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STUDY ON CHANGES IN SERUM SODIUM LEVELS IN PATIENTS WITH INTRACEREBRAL HEMORRHAGE AND RELATED FACTORS

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ABSTRACT

Objective: *To describe the variations in serum sodium levels in patients with intracerebral hemorrhage (ICH) and to analyze associated factors.*

Subjects and methods: *A prospective longitudinal descriptive analytical study was conducted on 112 patients diagnosed with ICH and treated at the Intensive Care Unit of Military Hospital 175 from June 2023 to December 2024.*

Results: *This study evaluated sodium disturbances in 112 ICH patients. Hyponatremia was observed in 59 patients (52.7%), primarily of mild severity (52.6%). The main causes were syndrome of inappropriate antidiuretic hormone secretion (SIADH, 35.6%) and cerebral salt-wasting syndrome (CSWS, 25.4%), while 39% of cases had unidentified etiologies. Hyponatremia was significantly associated with hypertension (OR = 2.6, p = 0.036), smoking (OR = 2.4, p = 0.048), and large hematoma volume (> 60 cm³, p = 0.028). Frontal lobe lesions showed a potential association with hyponatremia (OR = 3.1, p = 0.076).*

Conclusion: *Hyponatremia is common among patients with intracerebral hemorrhage and is associated with hypertension, smoking, and hematoma volume. SIADH and CSWS are the leading causes; however, further research is needed to clarify the cases with unknown etiology.*

Keywords: *Intracerebral hemorrhage, Frontal lobe, Syndrome of inappropriate antidiuretic hormone secretion (SIADH).*

1. INTRODUCTION

Intracerebral hemorrhage (ICH) is a critical medical emergency characterized by spontaneous bleeding into the brain parenchyma and is associated with a high mortality rate. This condition disrupts normal physiological processes, including the maintenance of serum electrolyte balance, particularly sodium homeostasis. Alterations in electrolyte balance-especially changes in serum sodium levels-play a significant role in both the pathophysiology and clinical management strategies of ICH. Several studies have demonstrated that electrolyte disturbances can exacerbate

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neurological injury and worsen patient outcomes [1], [2].

Acute stroke patients, including those with ICH, commonly present with significant electrolyte abnormalities, among which hyponatremia is the most frequent [2], [3]. Hyponatremia has been associated with increased disease severity in ICH patients and is also correlated with hypoalbuminemia [4]. Approximately 24% of patients with spontaneous ICH develop hyponatremia, often due to the syndrome of inappropriate antidiuretic hormone secretion (SIADH), and this condition is linked to prolonged hospitalization and a higher complication rate [5].

Early detection and appropriate management of sodium imbalances may contribute to prognostication and play a critical role in improving the clinical outcomes of patients with ICH [1]. Therefore, the present study aimed to describe the variations in serum sodium levels in patients with intracerebral hemorrhage and to analyze associated factors.

2. SUBJECTS AND RESEARCH METHODS

** Study subjects*

This study was conducted on 112 patients who were admitted to the Intensive Care Unit of Military Hospital 175 with a confirmed diagnosis of intracerebral hemorrhagic stroke between June 2023 and December 2024.

- Inclusion criteria:

+ Diagnosis of intracerebral hemorrhage based on the World Health Organization (WHO) 1989 definition of stroke.

+ Radiological confirmation of intracerebral bleeding on CT scan.

+ Patients or their legal representatives provided informed consent to participate in the study.

- Exclusion criteria:

+ History of heart failure, chronic kidney disease, adrenal insufficiency, hypothyroidism, pituitary disorders, brain or meningeal tumors, tuberculous meningitis, secondary hemorrhage following cerebral infarction.

+ Use of anticoagulant medications or presence of coagulopathy-related conditions.

+ Patients or their families who declined to participate in the study.

** Research methods*

- Study design:

This was a prospective longitudinal descriptive study with analytical components.

