

Clinico-etiological profile of hyponatremia among elderly age group patients in a tertiary care hospital in Sikkim

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ABSTRACT

Background: Hyponatremia is a common condition observed in hospitalized patients. The incidence is much more in the elderly patients owing to impaired ability to maintain water and electrolyte homeostasis. It is important to evaluate and understand the causes and patient characteristics in order to deliver precise management. **Materials and Methods:** Study was conducted at a teaching referral hospital in Sikkim and total of 100 elderly patients, diagnosed with hyponatremia, were enrolled in the study. Detailed medical history, clinical and laboratory examination were performed and data including treatment details were collected. Descriptive analysis was performed and results were correlated with patient characteristics. **Results:** Mean age of the patients was 73.87 ± 6.54 years with a male to female ratio of 1:0.96. About 81% of patients were symptomatic among which lethargy (50%), drowsiness (40%), and abnormal behavior (39%) were common symptoms. Most patients (51%) had profound hyponatremia and Syndrome of inappropriate antidiuretic hormone secretion (SIADH) (36%) and drugs (26%) were the most common cause of hyponatremia in this study. The common treatment given in this study was 0.9% NaCl (71%). Mortality of patients in this study was 20%. **Conclusion:** Clinicians need to be aware of the common occurrence of hyponatremia in the elderly, especially acutely sick elderly. A systematic approach to its diagnosis with the application of simple standardized diagnostic algorithms can significantly improve the assessment and management of hyponatremia as the outcome in profound hyponatremia is governed by etiology, and not by the serum sodium level.

Keywords: Clinico-etiological profile, elderly, hyponatremia

Introduction

Disorders of sodium and water metabolism are common in clinical practice. Both hyponatremia and hypernatremia can cause substantial morbidity and mortality and ironically, incorrect treatment can add to the problem.

Hyponatremia is defined as a serum sodium concentration of <135 mEq/L.^[1] Patients with clinically significant hyponatremia present with nonspecific or neurologic symptoms attributable to cerebral edema. When coupled with a recent history of altered fluid balance, these symptoms suggest the possibility of hyponatremia.^[2]

Studies suggest that hyponatremia may be present in 15%–30% of patients in chronic care facilities.^[1] The incidence is much more in the elderly mainly owing to the impaired ability to maintain water and electrolyte homeostasis in response to dietary and environmental changes.^[3] The management of these cases needs modification due to physiological changes with age affecting the renal and other systems.

Data regarding the incidence of hyponatremia in the elderly in India is limited. This study was conducted to evaluate the common clinical features and etiology of hyponatremia in the elderly hospitalized patients and to correlate the hyponatremia with comorbid conditions, if any.

Materials and Methods

After obtaining approval from the Institutional Ethical Committee, 100 consecutive consenting inpatients in the Department of

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General Medicine, age ≥65 years and both sexes with documented hyponatremia, were enrolled in the study. Postoperative patients and patients with pseudohyponatremia (defined by hyponatremia in the absence of any obvious etiology and presence of hyperproteinemia and/or hypertriglyceridemia) were excluded from the study.

Detailed clinical assessment was done and recorded on a predesigned proforma and managed in a Microsoft Excel

Table 1: Age and Sex distribution

Age Group	Female (n)	Male (n)	Grand Total (n)
65-69	9	17	26
70-74	16	11	27
75-79	10	13	23
80-84	10	6	16
85-89	4	4	8
Grand Total	49	51	100

Table 2: Severity of hyponatremia

Severity of Hyponatremia	Patients (n)
Mild Hyponatremia	23
Moderate Hyponatremia	26
Profound Hyponatremia	51

Table 3: Association of Symptoms with Severity of Hyponatremia

Symptoms	Mild Hyponatremia	Moderate Hyponatremia	Profound Hyponatremia
	(n)	(n)	(n)
Asymptomatic	16	2	1
Nausea	1	9	25
headache	2	6	21
Lethargy	5	14	31
Dizziness	2	6	15
Muscle cramps	2	5	7
Abnormal behaviour	1	11	27
Drowsiness	2	10	28
Seizures	0	0	3
Others	0	0	0

