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Clinical profile of hyponatremia in critical care patients in a tertiary care centre in India.

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ABSTRACT

INTRODUCTION: Disorders of sodium and water metabolism are frequently encountered in patients admitted to the Intensive Care Unit (ICU), and may even be acquired there. A systematic approach is needed to evaluate the causes of hyponatremia for better patient care.

MATERIAL AND METHODS: 100 adult patients with admission serum sodium levels <135 mEq/L in the ICU were recruited for this study over 18 months. Through history taking and appropriate laboratory investigations, the prevalence, causes, morbidity and mortality of hyponatremia were assessed. Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) was diagnosed using Schwartz and Bartter clinical criterion.

RESULTS: 23 cases were deemed to have pseudohyponatremia likely caused by dyslipidemia or hyperproteinemia, whereas remaining 77 cases had true hyponatremia. Values of arterial and venous sodium have a positive correlation indicating agreement between the parameters. Majority of subjects were males (61%). Causes of hyponatremia include: neurological causes in 34 cases (44.2%), followed by gastrointestinal cause 18 cases (23.4%), respiratory cause 15 cases (19.5%), cardiac cause 5 cases (6.5%), and other causes 5 cases (6.5%). Most frequently encountered diagnosis included cerebrovascular accident (16 cases), pneumonia (10 cases), metabolic encephalopathy (10 cases), acute gastroenteritis (8 cases) and tubercular meningitis (6 cases). Of 77 cases studied, 18 cases (23.4%) had hypovolemic hyponatremia (due to acute gastroenteritis), 51 cases (66.2%) had euvolemic hyponatremia (due to SIADH, likely caused by cerebrovascular accident, pneumonia or metabolic encephalopathy) and 8 cases (10.4%) had hypervolemic hyponatremia (due to chronic renal failure or congestive cardiac failure). Mortality in this population was 11.7%, and was seen mainly in patients of severe hyponatremia.

CONCLUSIONS: Severity of hyponatremia, male gender and neurological symptoms correlated significantly with morbidity and mortality in this cohort and the information from this study can be used to better identify patients at risk of adverse outcomes due to hyponatremia in critical care setting.

KEY WORDS: Hyponatremia, ICU, SIADH, pseudohyponatremia.

INTRODUCTION

Hyponatremia is the most common electrolyte disorder ranging from 5.2 to 28.8% in hospitalized patients [1]. It represents excess of body water relative to body sodium content and is frequently referred to as serum sodium level <135mEq/L [2]. Mild hyponatremia is defined as plasma sodium levels 130-135 mEq/L [3]. Severe hyponatremia (plasma sodium <125mEq/L) may be life threatening and is associated with substantial morbidity [4].

True hyponatremia is hypotonic hyponatremia. It is of 3 subtypes: hypovolemic, hypervolemic or euvolemic hyponatremia, of which various pathophysiologies and factors are at play [5]. In the vast majority of cases, hyponatremia occurs as a result of a proportional excess of water relative to the plasma sodium. Lack of sodium alone is very rarely the cause of hyponatremia. Sodium loss can lead to a state of volume depletion, with volume depletion serving as a signal for the release of anti diuretic hormone (ADH). As a result of ADH-stimulated water retention, blood sodium becomes diluted and hyponatremia results. The increase in ADH is secondary to either physiologic but excessive ADH release (as occurs with nausea or severe pain) or inappropriate and non-physiologic secretion of ADH ie. Syndrome of Inappropriate Antidiuretic hormone (SIADH). SIADH is often categorized under euvolemic hyponatremia along with hyponatremia due to inadequate urine solute, hyponatremia due to hypothyroidism or central adrenal insufficiency [5].

This study aims to describe the clinical profile of patients admitted with hyponatremia in a mixed surgical and medical ICU. Disorders of sodium and water metabolism are frequently encountered in patients admitted to the Intensive Care Unit (ICU), and may even be acquired there. A systematic approach is needed in which the detailed history, physical examination, routine blood and urine tests, and relevant diagnostic tests such as morning serum cortisol levels, thyroid function tests and arterial blood gases are used to assess and treat critically ill patients without causing significant morbidity and mortality.

