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Original Research Article

Profile of hyponatremia in a tertiary care centre in North India

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ABSTRACT

Background: Hyponatremia is the commonest electrolyte imbalance. Hyponatremia is a heterogenous disorder and classified into hypovolemic, euvolemic and hypervolemic types depending on the volume status of the patient. Approach is based on etiology and type of hyponatremia. The aim of the present study was to determine the profile of hyponatremia in adult patients including underlying etiology, type, clinical features and outcome
Methods: The study was conducted at BRD medical college Gorakhpur, India between July 2014 to August 2015 after approval by the ethical committee. Consenting patients >18 years of age with hyponatremia (<130meq/l) were included and investigated as per protocol. Based on volume status and urinary sodium patients were classified as euvolemic, hypervolemic and hypovolemic.
Results: N = 250, mean age 53.9 years. 56% males, 154(61.6%) patients had euvolemic, 53 (21.2%) hypervolemic and 43(17.2%) hypovolemic hyponatremia. The most common causes for euvolemic, hypervolemic, hypovolemic hyponatremia were CNS infections, CLD and acute gastroenteritis respectively. Neurologic symptoms were more common in severe as compared to mild hyponatremia (69.7% versus 8.1%). Seizures attributable to hyponatremia were seen in 44 patients (17.6%), all with severe hyponatremia. Overall mortality was 14%. Deaths were more frequently seen in patients with severe hyponatremia as compared to patients with mild hyponatremia (25.5% vs. 4.7% P = 0.035).
Conclusions: Euvolemic hyponatremia is the most common type seen in hospitalized patients and is associated mainly with intracranial pathologies. Severe hyponatremia is significantly associated with neurological manifestations and higher mortality.

Keywords: Hyponatremia, Serum osmolality, Urine osmolality, Urinary excretion of sodium

INTRODUCTION

Hyponatremia defined as serum sodium less than 135 meq/l is the most common electrolyte disorder among hospitalized patients.[1-5] It is associated with mortality and morbidity ranging from 5-50 % depending on severity and acuity of onset.[6]

Hyponatremia occurs in a broad spectrum of patients. It affects all age groups and both sexes equally but is most commonly found in elderly persons because of an increase frequency of comorbidities, that can lower serum sodium levels (example cardiac ,hepatic or renal failure).[7-9]

Patients in whom the serum sodium concentration is greater than 130 mEq/L are usually asymptomatic, whereas those in whom these values are lower may have symptoms. Symptoms occurring early in hyponatremia are usually anorexia, nausea, vomiting. Some patients may have headache and irritability. As serum sodium levels falls further patients develop neuropsychiatry symptoms. These symptoms range from restlessness, altered consciousness, lethargy, seizures to coma. There

are serious neurological sequelae associated with hyponatremia and its management.[10]

As the symptomatology varies markedly the diagnosis of hyponatremia is difficult to establish. Thorough evaluation for hyponatremia mandates accurate history taking and clinical examination along with various investigations. Prompt recognition and optimal management of hyponatremia in hospitalized patients may reduce in-hospital mortality and symptom severity, allow for less intensive hospital care, decrease the duration of hospitalization and associated costs, and improve the treatment of underlying comorbid conditions and patient's quality of life.

Hyponatremia is not a homogenous disorder and depending upon the volume status of the patient can either be euvolemic, hypervolemic or hypovolemic.[1,11] Each etiology and type of hyponatremia requires a different approach to treatment. The etiological profile may depend upon the climate, disease distribution pattern and peripheral services, which vary from region to region.

The etiological profiling and outcomes of patients with hyponatremia at admission in an acute care setting, especially in the tropical regions has not been studied. Therefore this study was done to find the incidence, types and outcomes of hyponatremia at admission in patients attending medical emergency.

METHODS

The present study was conducted in Department of Medicine, B.R.D Medical College Gorakhpur between July 2014 to August 2015 after approval by the ethical committee.

All patients who had hyponatremia (130 mEq/L) on initial serum electrolyte analysis by ion electrode method were considered for study. The electrolyte analysis was done by ESCHWEILER combi line machine. Patient who did not give consent were excluded from the study.

Patients were evaluated clinically to access their fluid status. Various tests were performed on these patients to determine the probable and underlying causes for hyponatremia. The routine investigations done in these patients were the haemoglobin, total count, differential count, erythrocyte sedimentation rate, electrocardiogram, chest x-ray, 24 hours urine sample for urine sodium, urine urea and urine glucose, blood sugar, urea and creatinine. Patients suspected with other causes were investigated accordingly. Other investigations like CSF analysis, thyroid function, cortisol levels, abdominal sonography, and computer tomographic scans were performed on some patients depending on the clinical suspicion. Wherever possible urine osmolality was also done. Based on serum sodium level, these patients were divided into mild hyponatremia with serum sodium 125-130 mEq/L, moderate hyponatremia with serum sodium 115-124 mEq/L and severe hyponatremia with serum sodium less than or equal to 115 mEq/L. Based on fluid status and urinary sodium these cases were further divided into euvolemic and hypervolemic and hypovolemic hyponatremia. 250 patient for whom detailed history and investigations were available and with serum sodium level less than or equal to 130mEq/L.

