International Journal of Frontiers in
Medicine and Surgery Research
Journal homepage: https://frontiersrj.com/journals/ijfmsr/
ISSN: 2783-0489 (Online)

(RESEARCH ARTICLE)

Check for updates

Analysis of syndrome of inappropriate anti-diuresis and cerebral salt wasting in patients with acute stroke

Mithun Somaiah, Shashank S Gowda, Shamantha G and Yedla Nischal *

Department of General Medicine, BGS institute, Bangalore, Karnataka, India.

International Journal of Frontiers in Medicine and Surgery Research, 2023, 03(02), 026–032

Publication history: Received on 07 June 2023; revised on 26 July 2023; accepted on 29 July 2023

Article DOI: https://doi.org/10.53294/ijfmsr.2023.3.2.0070

Abstract

Hyponatremia in hospitalized patients can significantly alter the morbidity, mortality, especially in chronic neurological patients. Most commonly, it is attributed to SIADH, and in stroke it occurs due to AVP secretion inappropriate to the osmotic threshold. The suppressed proximal renal tubular transport in this condition can lead on to bicarbonaturia and hypouricemia. CSW, on the other hand, is essentially a volume depleted state, which occurs due to the combined effects of decreased sympathetic outflow and increased natriuretic peptides. This resultant natriuresis leads to volume depletion and an appropriate AVP response. The treatment for SIADH AND CSW varies, and the outcomes vary considerably too. Hence, we performed this study to study the clinical profile of stroke patients with hyponatremia, and to identify the factors associated with the same.

Keywords: SIADH; CSW; Hyponatremia; Volume Depleted State; Cerebral Oedema

1. Introduction

Hyponatremia is the most common electrolyte abnormality seen in hospitalized patients and is also the most common electrolyte imbalance seen in critically ill neurologic patients. It can significantly alter the morbidity, mortality of the underlying disease [1].

The causes of hyponatremia are varied, but in neurologically ill patients, are most attributed to Syndrome of Inappropriate Anti-diuresis and Cerebral Salt Wasting. Both these entities are cerebral in origin but have distinct pathophysiology, prognosis, and treatment options. The importance of distinguishing both lies in the fact that the therapy indicated for one if used for the other, can be deleterious [2,3].

The distinction between the two requires a battery of investigations since there is considerable overlap between the two conditions, and no single parameter can define either entity.

SIADH is a subclinically volume-expanded state due to inappropriate anti-diuresis. [3] This causes excessive volume overload over the body's sodium content leading to euvolemic hyponatremia. In stroke SIADH occurs due to AVP secretion inappropriate to the osmotic threshold. The suppressed proximal renal tubular transport in this condition can lead on to bicarbonaturia and hypouricemia. The effective treatment is fluid restriction. Hypertonic saline therapy is reserved for cases of severe hyponatremia.

CSW, on the other hand, is essentially a volume depleted state, which occurs due to the combined effects of decreased sympathetic outflow and increased natriuretic peptides. This resultant natriuresis leads to volume depletion and an

* Corresponding author: Yedla Nischal

appropriate AVP response. So the treatment for SW includes an aggressive volume replacement regimen with isotonic saline or in severe cases, hypertonic saline.

Thus most CSW patients meet the criteria for SIADH and have elevated AVP levels but worsen with the treatment protocol given for SIADH. This observation lead to the description of CSW as a separate entity and widespread studies were carried out to distinguish the two entities [5,6].

At present the two entities are differentiated using a combined analysis of sodium levels, plasma osmolality, uric acid, effective arterial blood volume, urine sodium, serum potassium, and hematocrit. BUN/creatinine ratio. Hyponatremia, especially Cerebral Salt Wasting, occurring in the setting of stroke has been shown to worsen the prognosis of stroke, increase morbidity, short and long-term mortality, and cause a poorer discharge disposition [7].

Hence, we performed this study to study the clinical profile of stroke patients with hyponatremia, and to identify the factors associated with the same.

2. Material and methods

This was a prospective observational study conducted in the Department of General Medicine, BGS Global Institute of Medical Sciences, Kengeri, Bangalore. This was conducted in 100 patients from August 2020 to June 2022 that had been diagnosed with stroke by history, neurologic and imaging modalities.

Patients with history of Head injury, CNS tumour, Pulmonary tuberculosis, Bacterial pneumonia, Bronchogenic carcinoma, Hematologic malignancies, those that have undergone surgery in the last 30 days, Meningitis or Encephalitis and Patients who had a history of Drug usage- SSRI, TCA, narcotics, NSAIDs, Antipsychotics, Carbamazepine, Cyclophosphamide, Clofibrate, Chlorpropamide were excluded.

The type of stroke determined using the imaging of brain - Ischemic / haemorrhagic, site and the vascular territory involved.