Table 4: Pre-disposing characteristics

Characteristics	Mild Hyponatremia (n)	Moderate Hyponatremia (n)	Profound Hyponatremia (n)	
Pre-existing disease	Diabetes mellitus	11	16	19
	Hypertension	15	16	37
	Liver disease	0	1	2
	Renal disease	3	7	9
	Chronic heart failure	1	1	4
	Hypothyroidism	3	1	2
	Others	10	11	22
Pre-disposing factor	Poor intake	6	5	20
	Vomiting	4	6	22
	Drugs	8	8	18
	Diarrhoea	3	2	4
	Sweating	0	0	1

spreadsheet. Collected data was systematically analyzed and presented as a frequency distribution. Descriptive statistics have been calculated for the continuous variables and categorical variables are expressed as percentages. For analytical statistics, Chisquared test was used where appropriate. For all statistical tests of significance, a P value of <0.05 was considered to reject the null hypothesis.

Patients with hyponatremia were classified based on serum sodium levels into mild (130–134 mEq/L), moderate (125–129 mEq/L), and profound (<125 mEq/L).

Results

Total of 100 patients were enrolled in the study with a mean age of 73.87 ± 6.54 years and male to female ratio of 1:0.96. Age and gender distribution of the study patients is mentioned in Table 1 [Figure 1].

The severity of hyponatremia is given in Table 2 and Figure 2. In this study, majority of the patients had profound hyponatremia.

Symptoms of hyponatremia and its association with the severity of hyponatremia are given in Table 3 and Figure 3. Majority of patients (81%) were symptomatic with most of the patients (62%) having more than 1 symptom. Lethargy (50%), drowsiness (40%), and abnormal behavior (39%) were common symptoms and seizure was the least commonly observed symptom (3%) and all with profound hyponatremia. About 19% of patients were asymptomatic with most of them having mild hyponatremia.

Hypertension (68%) and diabetes mellitus (46%) were common pre-existing diseases, while drugs (34%), vomiting (32%), and poor intake (31%) were common predisposing factors observed among the study patients [Table 4 and Figures 4, 5].

Causes of hyponatremia are given in Table 5 and Figure 6. Majority of the patients had single etiology (86%). SIADH (36%) and drugs (26%) were the most common causes and hypothyroidism (3%) and renal loss (5%) being the least

