyponatremia was independently related with increased in-hospital mortality (OR 2.98, p = 0.01) after altering for age, ICU admission, and GCS at admission. ICU admission and lower GCS at admission were also strong predictors of mortality (Table 4).

Table 4: Multivariate Logistic Regression Analysis for In-Hospital Mortality

Variable	Adjusted Odds Ratio (95% CI)	p-value
Hyponatremia	2.98 (1.21 – 7.32)	0.01
Age (per year increase)	1.07 (1.02 – 1.12)	0.005
ICU Admission	4.21 (1.85 – 9.55)	<0.001
GCS at Admission	0.85 (0.78 – 0.93)	0.002

Discussion

Hyponatremia is a common electrolyte disorder in stroke patients which is frequently observed and has been linked to adverse clinical outcomes, including prolonged hospital stays, increased mortality, and poorer neurological recovery. Our study aimed to evaluate the prevalence of hyponatremia among stroke patients and its impact on clinical outcomes. The findings indicate that hyponatremia at admission is significantly linked to increased in-hospital mortality, prolonged hospitalization, and higher rates of ICU admission, consistent with previously published literature. The prevalence of hyponatremia was 30% in our study aligning with earlier reports, such as a prospective study conducted in 2014 that found a comparable rate of 35.3% [13]. However, variations in prevalence have been noted in different populations, with Rodrigues et al. reporting a lower frequency of 16% in ischemic stroke patients [9]. The discrepancy in prevalence may be attributed to differences in patient selection, definitions of hyponatremia, and the inclusion of both ischemic and hemorrhagic stroke cases in some studies. The underlying mechanisms of hyponatremia in stroke patients remain debated, but the cerebral salt wasting (CSW) and syndrome of inappropriate antidiuretic hormone secretion (SIADH) are frequently implicated [7,14].

Results of our study show that patients with hyponatremia were significantly older than normonatremic patients. The similar trend that has also been reported in prior studies [12]. Aging is associated with changed sodium homeostasis due to reduced renal function and decreased thirst response. Moreover, the higher prevalence of hypertension in the hyponatremic group (72.2% vs. 57.1%, p = 0.01) is noteworthy, as hypertension has been independently linked to both stroke severity and electrolyte disturbances [9].

The clinical outcomes seen in this study further highlight the predictive significance of hyponatremia in stroke patients. Patients with hyponatremia had significantly longer hospital stays (9.2 ± 3.1 vs. 6.8 ± 2.4 days, p < 0.001), higher ICU admission rates (26.7% vs. 14.3%, p = 0.006), and lower Glasgow Coma Scale (GCS) scores at both admission and discharge. These findings are in line with previous published research that has identified hyponatremia as an independent predictor of prolonged hospitalization and critical care requirements [12,15]. The association between hyponatremia and decreased GCS scores may be attributed to the exacerbation of cerebral edema and osmotic imbalances, leading to neurological worsening and delayed recovery [16].

Importantly, the functional outcomes assessed using the modified Rankin Scale (mRS) further highlight the negative impact of hyponatremia, with a significantly higher proportion of patients exhibiting poor functional recovery (mRS ≥ 3) at discharge (55.6% vs. 38.1%, p = 0.004). This bring into line with conclusions from previous studies, such as Rodrigues et al., who reported that hyponatremia was an independent predictor of poor NIHSS scores at both admission and discharge, as well as unfavorable discharge dispositions [9]. Additionally, a 2022 study demonstrated that lesser serum sodium levels were independently allied with a poor three-month functional outcome (OR = 1.647, 95% CI = 1.012-2.679) [17]. The worsening of cerebral edema and osmotic demyelination following aggressive correction of hyponatremia may contribute to these poor neurological outcomes [12,15].

In-hospital mortality was significantly higher among hyponatremic patients (15.6% vs. 5.7%, p = 0.005), with multivariate logistic regression confirming that hyponatremia was independently associated with increased mortality (OR = 2.98, p = 0.01) after altering for age, ICU admission, and GCS at admission. These results are aligned with prior studies that have demonstrated a significant correlation among hyponatremia and increased short-term and long-term mortality in stroke patients [18]. Huang et al. reported that hyponatremia was a noteworthy predictor of three-year mortality following ischemic stroke (HR = 2.23, 95% CI = 1.30-3.82, p = 0.003) [18]. Additionally, Soiza et al. found that hyponatremia was independently linked to higher rate of mortality in acute stroke patients younger than 75 years [19]. However, a multicenter study in China found no significant association between hyponatremia and in-hospital mortality (p = 0.905), highlighting the need for further research to clarify this relationship [20].

Regarding in-hospital complications, our study found that hyponatremic patients had significantly higher rates of aspiration pneumonia (22.2% vs. 11.9%, p = 0.02) and seizures (15.6% vs. 8.6%, p = 0.05). These findings are consistent with prior studies indicating that hyponatremia is linked to an increased risk of aspiration due to reduced consciousness and impaired swallowing reflexes [16]. Seizures, a well-documented consequence of electrolyte disturbances, have been attributed to neuronal excitability changes induced by hyponatremia [16]. However, the incidence of deep vein thrombosis (DVT) was not significantly different among the two groups (8.9% vs. 4.8%, p = 0.19), suggesting that hyponatremia does not independently contribute to thromboembolic complications in stroke patients.

Our study has certain limitations. Initially, being a single-center observational study, causality cannot be established. Second, we assessed the impact of hyponatremia on disability and mortality using only sodium levels at admission without considering the severity or duration of hyponatremia. Third, our study focused only on in-hospital mortality without long-term follow-up, limiting our ability to determine its impact on post-discharge outcomes. Future studies should explore whether timely and targeted correction of hyponatremia can progress functional results and decrease mortality in stroke patients.

Conclusions

Hyponatremia is a recurrent electrolyte disturbance in acute ischemic stroke patients and is connected with increased ICU admissions, prolonged hospitalization, poor neurological recovery, and higher in-hospital mortality. Given its significant prognostic implications, routine monitoring and careful management of sodium levels in stroke patients are crucial. Further research is required to determine whether interventions intended at correcting hyponatremia can improve clinical outcomes and survival rates in this patient population.

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