After ruling out the exclusion criteria, serial serum sodium levels were done. In patients with hyponatremia, plasma osmolality was measured to differentiate between true and pseudo-hyponatremia. Cerebral causes of hyponatremia were identified and classified as SIADH/CSW and treated as per the standard protocol.

2.1. Methodology

2.1.1. On Day 1

- Demographics of all patients noted down including socio economic status according to B G Prasad Classification
- Clinical Evaluation
- Clinical Estimation of Extracellular fluid volume - estimated by JVP (Jugular venous pressure elevation), Peripheral edema, Negative / positive fluid balance by input /output and Blood pressure levels
- Serum Sodium
- Plasma osmolality
- Serum potassium
- Serum uric acid
- Haematocrit
- BUN/ Creatinine ratio
- Serum albumin
- Urine Sodium were measured.

Based on Day 1 values, a provisional diagnosis of SIADH / CSW was made.

Sodium correction was carried out using the standard protocols i.e., fluid restriction in case of SIADH and intravenous saline in case of suspected CSW; hypertonic saline where severe hyponatremia was encountered.

2.1.2. On Day 3, values noted were

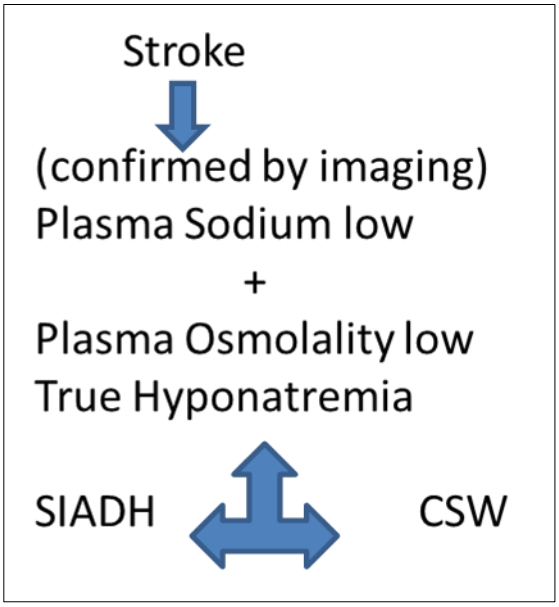
- Serum sodium
- Serum uric acid

- Haematocrit
- Serum albumin were measured
- At the time of discharge / death (approximately 7-10 days after the onset of hyponatremia in stroke), the outcome of patients was noted.

Investigations performed during the hospitalization

- Chest X-ray
- CT scan brain/ MRI brain
- Plasma osmolality
- Urine sodium
- Plasma sodium
- Serum Potassium
- Haematocrit
- Serum Uric acid
- Serum Albumin
- BUN / Creatinine ratio

2.2. Diagnostic approach followed in our study



Assess

- Clinical volume status
- Urine Sodium
- Serum Uric acid
- BUN/ creatinine ratio
- Serum Potassium
- Haematocrit
- Serum Albumin

2.3. Statistical analysis

The data is represented in the form of frequencies, percentages, mean values and Standard Deviation or the median, depending on their distribution.

A Chi Square test was used to assess differences in categoric variables between groups.

Kaplan Meyer was performed

A p value of <0.05 was considered significant for all the statistical tests.

All the data was analysed with the statistical software SPSS.

3. Results

In our set of stroke patients, the majority of patients, around 33% (n= 33) were middle aged i.e.; 61 to 70 years of age, 25% of patients belonged to age group 71 to 80, 20% of patients above >80 years, and 6% of patients < 50 years. Majority of the patients with hyponatremia in stroke belong to age group 61 to 70 years.

The prevalence of Stroke with Hyponatremia was high in Males (69%) compared to females (31%) among the total 100 patients of our study group.

The mean age of males with hyponatremia in stroke is 66.7 (+ 10.97), lower than the females i. e 72.5 (‡ 11.93)

Table 1 Frequency of clinical features in stroke patients with hyponatremia

Clinical Features	**Percentage**
Motor weakness	88%
(Hemiplegia/Hemiparesis/Monoparesis)	(Rt sided 41, Lt sided 47)
Speech involvement (Aphasia or Dysarthria)	48% (39% Dysarthria, 11 % Aphasia)
Cranial nerve involvement	63% 7th Nerve (61% UMN 7th nerve, 2% LMN)3rd nerve, 1 % LMN 7th & nerve with gaze palsy and 1% LMN 9 &10 Nerves
Altered sensorium	34%
Seizures	10%
Gait disturbances/Cerebellar signs	5%

3.1. Association of modifiable risk factors in stroke patients with hyponatremia

In our study 4% of the patients had history of chronic smoking, while 7% of people had history of alcohol consumption. In our study frequency of diabetes 45%, hypertension 69%, No history of diabetes and hypertension 16%.

