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EVALUATION OF CEREBRAL SALT WASTING AND SYNDROME OF INAPPROPRIATE ANTI-DIURETIC HORMONE SECRETION IN PATIENTS WITH STROKE

Dr. Shweta Meghnath Lokare[1], Dr.Bibifatima Bawakhan[2], Dr. Ameena Meah[3], Dr. Sneha Savanur[*]

Assistant Professor[1'2], Associate Professor[3'*]

Department of General Medicine[1'3'*], Department of Biochemistry[2]

Vydehi Institute of Medical Sciences and Research Centre[1'3'*], Karwar Institute of Medical Sciences[2], PES University Medical College*

Corresponding Author*: Dr. Sneha Savanur, Associate Professor, Dept.of General Medicine, PES University Medical College, Bengaluru.

ABSTRACT

Background - Hyponatremia has numerous causes, but in neurologically ill patients, Syndrome of Inappropriate Antidiuresis (SIADH) and Cerebral Salt Wasting (CSW) are the most common. Both these entities are cerebral In origin but have distinct pathophysiology, prognosis and treatment options. Thus most CSW patients meet the criteria for SIADH and have elevated AVP levels but worsen with the treatment protocol given for SIADH. Hence, we conducted this prospective study to describe the aetiology of hyponatremia in patients of stroke.

Materials and Methods- This was a prospective observational study was included all inpatients of stroke either ischemic or haemorrhagic admitted in the Department of General Medicine at a tertiary care hospital. A total of 50 patients were included in the study over a duration of 22 months between 22 Nov 2020 to Aug 2022. Patients willing to participate in the study, age more than 18years with established cases of stroke (ischemic or haemorrhagic) on the basis of clinical history, examination and brain imaging were included in the present study.

Results- Among SIADH patients, 83.3% had ischemic stroke and 16.7% had hemorrhagic stroke. Among cerebral salt wasting patients, ischemic stroke was found in 100% of patients. The difference in stroke type seen in the various conditions did not reach statistical significance($p>0.05$).

Conclusion Hyponatremia in the setting of stroke occurs in 14% of patients. The prevalence is higher in males and among the middle aged. Hyponatremia was more common in ischemic stroke than hemorrhagic stroke.

Keywords- ischaemic stroke, dyselectrolytenia, natriuresis

INTRODUCTION

Hyponatremia is the most prevalent abnormality in hospitalized patients and the most prevalent electrolyte imbalance in neurocritically ill patients. It can significantly alter the disease's morbidity and short- and long-term mortality. (1)

Hyponatremia has numerous causes, but in neurologically ill patients, Syndrome of Inappropriate Antidiuresis (SIADH) and Cerebral Salt Wasting (CSW) are the most common. Both these entities are cerebral In origin but have distinct pathophysiology, prognosis and treatment options. The importance of distinguishing between the two lies in the fact that the treatment indicated for one can be harmful if administered to the other. (1-3)

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Since there is considerable overlap between the two conditions, distinguishing between them requires a battery of parameters; no single parameter can define either entity. (4)

SIADH is a subclinical volume expanded state due to inappropriate anti-diuresis. This leads to euvolemic hyponatremia as a result of an excess of volume over sodium levels in the body. In stroke SIADH occurs due to AVP (Arginine vasopressin) secretion inappropriate to the osmotic threshold. The suppressed proximal renal tubular transport in this condition can lead on to bicarbonaturia and hypouricemia. Fluid restriction is an effective therapy. The administration of hypertonic saline is reserved for cases of severe hyponatremia.(5-6)

CSW, on the other hand, is essentially a state of volume depletion brought on by the combined effects of decreased sympathetic outflow and increased natriuretic peptides. This resultant natriuresis leads to volume depletion and an appropriate AVP response. So the treatment for CSW includes an aggressive volume replacement regimen with isotonic saline or in severe cases, hypertonic saline. (6,7)

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.