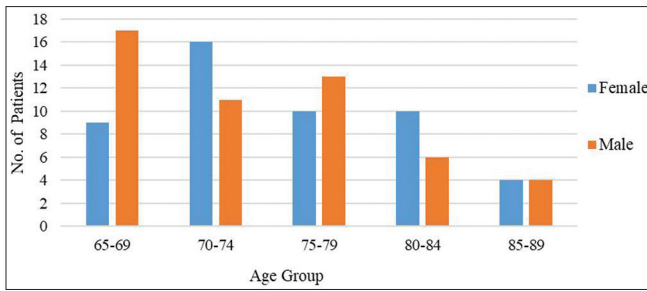


Figure 1: Age and sex distribution

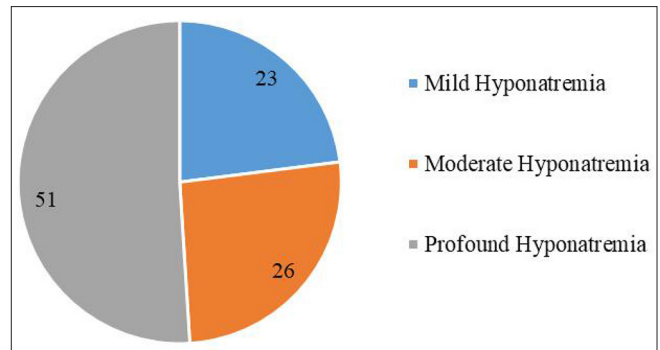


Figure 2: Severity of hyponatremia

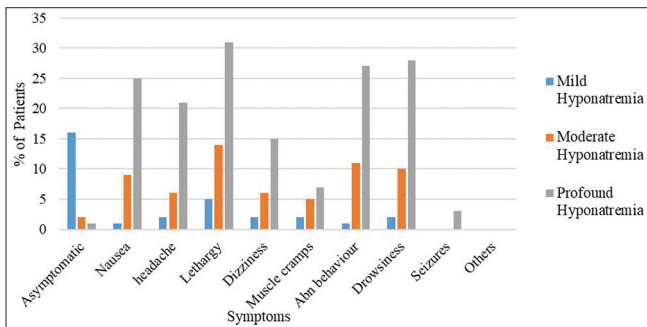


Figure 3: Association of symptoms with the severity of hyponatremia

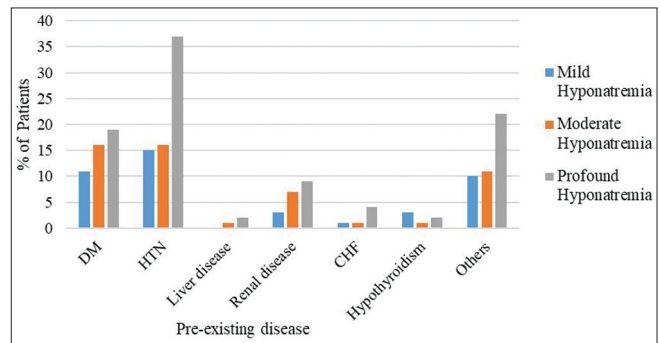


Figure 4: Association of pre-existing diseases with the severity of hyponatremia

Table 5: Aetiology of Hyponatremia

Aetiology	Patients (n)
SIADH	36
Drugs	26
Dilution	23
GI Loss	16
Poor Intake	7
Renal loss	5
Hypothyroidism	3

Table 6: Causes of SIADH

Causes of SIADH	No. of Patients
Neurological disorders	Cerebrovascular accident 13 Meningitis 4 Subdural hygroma 1
Pulmonary disorders	Pneumonia 13 Tuberculosis 1
Drugs	SSRIs 2
Carcinoma lung	1
Rheumatoid arthritis	1

Table 7: Drugs which caused Hyponatremia

Drugs which caused Hyponatremia	Patients (n)
Diuretics	Thiazide 9 Loop diuretics 5 Loop diuretics + spironolactone 4
Antidepressants	3
Anticonvulsants	2
Chemotherapeutic agents	2
Antitubercular agents	1

common. Causes of SIADH are given in Table 6. Drugs that caused hyponatremia are given in Table 7.

Majority of the patients had euvoolemia (48%) followed by hypervolemia (28%) and the least common being hypovolemia (24%) [Table 8 and Figure 7].

Levels of biochemical parameters in different levels of hyponatremia are given in Table 9.

In majority of the patients, more than 1 method of correction was used. The common treatment given in this study was 0.9% normal saline (NS) (71%). Twenty patients had associated hypokalemia, which was treated with intravenous and/or oral potassium supplement. Treatment strategy for correction of hyponatremia is given in Table 10 and Figure 8.

Mortality of patients in this study was 20%. Outcomes of the patients in different age groups, gender, hyponatremia level, and hydration status groups are given in Table 11 and Figures 9–12. There was no statistically significant correlation observed between any of characteristics and mortality.

Discussion

Hyponatremia has been associated with considerable morbidity and mortality in several chronic diseases, most notably in patients with congestive heart failure (CHF) and chronic liver

disease (CLD).^{14,5} Hyponatremia also leads to increased health care cost and the majority of these costs are attributable to the incremental resource utilization for patients who were not admitted specifically for hyponatremia, but whose hospitalization was prolonged due to hyponatremia.