MATERIAL AND METHODS

After attaining consent of the institutional ethical committee, adult cases admitted in the Intensive Care Unit of Bharati Hospital and Research Centre, Pune from September 2014 to February 2016 with hyponatremia were included in this study. Patients' serum sodium levels were evaluated on admission. Patients with serum sodium levels <135 mEq/L (with or without pre-existing hyponatremia-related complications) were further assessed after giving appropriate informed written consent as per Good Clinical Practice (GCP) Guidelines. Patients underwent history recording, clinical examination, and relevant laboratory investigations in order to determine the cause of hyponatremia. Special investigations were sent as per the requirement of the case, which included serum cortisol levels; T3, T4, TSH levels; serum and urine osmolality, spot urine sodium or radiological investigations such as CT/MRI. Pseudohyponatremia was diagnosed by determining serum osmolality in all patients. Normal serum osmolality along with serum sodium less than 135mEq/L suggested pseudohyponatremia.

SIADH was diagnosed using the Schwartz and Bartter clinical criterion [6]. Osmometer was used for the determination of serum osmolality and urine osmolality as per requirement. P-value was determined by Chi-Square test. P-value <0.05 is considered to be statistically significant..

RESULTS

Among the 100 cases, the differentiation between pseudohyponatremia and true hyponatremia was made. In the present study, there were 23 cases who were deemed to have pseudohyponatremia, whereas remaining 77 cases had true hyponatremia. Among the patients deemed to have pseudohyponatremia, 13 patients (56.5%) had hyperlipidemia. Other causes of pseudohyponatremia included hyperproteinemia (dehydration, HIV, Lupus).

The average value of arterial sample was 120.64 ± 7.55 mEq/L, and venous sample was 121 ± 7.91 mEq/L. The values of arterial and venous sodium have a positive correlation indicating agreement between the parameters. The mean ± standard deviation of age of the entire study group is 59.7 ± 16.2 years. The mean age for females is 61.4 years, and mean age for males is 58.7 years. The age range for males was from 18 to 83 years, and 20 to 85 years in females. As reflected in the total number of patients, majority were males in most of the age groups except >80 years in which more females were present. Age group of less than 20 years comprised only of males (not significant). The study population mostly consisted of patients above the age of 40 years (84.4%). The distribution of severity of hyponatremia did not differ between the age groups. (Figure 1)

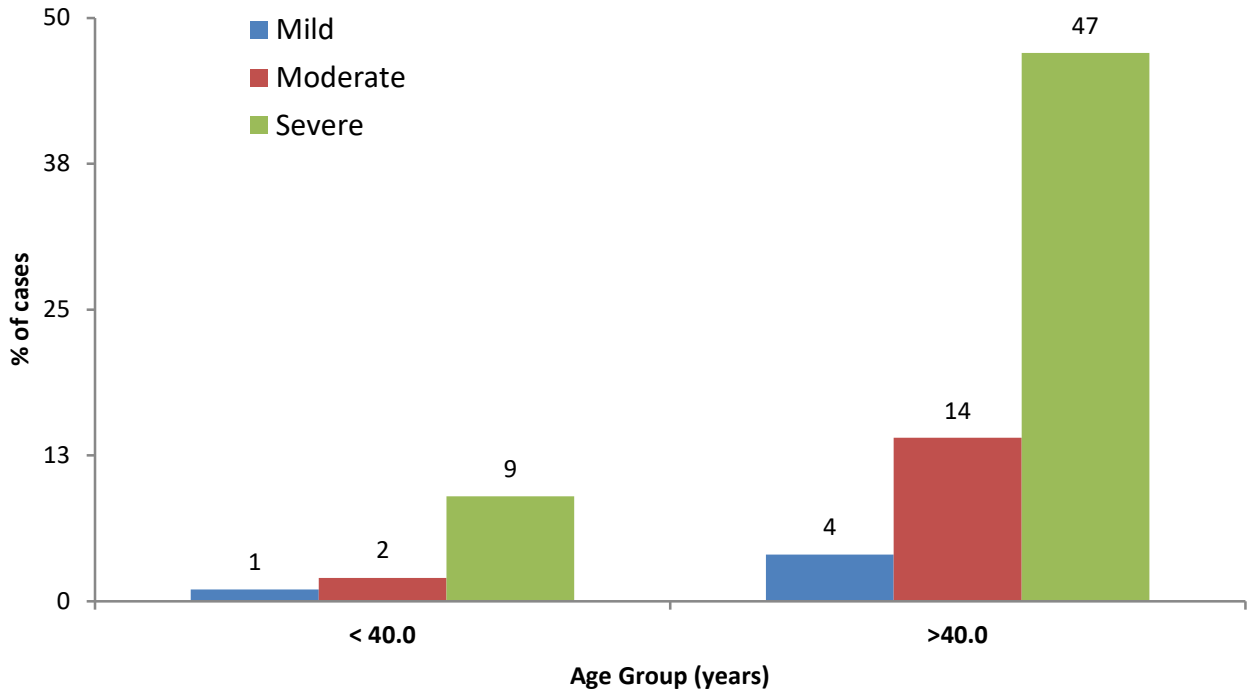

Figure 1. Age distribution of cases with hyponatremia. Value expressed in number of patients, where n=77.