- Sample size: A convenience sampling method was applied, including all patients diagnosed with intracerebral hemorrhagic stroke who were treated in the Intensive Care Unit of Military Hospital 175 from June 2023 to December 2024 and met the inclusion and exclusion criteria.

- Study parameters and variables

+ General characteristics of the study population: Age, sex, reason for hospital admission; onset characteristics (gradual, exertional, sudden); time from symptom onset to hospital admission; pre-hospital treatment history; medical history including hypertension, diabetes mellitus, previous stroke, hyperlipidemia, smoking, alcohol use. Patients were categorized into hyponatremia and normonatremia groups for comparative analysis.

+ Serum sodium variation: Plasma electrolyte testing was performed to evaluate increases or decreases in serum sodium levels during the first 72 hours after hospital admission. The severity of hyponatremia was also assessed.

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+ Correlation analyses: Association between hyponatremia and past medical history or location of brain injury; Association between size of cerebral lesion and serum sodium level.

- Data collection and statistical analysis:

Collected data were entered and stored using Microsoft Excel 365. Statistical analysis was performed using SPSS version 22.0.

3. RESULTS

This prospective observational study included 112 patients diagnosed with intracerebral hemorrhage and treated at the hospital from January 2023 to December 2024. Among them, 59 patients (52.7%) exhibited hyponatremia, 20 (17.9%) had hypernatremia, and 33 (29.4%) maintained normal serum sodium levels during hospitalization.

Table 3.1. Demographic, clinical, and medical history characteristics of patients (n = 112)

Variable		Frequency (n)	Percentage (%)
Mean age (years)		**61.4 ± 10.2**	
Sex	Male	74	66.1
	Female	38	33.9
Reason for hospital admission	Hemiparesis	64	57.1
	Altered consciousness	30	26.8
	Headache, nausea/vomiting	18	16.1
Time from symptom onset to admission (hours) (mean ± SD)		18.5 ± 7.9	
Onset characteristics	Sudden	72	64.3
	Exertional	26	23.2
	Gradual	14	12.5
History of prior treatment	Yes	52	46.4
	No	60	53.6
Medical history	Hypertension	67	59.8
	Diabetes mellitus	15	13.4
	Dyslipidemia	21	18.8
	Previous stroke	10	8.9
	Smoking	40	35.7
	Regular alcohol consumption	28	25.0

The study population included 112 patients with a mean age of 61.4 ± 10.2 years; 66.1% were male. The most common reason for admission was hemiparesis (57.1%), followed by altered consciousness (26.8%) and headache/nausea (16.1%). The average time from symptom onset to hospital admission was 18.5 ± 7.9 hours, with 64.3% presenting with sudden onset. The most common comorbidities were hypertension (59.8%), smoking (35.7%), and dyslipidemia (18.8%).

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Table 3.2. Severity of hyponatremia in patients with intracerebral hemorrhage (n = 59)

Severity of hyponatremia	Frequency (n)	Percentage (%)
Severe (<125 mmol/L)	10	16.9
Moderate (125-129 mmol/L)	18	30.5
Mild (130-134 mmol/L)	31	52.6
Total	**59**	**100**

Among 59 patients with hyponatremia, mild hyponatremia (130-134 mmol/L) accounted for the majority (52.6%), followed by moderate (30.5%) and severe cases (16.9%).