At present the two entities are differentiated using combined analysis of sodium levels, plasma osmolality, effective arterial blood volume, urine sodium, serum potassium, BUN(blood urea nitrogen)/creatinine ratio. (8,9)

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. Hence, we conducted this prospective study to describe the aetiology of hyponatremia in patients of stroke.

MATERIALS AND METHODS :

This was a prospective observational study was included all inpatients of stroke either ischemic or haemorrhagic admitted in the Department of General Medicine at a tertiary care hospital. A total of 50 patients were included in the study over a duration of 22 months between Nov 2020 to Aug 2022. Patients willing to participate in the study, age more than 18years with established cases of stroke (ischemic or haemorrhagic) on the basis of clinical history, examination and brain imaging were included in the present study.

Patients with history of gastroenteritis, brain tumour, head trauma, pulmonary Koch's, bacterial pneumonia, bronchogenic carcinoma, leukaemia, lymphoma, those that recently underwent major surgery and those with intake of drugs that can cause hyponatremia were excluded from the present study.

METHODS OF COLLECTION OF DATA: The diagnosis of stroke is established on clinical history , physical examination and brain imaging. A written and informed consent was sought from patient. A pre-structured and pretested proforma was used to collect the data. Relevant

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baseline data including age and sex, detailed medical history including conventional risk factors, clinical examinations and relevant investigations.

Method of Statistical Analysis:.

The following methods of statistical analysis have been used in this study. Data was entered in Microsoft excel and analysed using SPSS (Statistical Package for Social Science, Ver.20) package,

The results were averaged (mean + standard deviation) for continuous data and number and percentage for dichotomous data are presented in Table and Figure.

Univariate analyses of the dichotomous variables encoded was performed by means of the Chi square test with Yates correction if required.

RESULTS

Out of 50 patients, 50% were in the age group 41-60 years and 40% in the age group 61-80 years. The mean age of the study population was.

Among 50 patients,45(90%) had motor weakness, 9(18%) had cranial nerve involvement, 7(14%) had speech disturbances, 5(10%) had loss of consciousness, 6(12%) had sensory disturbance,2(4%) had seizures, 2(4%) had cerebellar involvement and 2(4%) had bowel and bladder involvement.

TABLE 1: ASSOCIATION OF DEMOGRAPHIC VARIABLES & CLINICAL VARIABLES WITH HYPONATREMIA

Clinical Variables	HYPONATREMIA		
	Without [n=43]	**SIADH [n=6]**	**CSW [n=1]**
AGE			
21 -40 %	7%	0%	0%
41 – 60 %	46.5%	66.7%	100%
61 – 80 %	44.2%	16.7%	0%
>80 %	2.3%	16.7%	0%
GENDER			
Male %	67.4	50	100
Female %	32.6	50	0
Types of Stroke			

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Ischemic %	79.1	83.3	100
Hemorrhagic %	20.9	16.7	0
TERRITORY			
ACA %	4.7	0	0
MCA %	83.7	66.7	100
PCA %	4.7	16.7	0
MCA-ACA %	2.3	0	0
MCA-PCA %	4.7	16.7	0
SIDE			
RIGHT %	34.9	33.3	0
LEFT %	62.8	66.7	100
BILATERAL %	2.3	0	0

Among 50 patients with stroke, 52% had DM, 50% had HTN, 30% had both DM and HTN, 6% had IHD and 4% had epilepsy.

Among 50 patients, 32% were smokers and 30% were alcoholics.

Among 50 patients, 40 (80%) patient had ischemic stroke and 10(20%) had hemorrhagic stroke. The majority of patients in our study i.e., 41 patients (82%), had stroke corresponding to the Middle Cerebral Artery territory.

In our study, most of the patients had Right sided stroke 64% (n=32), 34% had left sided stroke (n=17) and 2% (n=1) had bilateral involvement.