Among the 77 patients with true hyponatremia studied, 47 (61%) were males, and 30 (39%) were females. The male to female ratio for the patients with true hyponatremia was 1.56 : 1.0. Of 77 cases studied, 5 cases (6.5%) had mild hyponatremia with serum sodium 130-135 mEq/L, 16 cases (20.8%) had moderate hyponatremia with serum sodium 125-130 mEq/L and 56 cases (72.7%) had severe hyponatremia with serum sodium less than 125 mEq/L. (Figure 2)

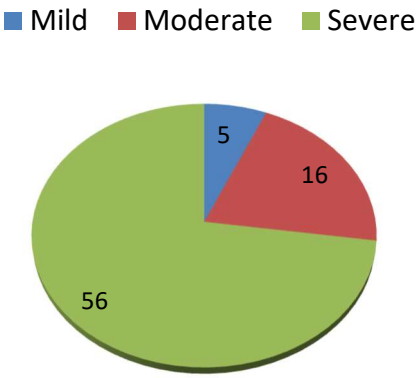

Figure 2. Distribution of patient population according to severity of hyponatremia.
Value expressed in number of patients where, n=77.

Most frequently encountered cases included cerebrovascular accident (16 cases), pneumonia (10 cases), metabolic encephalopathy (10 cases), acute gastroenteritis (8 cases) and tubercular meningitis (6 cases). Of the 77 patients diagnosed with hyponatremia, the majority 34 cases (44.2%) had a neurological cause, followed by gastrointestinal cause 18 cases (23.4%), respiratory cause 15 cases (19.5%), cardiac cause 5 cases (6.5%), and other causes 5 cases (6.5%). (Figure 3)

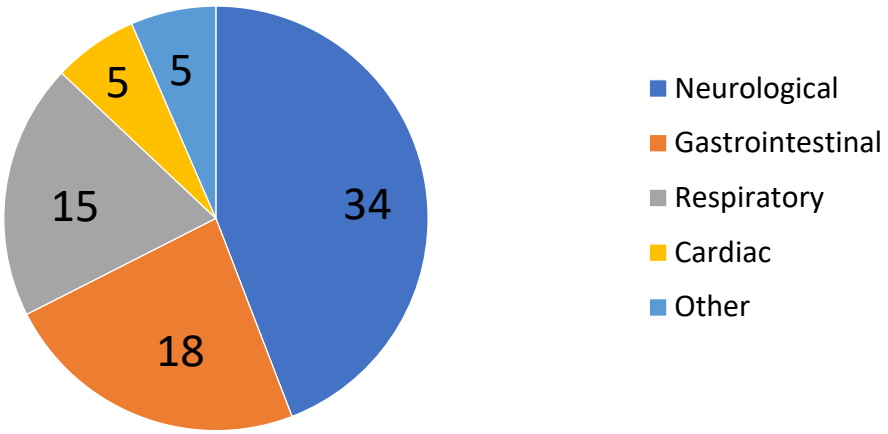

Figure 3. Distribution of patient population according to severity of hyponatremia.
Value expressed in number of patients where, n=77.

Of 77 cases studied, 18 cases (23.4%) had hypovolemic hyponatremia, 51 cases (66.2%) had euvolemic hyponatremia and 8 cases (10.4%) had hypervolemic hyponatremia. In patients with euvolemic hyponatremia, syndrome of inappropriate anti diuretic hormone (SIADH) was the most common cause. Out of 51 patients in the study who presented with euvolemic hyponatremia, 47 patients (92.2%) were diagnosed with SIADH, 3 patients (5.8%) with hypothyroidism and 1 patient (2.0%) with Addison's disease. Among those with SIADH, the causes included patients diagnosed with COPD, CVA, pneumonia, tubercular meningitis, pulmonary tuberculosis, metabolic encephalopathy, cerebral malaria, viral encephalitis and bacterial meningitis. (Table 1)

Table 1. Causes of euvolemic hyponatremia.