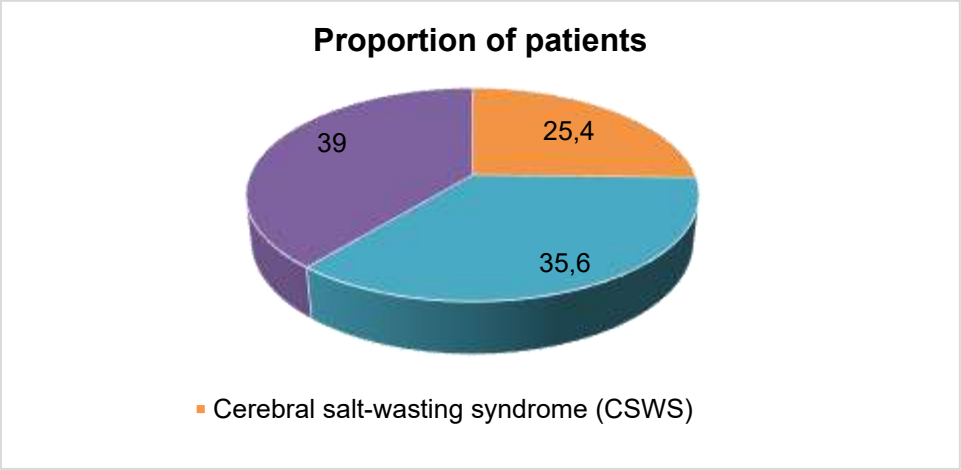

Figure 3.1. Causes of hyponatremia in patients with intracerebral hemorrhage

The most common cause was the syndrome of inappropriate antidiuretic hormone secretion (SIADH: 35.6%), followed by cerebral salt-wasting syndrome (CSWS: 25.4%). However, in 39% of cases, the underlying cause could not be determined.

Table 3.4. Association between hyponatremia and medical history, brain lesion location (n = 96)

Characteristic		Hyponatremia (n = 59)	Normonatremia (n = 33)	OR (95% CI)	p-value
Medical history	Hypertension	47 (79.7%)	20 (60.6%)	2.6 (1.0-6.8)	0.036
	Diabetes mellitus	12 (20.3%)	3 (9.1%)	2.5 (0.6-9.8)	0.188
	Smoking	30 (50.8%)	10 (30.3%)	2.4 (1.0-5.9)	0.048
Lesion location	Frontal lobe	14 (23.7%)	3 (9.1%)	3.1 (0.8-11.6)	0.076
	Basal ganglia	18 (30.5%)	12 (36.4%)	0.8 (0.3-2.0)	0.542
	Ventricular system	27 (45.8%)	18 (54.5%)	0.7 (0.3-1.7)	0.395

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Patients with hyponatremia had a higher prevalence of hypertension compared to the normonatremic group (79.7% vs. 60.6%, OR = 2.6, p = 0.036). Similarly, smoking was more common in the hyponatremia group (50.8% vs. 30.3%, OR = 2.4, p = 0.048). Frontal lobe involvement showed a trend toward association with hyponatremia (23.7% vs. 9.1%, OR = 3.1), though the difference was not statistically significant (p = 0.076).

Table 3.5. Association between hyponatremia and hematoma volume

Hematoma Volume (cm^3)	Hyponatremia (n = 59)	Normonatremia (n = 33)	p-value
<30	21 (35.6%)	20 (60.6%)	0.028
30-60	23 (39.0%)	10 (30.3%)	
>60	15 (25.4%)	3 (9.1%)	

Patients with hyponatremia had a higher proportion of large hematoma volumes (>60 cm^3) compared to those with normal sodium levels (25.4% vs. 9.1%, p = 0.028). Conversely, patients with normonatremia were more likely to have small hematomas (<30 cm^3, 60.6% vs. 35.6%).

4. DISCUSSION

In a cohort of 96 patients with intracerebral hemorrhage (ICH), the incidence of hyponatremia (serum sodium <135 mmol/L) was 52.7%, notably higher than previously reported. Large-scale studies of spontaneous ICH have shown that hyponatremia at admission typically occurs in only 10-20% of cases. For example, Kuramatsu et al. reported hyponatremia in 15.6% of ICH patients and found that it doubled the risk of in-hospital mortality [6]. Similarly, Carcel et al. observed hyponatremia in 12% of cases, with an independent association with increased 90-day mortality (18% vs. 11%, OR ≈ 1.8) [7]. A more recent study by Qian et al. involving 960 ICH patients reported that 19.6% developed hyponatremia within the first 7 days, and that this was an independent predictor of 90-day mortality (OR ≈ 2.76) [8]. The disproportionately high rate of hyponatremia in the present cohort may reflect more severe clinical presentations or a higher burden of comorbidities.