Table 2 Frequency of heart diseases among stroke patients with hyponatremia

Heart disease	**Frequency**	**Percentage (%)**
Present	30	30.0
Absent	70	70.0
Total	100	100.0

Table 3 Frequency of each type of stroke among stroke patients with hyponatremia

Type of stroke	**Frequency (n)**	**Percentage (%)**
Infarct (Ischemic stroke)	86	86
Haemorrhage (Intracerebral bleed)	11	11
Infarct with haemorrhage	3	3
Total	100	100

The above table shows, out of the total 100 patients with stroke and hyponatremia, 86% (n=86) had ischemic stroke. Haemorrhagic stroke was seen in 11% (11) patients and 3% patients (3) had infarct with haemorrhage.

75 of the total 100 patients (75%) had stroke in Middle Cerebral Artery territory, followed by 8 patients (8%) in Posterior cerebral artery and 6 patients (6% with Anterior Cerebral circulation involvement.

Table 4 Frequency of SIADH / CSW among stroke patients with hyponatremia

SIADH/CSW	Frequency(n)	Percentage (%)
SIADH	15	15
CSW	6	6
Not Elevated	79	79
Total	100	100

In our study 21% evaluated 6% CSW and 15% SIADH.

In our study minimum duration 1 day maximum duration 36 days standard deviation 10 and median is 7, while the minimum duration of survival was 1 day maximum duration 36 days standard deviation 10 and median is 7.

Table 5 Outcome of stroke patients with Hyponatremia

Outcome	Frequency	Percent
DEATH	2	2
DISCH/AGAINST	8	8
DISCHARGED	90	90
Total	100	100

In our study 90% patients discharged with MRS score 2 to 3, 8% discharged against advise and 2% death rate.

4. Discussion

In our observational study, we had analysed 100 patient's clinical profile of stroke with hyponatremia.

4.1. Age wise distribution in stroke patients with hyponatremia

Hence, this observational study, we found that majority of the patients of hyponatremia with stroke belonged to mean age 66 years (61 to 70 years of age. It closely resembled study done by Maniram et al, who opined maximum numbers of hyponatremia patients are seen in old ages (Above 50 years of age).

In our observational study, majority of patients were male (69%) than female (31%). As compared to study done by Maniram et al, hyponatremia was noticed in 53% of female patients whereas in male stroke patients this was found to be 54.22%; as is seen there is very little difference between these two values (p value = 0.975) 50 is similar to our study.

Frequency of each clinical features with patients of stroke with hyponatremia

In our study, hemiplegia was the most common clinical feature. It was reported in 88% of patients, followed by cranial nerve involvement in 63% patients.

In the present study, 34% of patients had altered sensorium which was similar to the findings of Saleem et al. [10] who opined Hyponatremia is one of the important causes of persistent altered sensorium in stroke patients.

In this study four patients (4%) were smoker among 100 stroke patients studied. The above study is not correlating with Donnan et al, [8] where smoking was strongest risk factor causing ischemic stroke. Mortality rates appeared higher for hyponatraemic subjects with current smoking (18%) as studied by Mohan et al.

In our study seven (7%) patients were found to be alcoholic. Our study does not correlate with study by Naik M, Rauniyar R.K. Sharma U.K.et al [9] who found H/O alcohol intake in 30.5% of stroke patients. For cerebral infarction chronic heavy drinking and acute intoxication have been associated with an increased risk among young adults. The deleterious effects of alcohol for stroke may occur through various mechanisms, including increasing hypertension, hyper coagulable states, and cardiac arrhythmias and reducing cerebral blood flow.

In above study 69% of stroke patient with hyponatremia had hypertension and which is found to be single most risk factor associated with stroke. This result correlating with Benerjee TK et al study which was conducted in Calcutta on urban population in which systemic hypertension emerged as single most important risk factor. Successful antihypertensive therapy decreases stroke incidence in asymptomatic persons, hypertensive patients with transient ischemic attacks and survivors of hypertensive stroke. The decrement in sodium level of the patients due to these medications can be a good explanation for the development of hyponatremia [52]

In our observational study, we found that 30% of cases were patient with Heart diseases including Coronary Artery Disease, Cardiomyopathy, valvular heart diseases and atrial fibrillation (AF). Earlier studies including these indices were not done. Hence need further researches in accordance with this association.

In our observational study, 10% of patient had old stroke. There were no earlier studies found in literature in this perspective. Hence needs further research on basis of findings of our study.

In the present study, Haemorrhagic stroke was seen in 11% (11) patients and 3% patients (3) had infarct with haemorrhage. This was similar to the findings of study done by Salem et al.10 SIADH was seen in 83 patients who had an ischemic stroke and 155 patients of haemorrhagic stroke.

In our observational study, total patients of SIADH and CSW were 21, in which patients with SIADH were 71.42% (no=15), while patients with CSW were 28.58% (no=6). Our study correlates with the study by Salem et al10, who showed that the prevalence of SIADH was 67% and CSW was 33%.