In previous studies, the incidence of hyponatremia in hospitalized patients was found to be about 1%–6%.^{11,6} The incidence of hyponatremia among elderly patients, in this study, was 25.98%, which is comparable to the reported incidence of 20%–36% in previous studies.¹⁷

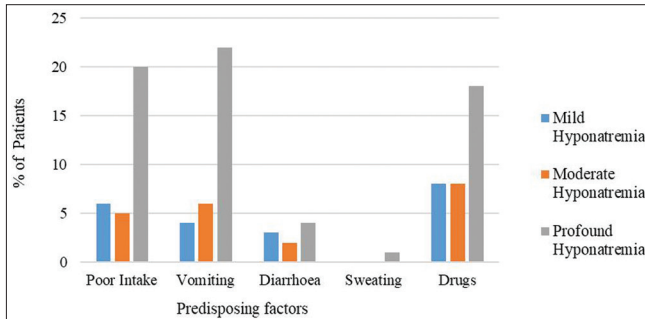


Figure 5: Association of predisposing factors with the severity of hyponatremia

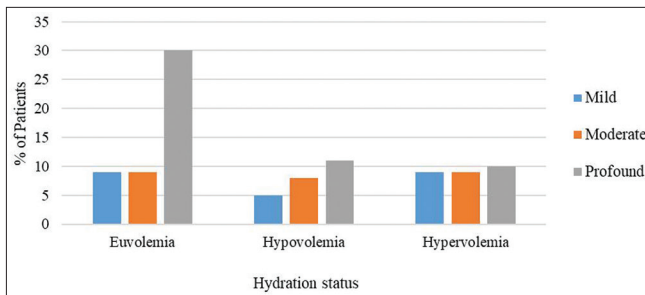


Figure 7: Association of hydration status with the severity of hyponatremia

In our study, the mean age of the patients was 73.87 ± 6.54 years, which was comparable to a hospital-based study by Rao *et al.* where the mean age was 72 years.¹⁷ Decreased glomerular filtration rate, impaired ability of the kidney to conserve sodium, increased release of antidiuretic hormone (ADH) to a given osmotic stimulus, various drugs taken by them, and concomitant illnesses predisposes an elderly patient to hyponatremia. Hawkins *et al.* noted that increasing age, after adjusting for sex, was independently associated with both

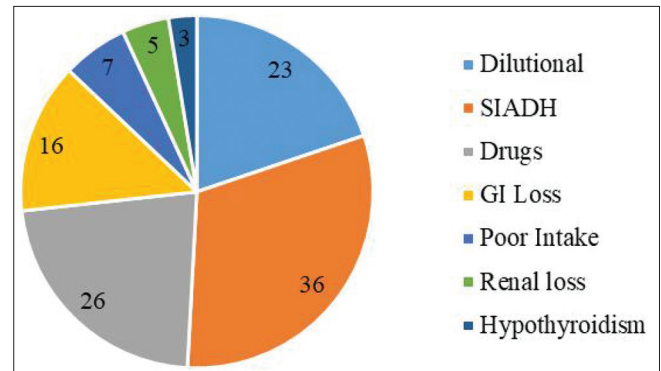


Figure 6: Etiology of hyponatremia

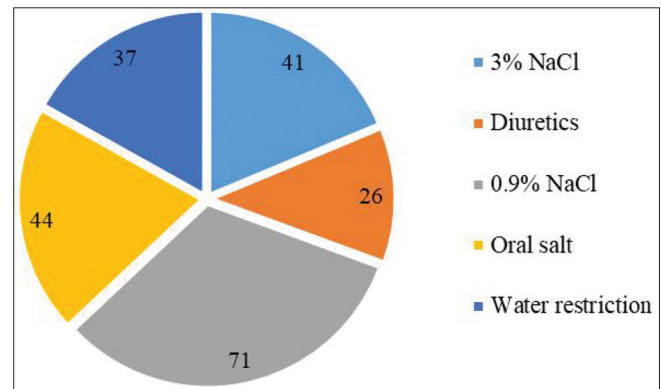


Figure 8: Treatment strategy for the correction of hyponatremia

Table 8: Association of Hydration status with Severity of Hyponatremia

Hydration status	Mild Hyponatremia (n)	Moderate Hyponatremia (n)	Profound Hyponatremia (n)
Euvolemia	9	9	30
Hypovolemia	5	8	11
Hypervolemia	9	9	10