The qualitative data are expressed in proportion and percentages and the quantitative data as mean and standard deviation. The difference in proportion is analysed by using Chi-square test and Fisher exact test wherever applicable and the difference in means is analysed by using student t test (unpaired). Significance level for tests has been determined as 95% ($p < 0.05$). The difference is significant if $p < 0.05$. 2×3 Fisher exact test has been used to find the significance of study parameters on categorical scale between two groups.

RESULTS

A total of 250 patients 140 (males) and 110 (females) were studied. The incidence of hyponatremia was 4% percent. The mean age of the patients was 53.9±16.46 years. 171 patients were more than 50 years and only 79 were less than 50 years.

Table 1 shows the distribution of grades of hyponatremia across different types. Mild hyponatremia was present in 87 patients, moderate in 98 and severe in 65. The mean value of serum sodium levels in patients with mild hyponatremia was 126 mEq/L, moderate hyponatremia was 120 mEq/L, severe hyponatremia was 113 mEq/L. According to clinical findings, 154 patients (61.6%) had euvolemia, 53 (21.2%) had hypervolemia and 43 (17.2%) had hypovolemia.

Table 1: Distribution of grades of hyponatremia across different types.

Type of hyponatremia	Grades of hyponatremia	No. of patients	Total (n=250)
Euvolemia	Mild	46	154 (61.6%)
	Moderate	48	
	Severe	60	
Hypervolemia	Mild	10	53 (21.2%)
	Moderate	24	
	Severe	19	
Hypovolemia	Mild	20	43 (17.2%)
	Moderate	11	
	Severe	12	

The gastrointestinal symptoms were predominantly nausea and vomiting and the neurological symptoms were headache, irritability, seizure. On clinical examination, 5.6% of patients were restless, 23.6% were unconscious and 28.8% were drowsy, 42% were conscious. Neurological signs were present in 7/86

patients with mild hyponatremia and 60/86 patients with severe hyponatremia. Seizure attributable to electrolyte abnormality were seen in 44 patients, all with serum sodium <115 mEq/L. Table 2 shows the type of hyponatremia in various etiologies. The most common association of euvolemic hyponatremia was with CNS infection (14 %) and stroke (12%). Hypervolemic was seen in CLD (8%), CHF (8%) and CKD (4%), hypovolemic was mostly associated with gastroenteritis (39.5%).

Table 2: Type of hyponatremia in various etiologies.

Diagnosis	Euvolumia	Hyper volumia	Hypovolumia	Total
Acute hepatic failure	2	0	1	3
Addisonian disease	4	0	0	4
AGE	0	0	17	17
AME	16	0	1	17
CHF	0	20	0	20
CKD	0	11	0	11
CLD	1	22	0	23
COPD	19	0	3	22
CVA	30	0	1	31
DKA	0	0	6	6
GTCS	1	0	1	2
Hypothyroidism	4	0	0	4
Malignancy	4	0	1	5
Metabolic encephalopathy	5	0	2	7
Pneumonia	20	0	4	24
Pulmonary TB	3	0	5	8
Septicemic encephalopathy	8	0	1	9
TBM	18	0	0	18
Nil	19	0	0	19
Total	**154**	**53**	**43**	**250**

The urinary sodium excretion in patients with clinical euvolemia, hypervolemia and hypovolemia was 66.8, 25 and 29.3 mEq/L respectively. The mean urea was 27.2 mg/dl in patients with euvolemic hyponatremia, 65.6 mg/dl in hypervolemic and 77.5 mg/dl in hypovolemic hypernatremia .The mean creatinine were 0.95 mg/dl, 1.8 mg/dl and 3.4 mg/dl in patients with euvolemic hypervolemic hypovolemic hyponatremia respectively.

Table 3: Correlation of hyponatremia grade and outcome.

Grades of hyponatremia	Death	Discharge	Total
Mild	4	82	86
	4.7%	95.3%	100%
Moderate	14	84	98
	14.3%	85.7%	100%
Severe	17	49	66
	25.8%	74.2%	100%
Total	**35**	**215**	**250**
	14.0%	**86%**	**100%**

The mortality was 14% in this study. Table 3 shows mortality according to severity of hyponatremia. Significantly more deaths were observed in severe hyponatremia (p= 0.035). Table 4 shows correlation of grades of hyponatremia and outcome in various etiologies.