In our study, the patients who recovered were 60%, while the patients who dies were 40%. A poorer discharge disposition was seen in the hyponatremia group in the study by Rodrigues. [12] This is not similar to the death rate reported by Saleem et al, 40%.58 In the studies, the presence of hyponatremia was found to significantly alter the treatment outcome in patients with stroke ($p<0.05$). Kuramatsu et al showed that in-hospital mortality was roughly doubled in hypernatremia compared with non hyponatremic patients (40.9% vs 21.1%), translating into a 2.5-fold increased odds ratio ($P<0.001$). Also, Multivariable analyses identified hyponatremia as an independent predictor of in-hospital mortality. (P-0.037). 14 Therefore, close monitoring of serum sodium must be carried out in all patients who are admitted with stroke and efforts must be made to determine the cause of hyponatremia, in order to properly manage such patients thereby decreasing the mortality rate.

Electrolyte disturbances are common at the time of presentation of patients with acute stroke associated with increased morbidity and mortality irrespective of types of location, and size of strokes and associated comorbidities. Hypocalcaemia and hypomagnesaemia were more common in ISCHS and hyponatraemia were common in ICH strokes in our study. Early detection and correction of electrolyte disturbances may prevent further morbidity and mortality in acute stages of strokes.

5. Conclusion

The most common clinical feature noted in our study was hemiplegia/hemiparesis, followed by Cranial nerve involvement noted in 63%, Speech disturbances in 48% patients, Altered Sensorium in 34%, Seizures in 10%, both gait disturbances and ataxia in 5% each.

In our study, Systemic hypertension, Diabetes, Smoking, Alcoholism and Dyslipidaemia were noted to have a statistically significant association with "hyponatremia in stroke" among patients aged more than 66 years.

The mean duration of hospital stay was significantly different in patients with hyponatremia ~ 10 days. The maximum duration of stay seen in one of the hyponatraemic patients was ~ 36 days. In our study stroke patients, an 90% cure rate, 8% discharge against medical advice and 2% death rate was seen.

Limitations of the study

- The study is small scale, will need larger scale studies for confirmation of the findings.
- The difference in clinical profile of patients with SIADH AND CSWS was not done in detailed respectively.
- Outcome of all the patients was not evaluated at the same fixed points of time successively, rather it varied according to the duration of hospital stay in different patients.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

IEC approval sought.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study

References

[1] McCance RA: Experimental sodium chloride deficiency in man. ProcR So Lond 119: 245-268, 1936

[2] Peters JP, Welt LG, Sims EA, Orloff J, Needham J: A salt-wasting syndrome associated with cerebral disease. Trans Assoc Am Physicians 63: 57-64, 1950

[3] Cort JH: Cerebral salt wasting. Lancet 266: 752-754, 1954

[4] Leaf A, Bartter FC, Santos RF, Wrong O: Evidence in man that urinary electrolyte loss induced by Pitressin is a function of water retention. J Clin Invest 32: 868- 878, 1953

[5] Schwartz WB, Bennett W, Curelop S, Bartter FC: A syndrome of renal sodium loss and hyponatremia probably resulting from inappropriate secretion of antidiuretic hormone Am J Med 23: 529-542, 1957

[6] Nelson PB, Seif SM, Maroon JC, RobinsonAG: Hyponatremia in intracranial disease: perhaps not the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). J Neurosurg 55: 938-941, 1981

[7] Wijdicks EF, Vermeulen M, ten Haaf JA, Hijdra A, Bakker WH, van Gijn J: Volume depletion and natriuresis in patients with a ruptured intracranial aneurysm. Ann Neurol 18: 211-216, 1985

[8] Naik M, Rauniyar RK, Sharma UK, Dwivedi S, Karki DB, Samuel JR. Clinico-radiological profile of stroke in eastern Nepal: a computed tomographic study. Kathmandu University medical journal (KUMJ). 2006; 4(2): 161-6.

[9] Donnan G, Adena M, O'Malley H, Mcneil J, Doyle A, Neill G. Smoking as a risk factor for cerebral ischaemia. The Lancet. 1989 Sep 16; 334(8664):643-7.

[10] Salem, Sheikh & Wani, Irfan & Gul, Azhara & Gupta, Satish & Verma, Sawan. (2014). Hyponatremia in stroke. Annals of Indian Academy of Neurology. 17. 55- 7. 10.4103/0972-2327.128554.

[11] Mahesar SA, Memon SF, Mustafa S, Javed A, Butt SM. Evaluation of Hyponatremia in Ischemic Stroke Patients in a Tertiary Care Hospital of Karachi, Pakistan. Cureus. 2019; 11(1):3926. Published 2019 Jan 21. doi: 10.7759/cureus.3926.