



A COMPREHENSIVE ANALYSIS OF SODIUM LEVEL CHANGES IN ISCHEMIC STROKE PATIENTS: IDENTIFYING RISK FACTORS AND HYPONATREMIA CONTRIBUTORS

Abdur Raheem Arshed¹, Ahmad Fiaz Raza², Ali Atiq³, Sameeha⁴, Syed Musa Raza⁵, Awais Habib⁶, Bilal Qammar^{7*}

¹King Edward Medical University, Lahore, Pakistan, Email: a.raheemarshed@gmail.com

²Shalamar Medical and Dental College, Lahore, Pakistan, Email: ahmadfayyaz985@gmail.com

³CMH, Lahore, Pakistan, Email: aliatiq006@gmail.com

⁴King Edward Medical University, Lahore, Pakistan, Email: sameeha.ismail357@gmail.com

⁵Shalamar Medical and Dental College, Lahore, Pakistan, Email: alrazams@gmail.com

⁶King Edward Medical University, Lahore, Pakistan, Email: awaishabib786@hotmail.com

^{7*}Shalamar Medical and Dental College, Lahore, Pakistan, Email: bilal.qamar.5680@gmail.com

***Corresponding Author:** Bilal Qammar

*Shalamar Medical and Dental College, Lahore, Pakistan. Email: bilal.qamar.5680@gmail.com

Abstract:

Background: The occurrence of hyponatremia is a prevalent electrolyte anomaly observed commonly in individuals diagnosed with both ischemic and hemorrhagic strokes. The substance mainly exhibits hypoosmolality and is indicative of the syndrome of inappropriate antidiuretic hormone secretion (SIADH) or cerebral salt-wasting syndrome (CSWS). This study aimed to assess the clinical range, such as frequency, severity, and association, of hyponatremia in stroke patients.

Objective: The primary objective of the research is to analyze the factors that play a critical role in the identification of hyponatremia in ischemic stroke patients during hospital admission and treatment.

Method: The study chose a quantitative primary method to evaluate and extract responses. 100 patients have been selected to volunteer in the study. All of the patients admitted to Hospital for Ischemic Stroke or else have a prior history of Ischemic Stroke. SPSS has been used to examine the response and generate the results in graphical format. Respondents have been chosen on the basis of an abnormal sodium concentration in their blood.

Result: It has been found in the results that abnormal sodium concentration is not limited to only one cause. Moreover, it has been found that BMI, coexisting disease or disorder, age, and gender play critical roles in the development of hyponatremia.

Conclusion: It has been concluded that the association of sodium concentration with the frequency and severity of hyponatremia in stroke patients is closely related to serum osmolality, urine sodium, and urine osmolality in the patient, along with other factors.

Keywords: Stroke Patients During Hospitalization, Ischemic Stroke, Instances of Stroke Patients During Hospitalization among Stroke Patients, Hypoosmolality, Hypothalamic Depressive Hormone Syndrome, and Sodium.

Introduction:

ⁱIndividuals diagnosed with ischemic stroke exhibit either increased, typical, or decreased concentrations of sodium. ⁱⁱAccording to a study by Mahaser, individuals who exhibit electrolyte abnormalities experience a greater rate of death during their hospital stay compared to those who maintain normal electrolyte balance. The observed rise in mortality among individuals with hyponatremia seems to be attributable to the deterioration of the underlying condition rather than the electrolyte imbalance per se. ⁱⁱⁱThis implies that hyponatremia could potentially serve as an indicator of more advanced disease and a less favorable prognosis. The presence of asymptomatic clinical hyponatremia has been associated with the development of seizures and cognitive instability, ultimately resulting in paralysis and cognitive impairment.