Table 9: Levels of Biochemical parameters in different Levels of Hyponatremia

Parameters	Hyponatremia			Total (n=100)
	Mild (n=23)	Moderate (n=26)	Profound (n=51)	
Serum Sodium (mEq/L)	131.22±20.96	127.15±18.62	118.47±26.96	123.66±6.58
Serum Potassium (mEq/L)	4.35±0.84	4.18±1.04	4.12±0.81	4.19±0.95
Blood Urea (mg/dl)	20.48±19.05	25.58±15.58	29.24±23.02	26.27±20.54
Serum Creatinine (mg/dl)	1.42±1.04	1.80±1.67	1.48±1.50	1.54±1.44
Random Blood sugar (mg/dl)	144.52±76.47	154.00±70.36	138.22±51.18	143.77±62.58
Serum Osmolality (Osm/L)	271.22±9.33	263.69±11.03	247.37±24.35	257.10±21.36
Urine Osmolality (Osm/L)	199.36±118.96	277.74±168.92	302.11±126.53	281.98±129.81
Urine Sodium (mEq/L)	45.07±27.63	63.95±53.00	81.90±64.18	71.19±56.96

hyponatremia at presentation and hospital-acquired hyponatremia.^[8] In our study, the prevalence of hyponatremia was almost equal in male and female patients comparable to study by Rao *et al.*^[7]

Symptoms of hyponatremia varied among study patients with 19% of the patients being asymptomatic. Most (85%)

asymptomatic patients had mild hyponatremia. Lethargy (50%) was the most common symptom. Most patients with serum sodium <125 mEq/L had neurological symptoms, such as drowsiness; however, patients with serum sodium ≤110 mEq/L showed severe neurological symptoms, such as seizures and unconsciousness. These findings are consistent with the available literature and previous studies.^[7,9,10]

Treatment	Patients (n)
3% NaCl	41
Diuretics	26
0.9% NaCl	71
Oral salt	44
Water restriction	37

Characteristics	Outcome		P	
	Death (n)	Discharge (n)		
Age Group (years)	65-69	6	20	0.9415
	70-74	7	20	0.6871
	75-79	3	20	0.6348
	80-84	3	13	0.9073
	85-89	1	7	0.9589
Gender	Female	9	40	0.9870
	Male	11	40	0.9899
Levels of Hyponatremia	Mild	1	22	0.1358
	Moderate	7	19	0.6184
	Profound	12	39	0.7708
Hydration status	Euvolemia	9	39	0.8577
	Hypovolemia	3	25	0.3938
	Hypervolemia	8	16	0.2580

The major pre-existing illnesses present among the patients, in our study, were hypertension (68%), diabetes mellitus (46%), and chronic kidney disease 1 (CKD) (19%). In our study, hypertension was a major risk factor for hyponatremia due to diuretic use. The studies on hyponatremia have not demonstrated a direct correlation between hyponatremia and hypertension, although the correlation of hyponatremia with the age and diuretic use is evident.^[4,11]

In our study, 26% of the patients had pre-existing renal disorder, heart failure, or CLD. Twenty-one out of these 26 patients were admitted to the hospital due to noncompliance with treatment. In majority of these patients, loop diuretics and fluid restriction were sufficient to correct hyponatremia. In a study by Saeed *et al.*, 37% of the patients had hyponatremia due to similar disorders (renal disorders 21%, liver disorders 7%, and CHF 9%).^[12] In our study, 6% of patients had pre-existing hypothyroidism, which is higher compared to reported 3.7% by Clayton *et al.*^[3]

SIADH was the most common cause of hyponatremia, in our study, representing 31% of cases, which is in line with reported 34.8% by Vurgese *et al.*^[13] Drugs was the second most common cause for hyponatremia, in our study, accounted for