DISCUSSION

We found the incidence of hyponatremia defined as serum sodium <130 mEq/L as 4% in a medical emergency ward. The incidence of hyponatremia varies based on the definition of hyponatremia. When taken as serum sodium <135 mEq/L it has an incidence as high as 15 –22% in general hospital population and when taken as serum sodium less than 130 mEq/L other studies have also found an incidence of 4- 6.9% .[12,13]

Hyponatremia was seen more commonly in patients above 50 year than in younger patients. Similar trends have also been seen in other studies.[13,14] The various factor responsible for hyponatremia in elderly may be decrease in glomerular filtration rate, increase ability of kidney to conserve sodium , increased release of arginine

vasopressin to a given stimulus , various drug taken by them, decreases appetite and concomitant illness.[15-17]

In this study euvolemic hyponatremia were present in 61.2% of patients. Other hospital based studies have also found euvolemic hyponatremia as the commonest type. The most common cause of euvolemic hyponatremia is SIADH. Euvolemic hyponatremia was most commonly with CNS infection (14%) and stroke (12%), both of which could lead to secondary SIADH.

These two causes were overall the most common etiologies of hyponatremia in our study. SIADH occurs more in elderly persons but in our study the mean age of patients of euvolemic hyponatremia was no different than from other groups.

Table 4: Correlation of hyponatremia grade and outcome in various etiologies.

Diseases	Mild		Moderate		Severe	
	Death	Discharge	Death	Discharge	Death	Discharge
Infection (COPD, Pneunomia, Pulmonary TB, Septicemic encephalopathy, TBM, AME)	2 (9%)	20	5 (10.2%)	44	11 (39%)	17
CVA	1 (9%)	10	2 (18.2%)	9	1 (11%)	8
CHF	1 (25%)	3	2 (25%)	6	5 (62.5%)	3
CLD	0	11	1 (11%)	8	0	3
Hypothyroidism	0	1	1 (100%)	0	0	1
GTCS	1 (50%)	1	0	0	0	0
Age	0	5	1 (14.3%)	6	0	5

We found that as serum sodium level decreases, the severity of symptom increases. Patients with serum sodium less than 115 mEq/L had severe neurological symptoms like seizure and unconsciousness. This further supports the fact that degree of hyponatremia could more or less predict the symptoms of hyponatremia. Across all grades of hyponatremia, patients with euvolemic hyponatremia were more symptomatic and had more severe symptoms as compared to other groups. Although the severity of symptoms is also dependant on the rate of fall of serum sodium this relationship cannot be concluded from our study as we had no pre-hospital value of serum sodium. The difference in underlying disease could be another reason for this.

Severe hyponatremia defined as sodium levels <115 mEq/L was infrequently seen with causes associated with hypovolemic or hypervolemic hyponatremia. Both of these had predominant moderate grade hyponatremia.

Serum urea and creatinine levels were within normal range in euvolemic patients and above normal in both hypo and hypervolemic patients. Also excretion of sodium was less than 30 mEq/L in both hypo and hypervolemic patients.

A urine sodium concentration <30 mmol/l suggests low effective arterial blood volume. Although patients with hypervolemia due to conditions like CHF etc are edematous, they usually have a low effective circulatory volume. This may explain the reason for increased urea and creatinine levels in both hypo and hypervolemic patients.

As shown in the Table 2, mortality was 4.7% in patients with mild hyponatremia, 14.3% in patients with moderate hyponatremia and 25.5% in patients with severe hyponatremia. This comparison does not take into account the underlying illness. When we compared mortality in sub groups of different illnesses, we found that in patients of CHF, CNS infection and sepsis there was a significant difference in mortality between patients with mild vs. severe hyponatremia. Hyponatremia as a risk factor of mortality in patients of CHF18 has also been shown in various other studies. The present guidelines on management of hyponatremia recommend a serum osmolality and urine osmolality based approach to management of hyponatremia. We could get urine osmolality done only in 65 patients. Out of them none of the patient had urine osmolality <100 mEq/L. So urine osmolality may not be a good clinical tool in patients of hyponatremia who are admitted.

Moreover urine osmolality is recommended to be done by freezing point depression method but most of the lab do not do it and out of 65 patients only 22 patients were done by freezing point depression method.

In resource limited setting and cost constraints it would be prudent to do only a urinary sodium measurement in patients of hyponatremia. Serum osmolality and urine osmolality even if done by appropriate methods may not give any additional information. Urinary excretion of sodium along with clinical history and examination is sufficient for categorisation of hyponatremia between euvolemic, hypervolemic and hypovolemic and its management.

CONCLUSION

Hyponatremia is a common electrolyte abnormality that affects morbidity and mortality. As it can be asymptomatic, it needs to be measured in all hospitalised patients. Simple measurement and clinical history and examination are helpful in classifying hyponatremia and aiding in its management.

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