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Hyponatremia in Acute Subarachnoid Hemorrhage: Frequency and Pathophysiology

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Abstract:

Background: *Hyponatremia is the most common electrolyte abnormality seen in patients with aneurysmal SAH. Clinically significant hyponatremia (*Serum Sodium <135 mEq/L*) requires treatment and there is a paucity of outcome studies based on this.*

Materials and Methods: *This prospective study was undertaken in the Department of Neurology, BSMMU. Patients with aneurysmal subarachnoid hemorrhage (SAH) were selected for this study from 1stJanuary 2020 to 31st October, 2022.*

Results: *A total of 64 patients were included in the study. Hyponatremia was observed in 24 (37.5%) patients. Among them, 14 (58.7%) developed hyponatremia within the first week after SAH. Serum osmolality was low in 70.8% of patients who developed hyponatremia. Urinary osmolality was also high for the same number (70.8%). Low serum osmolality and high urine osmolality were significantly ($p<0.05$) higher than that of normal values of serum and urine osmolality in hyponatremia patients.*

Conclusion: *Hyponatremia is common after subarachnoid hemorrhage. SIADH is the commonest cause of hyponatremia after subarachnoid hemorrhage.*

Keywords: *Aneurysmal subarachnoid hemorrhage, hyponatremia, SIADH.*

Introduction:

Hyponatremia is the commonest electrolyte abnormality to occur after subarachnoid hemorrhage[1]. One study showed that 19.6% of patients admitted with SAH developed significant hyponatremia[2]. Hospital stay is longer in patients who developed hyponatremia, which suggests that appropriate treatment of hyponatremia could reduce duration of admission, as well as diminish the likelihood of associated morbidity and mortality. The etiology of hyponatremia after SAH is diverse and includes syndrome of inappropriate antidiuretic hormone secretion (SIADH), cerebral salt wasting syndrome (CSWS), acute ACTH/glucocorticoid deficiency, excessive fluids, and diuretic therapy. So, appropriate therapy must be targeted to the correct etiology to restore eunatremia[3]. However, there is considerable dispute as to which of these diverse etiologies most commonly cause hyponatremia after SAH. A number of small studies have suggested that cerebral salt wasting syndrome (CSWS)[4,5,6,7] is the most common cause due to the finding that, plasma atrial natriuretic peptide (ANP)[4,6] and brain natriuretic peptic (BNP)[8] concentrations both rise after SAH. However, these studies were all small and underpowered. In contrast, recent data have suggested that the presence of elevated plasma BNP concentrations could not be regarded as a reliable predictor of either blood volume status orthedevelopmentofhyponatremia[9]. Elevated plasma BNP concentrations may therefore not necessarily mediate the development of hyponatremia.

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Two retrospective studies have failed to substantiate cerebral salt wasting as a cause of anything more than a minority of cases of hyponatremia after SAH and strongly support SIADH as the predominant cause of hyponatremia[2]. These studies are at variance with those derived from a recent retrospective study of similar size, where 35.4% of severe hyponatremia (<130mmol/L) was considered to be due to SIADH, with a substantial proportion; 22.9%; considered to be secondary to CSWS[10]. However, the patient cohort had more severe SAH than in our study and only those patients with plasma Na <130 mmol/L were analyzed in detail. Most patients in this study also developed hyponatremia more than7 days after SAH, which is later than the natural history of hyponatremia[10]. So, the two largest studies to date are not comparable due to fundamental difference in cohort and methodology. It is now apparent that acute ACTH deficiency is more common than previously recognized after neurosurgical insult[11]. Data from patients who have sustained traumatic brain injury (TBI) reveals that life-threatening hyponatremia[12] and hypotension may require pressor support[13]. Recent studies[14,15] had found that, between 7.1% and 12% of patients became cortisol deficient immediately after SAH. Both of these studies were prospective but small, and analysis of cortisol dynamics was taken place at a single point after SAH. It has been shown that plasma cortisol levels fluctuate significantly after other intracerebral insults such as TBI[1], so transient cortisol deficiency may have been missed, leading to an underestimation of the true frequency of acute cortisol deficiency. It is likely that at least some of those who develop hyponatremia after SAH are suffering from acute ACTH deficiency due to pituitary injury.

Materials and Methods:

This study was conducted in Department of Neurology, BSMMU from 1st January 2020 to 31st October 2022. A total 64 patients with non-traumatic subarachnoid hemorrhage were enrolled in this study. Informed written consent was taken from all patients or attendants. Clinically suspected subarachnoid hemorrhage patients were confirmed by plain CT scan of brain. To locate the aneurysm CTA of brain or Cerebral DSA were done. Serum electrolytes of all selected patients were done. Those who had hyponatremia (serum sodium level < 135 mmol/l); both serum and urinary osmolality were done to evaluate the causes of hyponatremia.