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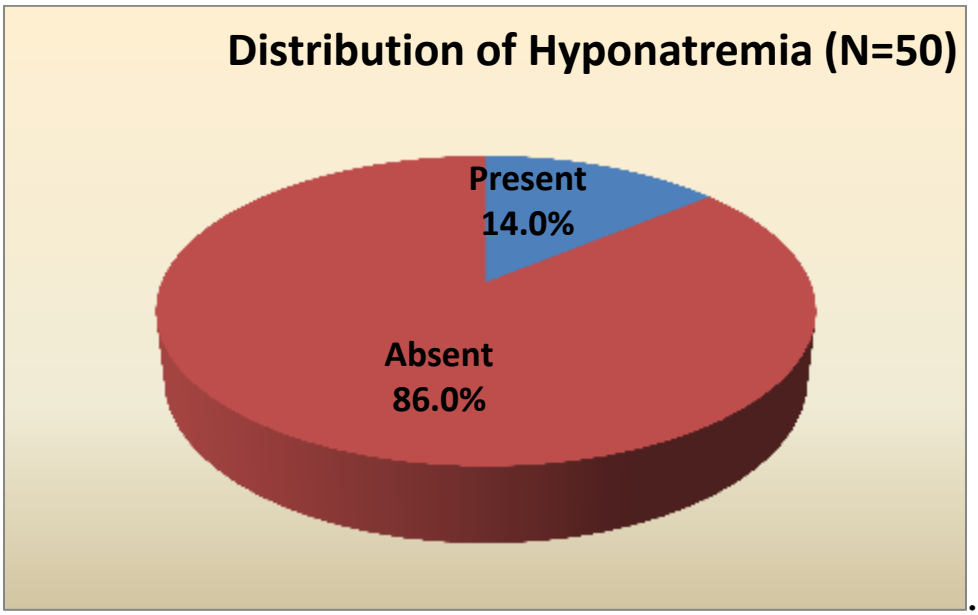
FIGURE 1. INCIDENCE OF HYPOATREMIA



Out of 50 patients, hyponatremia was present in 7(14%) of patients.

TABLE 2 :- SEVERITY OF HYPONATREMIA.

Serum sodium in mEq/l	n	(%)
>134	42	84%
130-134	1	2%
125-129	2	4%
<125	5	10%
Total	50	100%

Among 50 patients, 42 (84%) had normal serum sodium, 1(2%) had serum sodium 130-134,2(4%) had serum sodium 125-129 and 5(10%) had serum sodium <125Meq/l
Of the 50 patients, 85.7% had SIADH (n=6) and 14.3% had CSW (n=1).

TABLE 3. MEAN SODIUM LEVELS

	n	mean	SD	MIN	MAX
SIADH	6	121.67	7.94	106	125
CSW	1	123	-	123	123
Normal	43	138.74	3.88	134	148
Total	7	136.38	7.37	106	148

Patients with SIADH group 6(100%) had normal volume status and patients with CSW group 1(100%) had decreased volume status. Patients with SIADH group 6(100%) had

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normal BUN/creatinine ratio and patients with CSW group 1(100%) had increased BUN/creatinine ratio. Patients with SIADH group 4(60%) had normal HCT,2(40%) had decreased HCT and patients with CSW group 1(100%) had increased HCT. Patients with SIADH group 6(100%) and CSW group 1(100%) had normal serum albumin. Patients with SIADH group 6(100%) and CSW 1(100%) had increased urine sodium levels.

In general, the occurrence of hyponatremia was noted most in the 41-60 year age group i.e., 71.4% (n=5), 14.2%(n=1) in 61-80 year age group and 14.2%(n=1) in the > 80 year age group. The difference in the hyponatremia prevalence among the various age groups didn't reached statistical significance ($p>0.05$)

In the SIADH group, males 50% (n=3) and females 50% (n=3) equally distrubuted.

In the CSW group males comprised 0f 100%(n=1). The variation in sex distribution among the various groups did not reach statistical significance.($p > 0.05$).

Out of the Ischemic stroke patients 15% had hyponatremia. (n=6).

Hyponatremia was seen in 10% (n=1) of patients with haemorrhagic stroke.

Among patients with hyponatremia, 85.7% had ischemic stroke (n=6) and 14.3% had haemorrhagic stroke (n=1).

Among SIADH patients, 83.3% had ischemic stroke and 16.7% had hemorrhagic stroke.