The objective of this research is to quantify the sodium deficit in individuals diagnosed with cerebral ischemia and ascertain if the occurrence of a sodium deficit among hospitalized patients may be attributed to ischemic stroke. The inclusion of the conventional hyponatremia scale utilized in our study was subsequent to a comprehensive examination of the existing body of scholarly literature. ^{iv}According to the recommendations of Shima et al., the classification of hyponatremia in adults is based on the serum sodium concentration. It is categorized as mild when the concentration ranges from 130 to 134 mmol/l, moderate when it ranges from 125 to 129 mmol/l, and severe when it is below 125 mmol/l.

^vThe presence of hyponatremia is correlated with a heightened likelihood of mortality, both during the period of hospitalization and following discharge. ^{vi}Clinical assessment is the primary method for diagnosing stroke, followed by the utilization of imaging modalities such as computed tomography (CT) or magnetic resonance imaging (MRI) to validate the diagnosis. Hyponatremia following a stroke is distinguished by an alteration in electrolyte levels due to a recent cerebral injury ^{vii}. The presence of hyponatremia in a patient is identified after the administration of an electrolyte test. Hyponatremia is prevalent in various clinical settings, but its occurrence in patients with ischemic stroke warrants special attention due to its potential impact on neurological outcomes and overall mortality.

^{viii}Hyponatremia is a prevalent electrolyte issue observed in neurological conditions such as stroke, hypothyroidism, and meningitis. This ailment is typically attributed to syndrome of inappropriate antidiuretic hormone secretion (SIADH) or cerebral salt wasting syndrome (CSWS) ^{ix}. The hormone known as antidiuretic hormone (ADH) is stored within the posterior pituitary gland. The primary regulator of bodily water balance, this hormone has an influence on renal function and facilitates an increase in the overall water content of the body. Typically, the physiological reaction to a reduction in plasma volume or an elevation in serum osmolality leads to the secretion of antidiuretic hormone (ADH) ^x. In the context of the syndrome of inappropriate antidiuretic hormone (SIADH), the synthesis of antidiuretic hormone (ADH) persists despite the presence of hypothermia and heightened functional blood flow ^{xi}. Consequently, the conventional negative feedback mechanism responsible for regulating ADH is rendered ineffective, leading to the continuous release of ADH ^{xii}. Hyponatremia is commonly found among ischemic stroke patients, with rates ranging from 11% to 43%. A study involving 925 patients showed that 11.6% were hyponatremic, with a higher prevalence of diabetes mellitus among them. Another study in Nigeria found that 32.8% of acute stroke patients had hyponatremia, with advanced age and altered consciousness significantly associated with its presence. This implies that presence of hyponatremia was affected by different variables age, altered consciousness in stroke, comorbidities and could potentially serve as an indicator of more advanced disease and a less favourable prognosis. There are many factors that

play a critical role in the development of hyponatremia in ischemic stroke patients during hospital admission and treatment. By gaining a comprehensive understanding of these factors, healthcare providers can devise more targeted and effective management strategies, ultimately improving patient outcomes and reducing the burden of post-stroke complications.

Material and Methods:

This study represents one of several cross-sectional investigations that were conducted from February 2023 to December 2023. The study involved a cohort of 100 patients, whose statistical data was analyzed across various health departments and stroke distributions. All the chosen patients belong to one of the reputable hospitals. The requisite information on a pre-designed questionnaire is filled for every patient diagnosed with hyponatremia and ischemic stroke. This encompasses inquiries about many aspects of the findings, such as age, gender, clinical manifestation, coexisting medical conditions, sodium levels, and duration of symptoms. The method of the examination revolves around patients that have been admitted to the hospital within the given timeline under the supervision of the doctors and other medical staff. The sodium concentrations were assessed continuously for a minimum of 24 hours following admission to the hospital, as documented in the medical records. There were no specific limitations on the day when hyponatremia levels were measured, save for considerations related to the patient's well-being. The statistical reports were generated using version 22 of the SPSS program (Statistical Package for Social Science), developed by IBM in New York, USA. The data is presented in a tabular format to convey statistical information. Descriptive statistics were employed to ascertain the frequency of hyponatremia values. The chi-square test is commonly used to analyze categorical variables, such as the extent of hyponatremia. It is challenging to establish a definitive association between parrots. However, a p-value of 0.001 is indicative of statistical significance. Before the research evaluation, it has been requested that patients show us recent CT scan reports. The CT scan data must originate from a radiologist who has completed a five-year tenure in the field. In addition, measurements were taken for serum sodium, serum osmolality, urine sodium, and urine osmolality. The study excluded individuals who had previously experienced gastroenteritis, brain damage, brain tumors, and pneumonia lasting two weeks. Patients with hemorrhagic stroke, transient ischemic stroke, recurrent stroke, venous thrombosis, viral, fungal, tuberculous, and fungal meningitis, as well as stroke, were excluded from the study based on clinical and brain imaging assessments. The syndrome of inappropriate antidiuretic hormone secretion (SIADH) can be distinguished from cerebral salt wasting syndrome (CSWS). This study focuses on the identification of acute ischemic stroke cases in individuals of both genders, ranging from 16 to 90 years old. Individuals who have a history of heart or kidney failure were not included in the study.