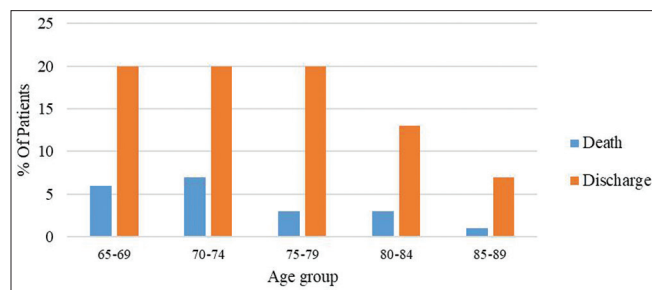


Figure 9: Outcome in different age groups

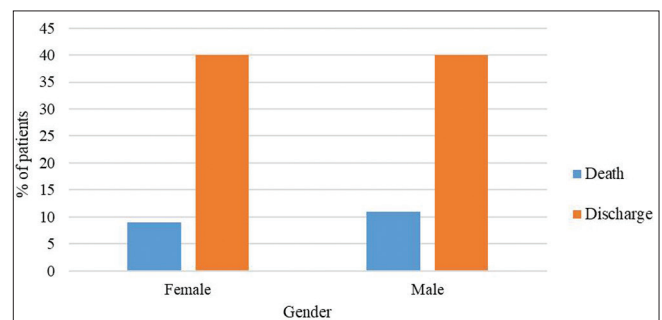


Figure 10: Outcome in different gender

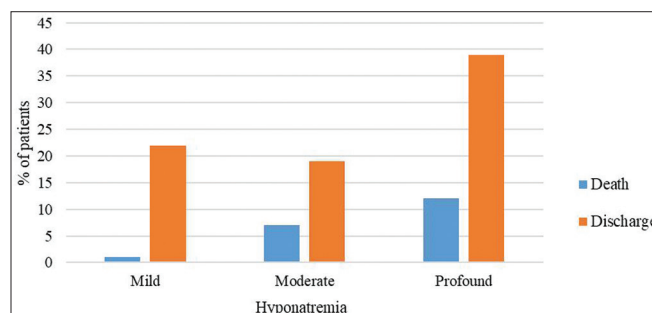


Figure 11: Outcome in different levels of hyponatremia

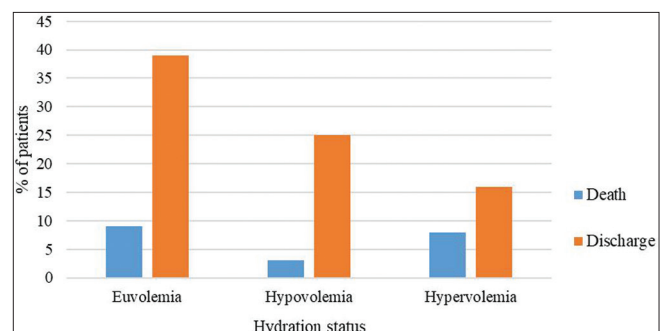


Figure 12: Outcome in different hydration status

26% of the study patients, out of which 18 patients were on diuretics (9 patients on thiazide diuretics, 5 patients on loop diuretics, and 4 patients on a combination of loop diuretic and spironolactone). It is reported that 14% of patients prescribed a thiazide diuretic in primary care, have sodium level below the normal range and this incidence is up to 33% in elderly patients.^[14] Thiazide is reported to be known cause of profound hyponatremia.^[15] In our study, 13 out of 51 patients of profound hyponatremia were on thiazide diuretic. Saeed *et al.* reported 33.3% while Huda *et al.* reported 63.6% hyponatremia cases associated with diuretic usage.^[12,16] Though JNC 8 recommends diuretics as the first-line drug for treatment of hypertension, a word of caution should be maintained while prescribing diuretics in the elderly and when required doses should be modified according to the body weight and should begin with the lowest dose. In our study, 2 patients had selective serotonin reuptake inhibitors (SSRIs) induced hyponatremia, which is much lower than 11.1% reported by Clayton *et al.*^[3] This is possibly because SSRIs are not usually prescribed for the patients in general medical and surgical wards.

In our study, 14% of the patient had multiple etiological factors for hyponatremia, which is in line with reported 10.9% by Nzerue *et al.* while it is much lower than reported 75% by Clayton *et al.*^[3,17] These studies emphasize the importance of establishing the various factors responsible for hyponatremia in the patient so that relevant corrective measures can be considered during the treatment.