SIADH is considered the predominant mechanism of hyponatremia following ICH. Qian et al. found that 64.9% of hyponatremia cases were attributed to SIADH, while 22.3% were due to cerebral salt-wasting syndrome (CSWS) [8]. Similarly, Gray et al. reported that up to 90% of hyponatremia cases were SIADH-related [5]. These findings are consistent with the known prevalence of SIADH after central nervous system injuries. Therefore, most cases of hyponatremia in ICH should be managed under the assumption of inappropriate ADH secretion, warranting fluid restriction and sodium correction.

Regarding associated factors, hypertension and smoking are well-established risk factors for ICH [9]. However, current and prior analyses, including that of Gray et al., did not show significant differences in the prevalence of these comorbidities between hyponatremic

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and normonatremic groups (e.g., hypertension: 79% vs. 83%, p = 0.77; smoking: 32% vs. 42%, p = 0.39) [5]. This suggests that while these factors contribute to the risk of ICH, they may not influence the development of hyponatremia post-hemorrhage. In contrast, hematoma volume appears to be more closely linked to hyponatremia. Carcel et al., in an analysis of 3,243 ICH patients, found significantly larger hematoma volumes in patients with hyponatremia (p = 0.046) [7]. A similar trend was observed in our cohort, where the median hematoma volume in hyponatremic patients was higher (32 mL vs. 22 mL), although this was not statistically significant in Gray et al.'s study (p = 0.30) [5]. Larger hematomas may increase intracranial pressure and stimulate neuroendocrine or inflammatory responses, including non-osmotic ADH release.

Data on lesion location and its association with hyponatremia remain inconclusive. Gray et al. reported no significant differences in hyponatremia prevalence across ICH locations (p > 0.05), and notably, none of the patients with brainstem or cerebellar involvement developed hyponatremia (p = 0.06) [5]. Although limited by small numbers, these findings highlight the importance of serum sodium monitoring even in clinically severe subtypes such as brainstem hemorrhages. Previous studies have consistently demonstrated a poor prognosis in ICH patients with hyponatremia. Kuramatsu et al. found that hyponatremia was associated with a doubling in-hospital mortality (40.9% vs. 21.1%) and was an independent predictor of death [6]. Carcel et al. similarly reported that hyponatremia increased 90-day mortality (18% vs. 11%, adjusted OR ≈ 1.8) [7]. These associations remained independent of known prognostic variables, including age, Glasgow Coma Scale, and ICH score [6], [8]. Collectively, the data underscore the importance of early identification and correction of hyponatremia in improving outcomes, though the precise mechanisms (e.g., impact on cerebral edema or cardiovascular events) warrant further investigation.

The findings presented here corroborate and expand upon existing literature on hyponatremia in ICH. While the observed prevalence was higher than reported elsewhere, the associations with SIADH and hematoma volume were consistent with prior studies [7]. In contrast, factors such as hypertension, smoking, and lesion location did not show strong associations with hyponatremia, aligning with findings by Gray et al. [5].

5. CONCLUSION

The study identified hyponatremia as a common electrolyte disturbance in patients with intracerebral hemorrhage, characterized by a high prevalence and association with several clinical factors such as hypertension, smoking, hematoma volume, and frontal lobe involvement. The syndrome of inappropriate antidiuretic hormone secretion (SIADH) and cerebral salt-wasting syndrome (CSWS) were identified as the primary underlying mechanisms. These findings contribute to a better understanding of the epidemiological and pathophysiological characteristics of hyponatremia in the context of intracerebral hemorrhage, underscoring the importance of early detection and management of sodium imbalance to improve patient outcomes and guide the development of more tailored clinical care strategies in the future.

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