Results:

Considering the descriptive analysis that includes demographic information, it can be observed that the age group that most commonly encounters hyponatremia with ischemic stroke is from 45 to elderly age. 37 respondents are 45 years old, making them 34%, and 29 respondents are elderly, identifying as 27%. Moreover, it has been found that females are more likely to be diagnosed with hyponatremia (54% with ischemic stroke) than males (56%), which could be due to exposure to estrogen and progesterone. It has been further found in the descriptive analysis that in most cases, patients have already been diagnosed with various diseases that could become sources of hyponatremia, as mentioned in the introduction section. In terms of the location of the hemisphere, it has been found that the severity and frequency of hyponatremia in ischemic stroke are completely avoidable. Correlation analysis has been used to test the difference in condition representation on either side of the hemisphere. Mean analyses have been performed to analyze the significance of serum osmolality, urine sodium, and urine osmolality. It has been found out that all the variables mentioned are important indicators that suggest the severity and frequency of hyponatremia. Moreover, BMI plays a critical role in the prevalence of hyponatremia, as individuals with a BMI

less than 18.5 represent underweight and those with a BMI greater than 30 represent obese individuals; these two groups are more susceptible. However, standards 18.5 to 24.9 show variety in the severity of hyponatremia. Although there are several intervention methods to manage the severity of healthcare hyponatremia, we have selected only two, which are fluid restriction and hypertonic saline. As one-way Anova has been chosen to evaluate the better option, the results show that fluid restriction with a significance level of 0.05 is the best option that is widely used in health care settings to stabilize the concentration of sodium. Anova results indicate that there is no statistically significant difference for respiratory distress, muscle weakness, vomiting, headache, and observed nausea as the p-values for all symptoms are greater than 0.05. This means that the differences in the means of these symptoms are not large enough to be considered statistically significant, and it is likely that any differences observed are due to chance. Research has shown that respiratory distress, muscle weakness, vomiting, headache, and observed nausea are common symptoms in various medical conditions. However, it is important to consider the clinical significance of the results and to interpret them in the context of the specific population and measurement tools used.

Discussion:

There are various reasons why these results have been obtained, for instance, in elderly people diagnosed with multiple diseases and disorders related to nephrology and the cardiac system. This can be related to the first part of the report, which stated that hyponatremia could be a by-product of multiple diseases and disorders. This study aimed to assess the extent of aberrant sodium levels in ischemic stroke patients without any other underlying conditions and what factors should be looked at to detect hyponatremia. The occurrence of a hyponatremia was seen, and it was shown that sodium levels exhibited a drop in individuals with ischemic stroke during their hospitalization period. Besides, stroke patients, the elderly in particular, are frequently treated with medications that can induce hyponatremia, including antihypertensive agents, antidepressants, and nonsteroidal anti-inflammatory drugs. Different heart and kidney diseases were observed as comorbidities among individuals with low sodium levels. The prevalence of stroke in both genders exhibits a positive correlation with elevations in coexisting diseases.^{xiii} The measurements of body mass index (BMI), blood pressure, and blood glucose levels were collected in a non-systematic manner. It has been found out that BMI also plays a crucial role in the development of hyponatremia, as people with a standard BMI have a low probability of developing the condition^{xiv}. During hospitalization, “inappropriate” administration of hypotonic solutions, infections, and other drugs, such as mannitol, could lower sodium levels in patients with acute stroke. Secondary adrenal insufficiency due to pituitary ischemia, syndrome of inappropriate antidiuretic hormone secretion, and cerebral salt wasting are additional stroke related causes of hyponatremia.