Vomiting is one of the strongest known stimuli for ADH release.^[18] In our study, vomiting was associated with infective/inflammatory illnesses (18 patients; gastroenteritis—10, viral fever—7, and pancreatitis—1), systemic illnesses (10 patients; renal disorder—6, acute and chronic liver diseases—3, and diabetic ketoacidosis—1), drug induced (2 patients; Digoxin—1 and Isoniazid—1), gastrointestinal obstruction (1 patient), and increased intracranial pressure 1 (ICP) (1 patient). It was also associated with poor intake and diarrhea in 10 and 7 patients, respectively.

Poor nutritional intake secondary to various other comorbidities was a major risk factor in this study. Total 31% of patients had a history of poor intake, which was associated with various causes, such as anorexia (14 patients; uremia—7, malignancy—3, CLD—2, and tuberculosis—2) and acute illnesses (11 patients). The conventionally fed fluids in India, orally or through Ryle's tube, are sugar based, such as fresh fruit juices, milk, tea and coffee, glucose water, and tender coconut water. Soups and canned juices with salt are not a part of our traditional meal, which may lead to the development of in-hospital hyponatremia. This is in line with the causes of hospital-acquired hyponatremia as reported earlier.^[19]

In our study, 48% of patients were euvolemic, 28% of patients were hypovolemic and 24% of patients were hypervolemic, which is line with reported by Bhattacharjee *et al.*^[9] Patients with

euvolemia were observed to have more severe symptoms of hyponatremia compared to the other groups.

In our study, a better response in terms of survival was observed among patients who were presented with central nervous system (CNS) symptoms of hyponatremia and responded to treatment than compared to those who did not show any CNS symptoms of hyponatremia, which is consistent with the data in the literature.^[20] In our study, 71% patients received NS, 44% patients were given oral sodium chloride supplementation, 41% patients were given hypertonic (3%) saline (3% NS), 37% patients were on fluid restriction, and 26% patients received loop diuretics. There are considerable differences in the treatment strategies for hyponatremia in recent studies on hyponatremia in hospitalized patients. In a study by Hoorn *et al.* on severe hyponatremia in hospitalized patients, 29% patients were given NS, 9% patients were advised fluid restriction, 10% patients received oral sodium chloride supplementation, 5% patients were given 3% NS, and 19% patients received no therapy for hyponatremia whereas in a study by Nzerue *et al.*, 82% patients received NS, 9% patients were given fluid restriction, 3% patients were given 3% NS while 6% patients were treated with other treatment modalities, such as withdrawal of drug causing hyponatremia.^[17,19]

The overall mortality among patients of hyponatremia, in our study, was 20% and 23.5% among patients with profound hyponatremia, which is comparable to the mortality between 20% and 27%, as in the literature in patients with hyponatremia.^[16,17] Mortality was not directly related to hyponatremia but to the severity of the underlying medical condition in the patients. However, the extent of contribution to death is debatable as even those patients who succumbed to their illness had received the correction of hyponatremia as per the standardized regimen of treatment followed in our study.

When the mortality outcomes were compared with respect to age, sex, and hydration status, there was no statistically significant difference. However, mortality was noted to be higher in females, in our study. The reason for this age-related decrease in the sodium pump function is unclear. Factors, such as female sex hormones, which are known to inhibit the Na-K-ATPase pump, are significantly diminished after menopause.^[21]

As this was a single arm, monocentric study with limited sample size, it is difficult to conclude precise clinico-etiological profile and its association with different characteristics and hence, multicenter, 2 arms with the control group, study with a large population is suggested for further evaluation.

Conclusions

Clinicians need to be aware of the common occurrence of hyponatremia in the elderly, especially acutely sick elderly. A systematic approach with the application of simple standardized diagnostic algorithms and establish mechanism of hyponatremia can significantly improve the assessment and

management of hyponatremia as the outcome in profound hyponatremia is governed by etiology, and not by the serum sodium level.

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Conflicts of interest

There are no conflicts of interest.

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