Cause of euvolemia (n=51)	**n**	**%**
1) SIADH	47	92.2%
2) Hypothyroid	3	5.8%
3) Addison's Disease	1	2.0%
Causes of SIADH (n=47)	**n**	**%**
1) CVA	14	29.8%
2) Pneumonia	9	19.1%
3) Metabolic Encephalopathy	7	14.9%
4) Tubercular Meningitis	6	12.8%
5) Pulmonary Tuberculosis	5	10.6%
6) Chronic Obstructive Pulmonary Disease	2	4.3%
7) Cerebral Malaria	2	4.3%
8) Bacterial Meningitis	1	2.1%
9) Viral Encephalitis	1	2.1%

Out of 9 patients (11.7%) in the study whose outcome was death, 66.7% patients suffered from severe hyponatremia. Cause of death in patients suffering from mild hyponatremia was contributed more to concomitant comorbidities rather than severity of hyponatremia. (Table 2)

Table 2. Cause of death.

	Severity of Hyponatremia		
	Mild	Moderate	Severe
Cause of Death	SLE 1	CVA 1	CVA 1
		Pneumonia 1	Chronic Renal Failure 1
			Cerebral Malaria 1
			Hepatic Cirrhosis 1
			Congestive Cardiac Failure 1
			Tubercular Meningitis 1
Total	1 case	2 cases	6 cases

DISCUSSION

True Versus Pseudohyponatremia

Out of 100 cases studied, there were 23 cases (23%) who were deemed to have pseudohyponatremia, whereas remaining 77 cases (77%) had true hyponatremia. Pseudohyponatremia was diagnosed by measuring serum osmolality and calculating osmolality in all patients. Normal measured serum osmolality, low calculated serum osmolality, and presence of serum sodium level <135 mEq/L suggested pseudohyponatremia. In our study, pseudohyponatremia could be attributed to hyperlipidemia 13 cases (56.5%), and hyperproteinemia in 10 cases (43.5%).

Correlation of Arterial Sodium with Venous Sodium

All patients were subjected to arterial blood gas in which arterial sodium was noted and compared to venous sodium. The average value of arterial sample was 120.64 ± 7.55 mEq/L, and venous sample was 121 ± 7.91 mEq/L. Similar to the present study, in a study by Nanda SK et al, the values of arterial and venous sodium have a positive correlation indicating agreement between the parameters [7].

Age and Sex Distribution

65 patients (84.4%) were above the age of 40 years in the present study. The ratio of patients above 40 years to patients below 40 years was 5.17 : 1.0. Similar trend was also observed by Hochman [8] and Vurgese [9] in their study, which showed that elderly patients were more prone for hyponatremia. The distribution of severity did not differ between the age groups in the present study as well as in the comparative studies. In the study by Baji PP et al [10], the mean age of patient population was 59.4,

whereas in our population it was 59.7. In similar studies by Anderson [11] and Vurgese the mean age was 58 years and 57.05 years respectively. Baji PP et al found that 72% patients were above 50 years of age, while the remaining were below 50 years of age. Similar finding was seen in our study, in which 71.4% of patients were above 50 years of age. In the present study, there were 47 (61%) males and 30 (39%) females with ratio 1.56 : 1.0. This ratio was similar to the ratio observed in the study by Baji PP et al.

Distribution of Hyponatremia according to Severity

Of 77 cases studied, 5 cases (6.5%) had mild hyponatremia with serum sodium 130-135 mEq/L, 16 cases (20.8%) had moderate hyponatremia with serum sodium 125-130 mEq/L and 56 cases (72.7%) had severe hyponatremia with serum sodium less than 125 mEq/L. Our study had more patients with moderate to severe hyponatremia (93.5%) as compared to the study by Hochman et al in which 61% patients had moderate to severe hyponatremia.

Distribution of Hyponatremia according to Volume Status

The hydration status of the patients was diagnosed on the basis of clinical examination. Patients were deemed hypovolemic if there were signs of dehydration present, such as reduced skin turgor or dry mucous membranes. Patients were deemed hypervolemic by presence of raised jugular venous pressure, congestive hepatomegaly, ascites, pulmonary oedema or peripheral oedema. Patients without these signs were deemed as euvolemic. The incidence of euvolemic and hypovolemic hyponatremia in our study was comparable to the studies by Hochman, Baji, Anderson et al. The incidence of hypervolemic hyponatremia however was less in our study as compared to the other studies. (Table 3)

Table 3. Comparison of the distribution of hyponatremia according to volume status in various studies.