Result:

Table-I

Distribution of demographic variables and history of patients with hyponatremia

Variables	Hyponatremia		p value
	Yes	No	
Age (years)	N (%)		
≤45 years	5 (33.3)	10 (66.7)	
45-60 years	10 (28.6)	25 (71.4)	
>60 years	9 (64.3)	5 (35.7)	
Mean ± SD	54.08 ± 2.57	50.33 ± 1.99	0.252[c]
Sex category			
Male	10 (34.5)	19 (65.5)	0.650[a]
Female	14 (40.0)	21 (60.0)	
Hypertension	10 (41.7)	14 (58.3)	0.594[a]
DM	11 (73.3)	4 (26.7)	*0.001[a]
Smoking	1 (10.0)	9 (90.0)	0.076[b]
Family history	0 (0)	2 (100.0)	0.524[b]
Drug abuse	0 (0)	1 (100.0)	0.999[b]

[a]Chi-squared test was done to measure the level of significance.
[b]Fisher's Exact test was done to measure the level of significance.
[c]Unpaired t test was done to measure the level of significance.
* Significant, Figure within parenthesis indicates percentage.

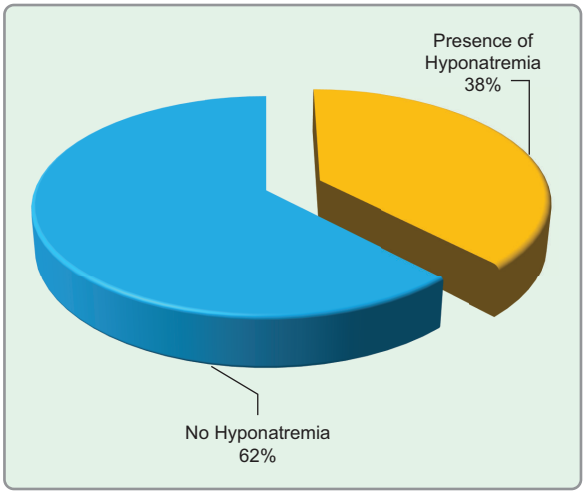

Fig.-1: *Pie chart showing prevalence of hyponatremia in aneurysmal SAH patients.*

Table-II

Time delay of Hyponatremia development from the ictus

Hyponatremia development within	Frequency	Percentage
1st week of ictus	14	58.3
2nd week of ictus	10	41.7
Total	24	100.0

Table-III

Distribution of location of aneurysm of the patients with hyponatremia

Location aneurysm	Hyponatremia Yes	Hyponatremia No	p value
ACOM	10 (50.0)	10 (50.0)	0.197[a]
PCOM right	4 (66.7)	2 (33.3)	0.999[b]
MCA right	2 (22.2)	7 (77.8)	*0.018[b]
MCA left	0 (.0)	3 (100.0)	0.057[b]
Basilar	0 (.0)	2 (100.0)	0.154[b]

[a]Chi-squared test was done to measure the level of significance.
[b]Fisher's Exact test was done to measure the level of significance.
* Significant,
Figure within parenthesis indicates percentage.

Table-IV

Distribution of serum osmolality and urine osmolality of the patients with hyponatremia

Variables	Low	High	Normal	p value
Serum osmolality	17 (70.8)	-	7 (29.2)	*<0.001
Urine osmolality	-	17 (70.8)	7 (29.2)	*<0.001

One proportion z test was done to measure the level of significant.
* Significant
Figure within parenthesis indicates percentage.

Discussion:

In the present study, among 64 patients with subarachnoid hemorrhage, 24 (37.5%) patients developed hyponatremia (serum sodium < 135mmol/l). Among them 14 (58.3%) patients developed hyponatremia within the 1st week of ictus, while 10 (41.7%) patients developed within the 2nd week of ictus. In a study conducted in 2013, the incidence of hyponatremia was 37% among 59 patients[16]. But another study conducted in Ireland revealed 49%of their patients developed hyponatremia[17]. They also found that, 85.7% of their patients developed hyponatremia within first week of ictus, while the rest (14.3%) developed in the second week of ictus[17]. Another study found 68.2% patients developed hyponatremia within first week (31.8%) developed in the second week[2]. So, the overall pattern is most of the patients develop hyponatremia within the first week of SAH; which is consistent with our study.

In our study 45- 60 years group mostly suffered from SAH, male to female ratio of 1:1.2. Previous study showed median age group was 53 years and male to female ratio was 1:0.89[17]. In another study, the mean age was 50.5 years[16]. They also found the male to female ratio as 1:0.97[16]. The age group of our study matches but sex category varies from some previous studies.

As aneurysm in SAH is more common in the anterior circulation, most of our patients (97%) had aneurysm in the carotid system. Aneurysm location may potentially influence the severity of hyponatremia as the carotid system is related to the hypothalamic-pituitary-adrenal axis[18]. But multiple studies failed to connect any possible connection between hyponatremia and location of

aneurysm[1,2,16,18]. So, further studies may address this issue.

In our study, among the 24 patients who suffered from hyponatremia 17 (70.8%) patients suffered from SIADH, as evidenced by presence of high urinary osmolality in presence of hypotonic plasma and absence of other contributing factors. SIADH was the predominant cause of hyponatremia in SAH in many previous studies like 62.9%[2], 63.6% [17]. But, SIADH must be differentiated from other causes of hyponatremia, especially cerebral salt wasting syndrome, as treatment modality depends upon the volume status of the patient.

The limitation of our study is that it was done at a single institute. Being a tertiary level referral institute, many patients reached the institute many days/months after the initial symptoms.

Conclusion:

Hyponatremia is a common systemic complication after acute subarachnoid hemorrhage. Among the different pathophysiology of hyponatremia SIADH is the most common.

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