Among cerebral salt wasting patients, ischemic stroke was found in 100% of patients.

The difference in stroke type seen in the various conditions did not reach statistical significance($p>0.05$).

In the MCA territory stroke patients, 12% developed hyponatremia. 33% of MCA-PCA territory stroke patients developed hyponatremia, while Hyponatremia was seen in 33% of the Posterior Cerebral Artery territory stroke.

DISCUSSION

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.

In our study we analysed 50 patients with stroke to study the occurrence of hyponatremia. The majority of stroke patients, 50% belonged to the middle age i.e., 41 – 60 years of age.

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The mean age of stroke occurrence was 60.2 (± 12.7). The mean age of stroke occurrence in males was 58.2 (± 11.12) and that of the females was 64.4 (± 15.04).

This is comparable to the population based study by Dalal et al [11] in Mumbai where the mean age for stroke was 66 years, and in Trivandrum by Sridharan et al [12] where the mean age was 67 years.

The majority of males belonged to 41-60 years age group. The prevalence of stroke in females, however was higher in the 60 to 80 year age group. Thus a higher age stratified prevalence for females was found, which is comparable to the data from the 2008 Mumbai stroke registry [11], where a mean of 63.4 years was recorded for females.

Of the stroke patients in our study group, 66% were male and 34% were female.

The prevalence of ischemic stroke was higher (80%), Hemorrhagic stroke was seen in 20%. This is comparable to the Mumbai stroke registry [11], where 80% of strokes were attributed to be ischemia and 17.7% to haemorrhage.

HYPONATREMIA

The prevalence of hyponatremia was noted in 14% of the stroke patients. The prevalence is comparable to the study by Kuramatsu et al [13] where prevalence was 15%. Rodrigues B [14] reported a prevalence of 16% and Soiza et al [15] 13.8%

Of the hyponatremic patients, there was a higher prevalence of SIADH (85%). CSW contributed to 15%. The study by Saleem et al [16] showed the respective prevalences to be 67% and 33% .

The prevalence of hyponatremia was the most in the 41-60 year age group (71.4%).

The trend of hyponatremia prevalence was more in males (57.1%) but did not reach statistical significance ($p>0.05$).

Hyponatremia was seen in 10% of patients with haemorrhagic stroke. The most common stroke type seen in hyponatremic patients was ischemic stroke (85.7%).

Among SIADH patients, 83.3% had ischemic stroke and 16.7% had hemorrhagic. Saleem et al [15] in his study, showed 35% and 65% respectively.

The majority of patients with SIADH had a Middle Cerebral Territory stroke, 66.7%, and 16.7% had posterior circulation stroke. Saleem et al [16 however, reported 86% and 13% respectively.

In CSW, 100% had Middle Cerebral Artery territory involvement .This was comparable with Saleem et al's study [16] who reported 85%.

In stroke patients 26%(n=13) had potassium imbalance out of which hypokalaemia present in 18%(n=9) and hyperkalaemia in 8%(n=4). Hypokalaemia was more common in ischemic stroke 16%(n=8) than in hemorrhagic stroke2%(n=1).

Prevalence of hypokalaemia 18% in our study is less compared to the study conducted by Hasan MK et al [17], who reported prevalence 27.14%.

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Prevalence of hyperkalemia in stroke patients was 8%(n=4), hyperkalemiawas more common in ischemic stroke6%(n=3) than hemorrhagic stroke2%(n=1).

In stroke patients 28%(n=14) had chloride imbalance out of which hypochloraemia present in 28%(n=14). Hypochloremia was more common in ischemic stroke 24%(n=12) than in hemorrhagic stroke 4%(n=2).

CONCLUSION

Hyponatremia in the setting of stroke occurs in 14% of patients. The prevalence is higher in males and among the middle aged.

Hyponatremia was more common in ischemic stroke than hemorrhagic stroke.

Hyponatremia occurs more with Middle and Posterior cerebral arterial territories involvement.

SIADH has a higher prevalence than Cerebral Salt Wasting.

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