Electrolyte levels of patients should be kept in check from the moment they arrive because potassium and sodium are the chief electrolytes of the body and a switch in their levels can adversely affect the body on a mass level. Hyponatremia is an important cause of persistent altered sensorium in stroke patients^{xv}. It can also give various other neurological sign and symptoms like seizures, which can deteriorate the level of consciousness of the patient, hence, a quantification of the severity of hyponatremia needs to be done in order to have a clear vision about what levels can cause such adverse outcomes and deal with the problem in an orderly manner.

Muscle weakness is a common symptom of hyponatremia, which can be attributed to the fact that sodium plays a crucial role in maintaining the proper functioning of the muscles^{xvi}. Sodium is involved in the regulation of muscle contractility, and low levels of sodium can lead to muscle weakness and fatigue^{xvii}. In severe cases, hyponatremia can lead to muscle cramps, seizures, and even coma. Vomiting is another common symptom of hyponatremia, which can be caused by a variety of factors^{xviii}. In some cases, vomiting can be a result of the body trying to eliminate excess

water, which can dilute the sodium concentration in the blood^{xvi}. In other cases, vomiting can be a symptom of other underlying conditions that can lead to hyponatremia, such as gastrointestinal infections or the use of certain medications. Headaches are also a common symptom of hyponatremia, which can be attributed to the fact that sodium plays a crucial role in maintaining the proper functioning of the brain^{xvi}. Sodium is involved in the regulation of brain water content, and low levels of sodium can lead to an increase in brain water content, which can cause swelling and pressure on the brain^{xvii}. In severe cases, hyponatremia can lead to brain herniation, which can be life-threatening. It is important to note that the diagnosis of hyponatremia should not be based solely on the presence of these symptoms^{xvii}. Other tests, such as urine sodium and serum osmolality, should be performed to confirm the diagnosis of hyponatremia and to determine the underlying cause of the condition^{xvi}. Treatment of hyponatremia depends on the severity of the condition and the underlying cause. In some cases, treatment may involve restricting fluid intake or administering intravenous fluids with a higher concentration of sodium.

Conclusion:

Thorough surveillance of blood sodium levels facilitated the identification of the precise rate of drop across various age groups and both genders. Our findings indicate that the majority of cases that developed hyponatremia contributed to previous diseases. The evaluation of the extent of hyponatremia can provide insights into the magnitude of detrimental consequences that a stroke patient may encounter, hence potentially mitigating the risk of mortality. Moreover, muscle weakness, vomiting, and headaches are all contributors to hyponatremia but should be diagnosed with other tests such as urine sodium and serum osmolality.

Appendix: Questionnaire

Section A: Demographics Information

Sr. No	Items	Responses
1	Age group	25 to 35 years old 35 to 45 years old 45 to 55 years old Above 55 years old
2	Gender	Male Female Others
3	Prior disease history	Yes No
4	Have you submitted a CT scan?	Yes No
5	Do you have any coexisting medical condition	Yes No

Section B: Survey Questions:

- The closed-ended questions are answered using the five-point LIKERT scale, where 1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, and 5 = strongly agree.