Hyponatremia	Hochman (%)	Baji (%)	Anderson (%)	Present Study (%)
Euvolemia	50	43	34	66.2
Hypovolemia	30.5	19	35	23.4
Hypervolemia	19.5	38	31	10.4

Distribution of Causes of Hyponatremia according to Volume Status Euvolemic Hyponatremia

Majority of the patients in this study had euvolemic hyponatremia 51 cases (66.2%), of which 47 cases (92.2%) were diagnosed to have SIADH by measuring serum and urine sodium, and serum and urine osmolality. In the study by Anderson et al also, SIADH was found to be the most common cause of euvolemic hyponatremia. Neurological causes of SIADH were most common in our study and included 14 cases of cerebrovascular accident (29.8%), 7 cases of metabolic encephalopathy (14.9%), 1 cases of bacterial meningitis (2.1%), 6 cases of tubercular meningitis (12.8%), and 2 cases of cerebral malaria (4.3%). Respiratory causes of SIADH were seen in 9 cases of pneumonia (19.1%) and 5 cases of pulmonary tuberculosis (10.6%) and 2 cases of COPD (4.3%). Majority of the patients with SIADH had severe hyponatremia.

Hypovolemic and Hypervolemic Hyponatremia

In the present study, 18 cases (23.4%) of hyponatremia were hypovolemic. Most common cause of hypovolemic hyponatremia was acute gastroenteritis (38.9%). Other causes include: pneumonia, enteric fever, hepatic cirrhosis, and diabetic ketoacidosis. 8 cases (10.4%) had hypervolemic hyponatremia in the present study. Causes of hypervolemic hyponatremia included 4 cases of chronic renal failure, 2 cases of congestive cardiac failure, 1 case of hepatic cirrhosis and 1 case of cor pulmonale.

Distribution of Presenting Symptoms of Hyponatremia According to Severity

Common symptoms as observed in mild hyponatremia included nausea (3 cases), vomiting (3 cases), drowsiness (6 cases) and headache (2 cases). Fatigue (11 cases), nausea (8 cases) and vomiting (6 cases) were frequently observed in moderate hyponatremia. Patients with severe hyponatremia presented with fatigue (34 cases), irritability (34 cases), drowsiness (35 cases), headache (15 cases) and seizures (12 cases). Neurological symptoms and signs were more frequently associated with increasing severity of hyponatremia. All of the cases in which seizures were present suffered from severe hyponatremia. Similar findings were present in the study by Baji PP et al. Thus, in our study, presence and type of symptoms correlated with severity of hyponatremia. Seizures, drowsiness, irritability, fatigue and headache were more common in patients with severe hyponatremia than in patients with mild or moderate hyponatremia.

Correlation of Level of Consciousness with Severity of Hyponatremia

Out of the 56 patients with severe hyponatremia in our study, it was found that 58.9% of patients had altered sensorium (37.5% drowsy, 21.4% unconscious). Unconsciousness was seen only in patients with severe hyponatremia. In the study by Baji et al, 11% of patients suffered from seizures, which is comparable to the present study. In both studies, drowsiness was found to be the most common neurological symptom.

Correlation of Severity of Hyponatremia with Mortality

The mortality rate of the present study was 11.7% (9 cases). On the other hand, in a study by Gill G et al [12], the mortality rate was 27% and in a study by Baji PP et al the mortality rate was 21%. Of the patients who died, 6 cases (66.7%) had severe hyponatremia. The diagnosis of the patients whose outcome resulted in death included neurological causes like cerebrovascular accident, cerebral malaria, and tubercular meningitis. The death of the few cases who had mild to moderate hyponatremia was attributable more to prior comorbidities rather than severity of hyponatremia.

Limitations of the Study

This study would have benefited from a larger sample size. This would have enhanced the generalizability of the results.

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CONCLUSIONS

This study has been undertaken to understand the etiology and common clinical features of hyponatremia in ICU hospitalized patients and to correlate the outcome of these patients with admission serum sodium levels. The percentage of patients who suffered from hypovolemic, hypervolemic and euvolemic hyponatremia was comparable to other studies. Most of the patients in the present study were found to have euvolemic hyponatremia, of which SIADH was the most common cause followed by hypothyroidism and hypoadrenalism. The commonest causes of SIADH were neurological and respiratory. The severity of hyponatremia correlated with the symptoms of hyponatremia. The frequency of neurological symptoms increased with the severity of hyponatremia. Mortality was more common in patients with neurological disease.

SUPPLEMENTARY INFORMATION

Funding: *No fund was received related to this study.*
Institutional Review Statement: *The study was conducted according to the guidelines of the Declaration of Helsinki.*
Informed Consent Statement: *Informed consent was obtained from all subjects involved in the study.*
Data Availability Statement: *The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.*
Conflicts of Interest: *The authors declare no conflicts of interest.*

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