	1	2	3	4	5
1. The location was in the right hemisphere.					
2. The location was in the left hemisphere.					
3. The sodium level was below 135 to 145 milliequivalents per liter (mEq/L).					
4. Serum osmolality was 275 to 295 mOsm/kg, which impacted the severity of ischemic stroke.					
5. Urine sodium is an important factor in analysing the severity of ischemic					

stroke.					
6. Urine osmolality frequency, severity, and association with hyponatremia.					
7. Frequency, severity, and association of hyponatremia if less than 18.5 BMI.					
8. Frequency, severity, and association of hyponatremia up to BMI from 18.5 to 24.9.					
9. BMI between 24.9 and 29.9 can vary the frequency and severity of hyponatremia.					
10. BMI greater than 30					
11. I observed nausea, which is associated with hyponatremia and ischemic stroke.					
12. I have observed headaches that are associated with hyponatremia and ischemic stroke.					
13. I have observed vomiting which is associated with hyponatremia and Ischemic Stroke					
14. I have observed muscle weakness, which is associated with hyponatremia and ischemic stroke.					
15. I have observed respiratory distress.					
16. Fluid restriction is an effective intervention strategy.					
17. Hypertonic saline is an effective intervention strategy.					

Age		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	19-25	11	10.4	11.0	11.0
	25-35	7	6.6	7.0	18.0
	35-45	15	14.2	15.0	33.0
	45-55	37	34.9	37.0	70.0
	55-and more	29	27.4	29.0	99.0
	11	1	.9	1.0	100.0
	Total	100	94.3	100.0	
Missing	System	6	5.7		
	Total	106	100.0		

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Respiratory distress	Between Groups	.062	1	.062	.039	.844
	Within Groups	156.528	98	1.597		
	Total	156.590	99			
Muscle weakness	Between Groups	.062	1	.062	.039	.844
	Within Groups	156.528	98	1.597		
	Total	156.590	99			
Vomiting	Between Groups	.062	1	.062	.039	.844
	Within Groups	156.528	98	1.597		
	Total	156.590	99			
Headache	Between Groups	.062	1	.062	.039	.844
	Within Groups	156.528	98	1.597		
	Total	156.590	99			
Observed nausea	Between Groups	2.956	1	2.956	1.574	.213
	Within Groups	184.034	98	1.878		
	Total	186.990	99			

Correlations		BMI	BMITWO	BMITHREE	BMIFOUR
BMI	Pearson Correlation	1	-.077	-.122	-.218*
	Sig. (2-tailed)		.447	.226	.029
	N	100	100	100	100
BMITWO	Pearson Correlation	-.077	1	-.436**	.636**
	Sig. (2-tailed)	.447		.000	.000
	N	100	100	100	100
BMITHREE	Pearson Correlation	-.122	-.436**	1	.029
	Sig. (2-tailed)	.226	.000		.772
	N	100	100	100	100
BMIFOUR	Pearson Correlation	-.218*	.636**	.029	1
	Sig. (2-tailed)	.029	.000	.772	
	N	100	100	100	100

* The correlation is significant at the 0.05 level (2-tailed).
 ** The correlation is significant at the 0.01 level (2-tailed).

Sodium level * hypertonic saline			
Sodium level			
Hypertonic saline	Mean	N	Std. Deviation
Agree	1.81	26	.402
Strongly agree	1.68	22	.477
Neutral	1.83	18	.383
Disagree	1.70	20	.470
Strongly disagree	1.50	14	.519
Total	1.72	100	.451

Sodium level * Fluid restriction			
Sodium level			
Fluid restriction	Mean	N	Std. Deviation
Agree	1.75	36	.439
Strongly agree	1.70	33	.467
Neutral	1.62	13	.506
Disagree	1.90	10	.316
Strongly disagree	1.63	8	.518
Total	1.72	100	.451

References:

- ⁱ Mahesar, S.A., Memon, S.F., Mustafa, S., Javed, A. and Butt, S.M., 2019. Evaluation of hyponatremia in ischemic stroke patients in a tertiary care hospital of Karachi, Pakistan. *Cureus*, 11(1).
- ⁱⁱ Liamis, G., Barkas, F., Megapanou, E., Christopoulou, E., Makri, A., Makaritsis, K., Ntaios, G., Elisaf, M. and Milionis, H., 2020. Hyponatremia in acute stroke patients: pathophysiology, clinical significance, and management options. *European Neurology*, 82(1-3), pp.32-40.
- ⁱⁱⁱ Chen, Z., Jia, Q. and Liu, C., 2019. Association of hyponatremia and risk of short-and long-term mortality in patients with stroke: a systematic review and meta-analysis. *Journal of Stroke and Cerebrovascular Diseases*, 28(6), pp.1674-1683.
- ^{iv} Shima, S., Niimi, Y., Moteki, Y., Takahashi, O., Sato, S., Inoue, T. and Okada, Y., 2020. Prognostic significance of hyponatremia in acute stroke: a systematic review and meta-analysis. *Cerebrovascular Diseases*, 49(5), pp.531-539.

- ^v He, L., Guo, Z.N., Qu, Y. and Jin, H., 2022. Hyponatremia is associated with post-thrombolysis hemorrhagic transformation and poor clinical outcome in ischemic stroke patients. *Frontiers in Molecular Neuroscience*, 15, p.879863.
- ^{vi} Kalita, J., Singh, R.K. and Misra, U.K., 2017. Cerebral salt wasting is the most common cause of hyponatremia in stroke. *Journal of Stroke and Cerebrovascular Diseases*, 26(5), pp.1026-1032.
- ^{vii} Balbi, A., Sadowski, J.A., Torrens, D., Jacoby, J.L., Yacoub, H.A. and Eynor, J.K., 2022. Hyperacute hyponatremia mimicking acute ischemic stroke. *The American journal of emergency medicine*, 51, pp.428-e5.
- ^{viii} Karunanandham, S., Rajappa, T. and Selvaraju, K., 2018. Hyponatremia in Patients Admitted with Stroke. *Journal of Clinical & Diagnostic Research*, 12(8).
- ^{ix} Al-Khazraji, A.K.K., 2016. Hyponatremia in a group of Iraqi patients with stroke. *Iraqi J Med Sci*, 14(2), pp.191-96.
- ^x Blessing, D., 2022. Remarks on Hyponatremia in Patients with Stroke.
- ^{xi} Khan, A., Khan, Z., Khan, S., Ullah, A., Ayub, G. and Tariq, M.N., 2023. Frequency of Hyponatremia and Its Impact on Prognosis in Ischemic Stroke. *Cureus*, 15(6).
- ^{xii} Soiza, R.L., Cumming, K., Clark, A.B., Bettencourt-Silva, J.H., Metcalf, A.K., Bowles, K.M., Potter, J.F. and Myint, P.K., 2015. Hyponatremia predicts mortality after stroke. *International Journal of Stroke*, 10(SA100), pp.50-55.
- ^{xiii} Bhattacharjee, K., Das, D., Kalwar, A., Debnath, B. and Kar, G., 2015. Relationship of Hyponatremia with immediate mortality in acute stroke. *J Evid Based Med Health Care*, 2(38), pp.6119-24.
- ^{xiv} Hakim, M. and Hasan, M., 2020. Hyponatremia as an independent predictor of mortality and functional outcome in stroke (4311).
- ^{xv} Study of electrolyte abnormality in acute stroke. Bandopadhyay M, Jatua SK, Adhikari M, Bhandari A. *Annals Intl Med Dental Res*. 2017;3:4–9.
- ^{xvi} Brenner, B. M. (2019). *Brenner and Rector's the kidney* (10th ed.). Elsevier.
- ^{xvii} Gross, P., Hix, J. K., & Kamel, K. S. (2014). Hyponatremia in the Syndrome of Inappropriate Antidiuretic Hormone Secretion: Diagnosis, Clinical Features, and Treatment. *American Journal of Medicine*, 127(4), 320-327.