



PROFILE OF HYPONATREMIA IN ELDERLY: STUDY FROM A TERTIARY TEACHING HOSPITAL OF EASTERN INDIA

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ABSTRACT

Background: Hyponatremia is the most common electrolyte disorder particularly in elderly population and among hospitalized patients.

Objectives: To investigate clinical manifestations, severity, etiological factors, comorbid conditions and outcome following treatment in elderly hyponatremic patients.

Methodology: Elderly patients (≥ 60 years) having serum sodium below 135 mmol/L at the time of presentation or fall during hospital stay were enrolled.

Results: Of total 50 patients, profound hyponatremia was found in 50% cases. 72% patients were symptomatic out of which altered sensorium was the most common presentation (41.6%). All patients of profound hyponatremia were symptomatic. Euvolemia, hypervolemia and hypovolemia was found in 54%, 24%, 22% cases respectively. Drug induced hyponatremia was the commonest etiology followed by SIADH. Loop diuretics were major culprit. Hypertension was the most common co-morbid condition followed by diabetes mellitus. Multiple co-morbidities were found in 34% cases. Mortality was recorded in 6% cases.

Conclusion: Hyponatremia in elderly is multifactorial and is associated with comorbidities. Diuretics should be used with caution in elderly.

KEYWORDS : Dyselectrolytemia, hyponatremia, elderly, SIADH

INTRODUCTION

Hyponatremia, defined as a serum sodium concentration < 135 mmol/L, is the commonest disorder of body fluid and electrolyte balance encountered in day to day medical practice.⁽¹⁾ Though the exact prevalence is not known, it is seen in 15-30% of hospitalised patients and more than 50% of the overall hyponatremia population comprises of hospitalised patients⁽²⁾. Though it can affect all age groups, is especially prevalent in frail, older population due to impaired response of water and electrolyte⁽³⁾. In elderly population, this condition can be an important contributor to the major geriatric ailments such as cognitive impairment, immobility and falls, bone demineralization and hip fractures.^(4,5,6,7) The reasons for the higher prevalence in elderly may be due to high prevalence of comorbid conditions like chronic congestive cardiac failure (CCF), chronic kidney disease (CKD), dehydration, neurological disorders including stroke, bronchopneumonia, malignancy; frequent use of drugs causing hyponatremia eg. thiazide diuretics, selective serotonin reuptake inhibitors (SSRIs), neuroleptic medications, carbamazepine; and age related changes in homeostatic mechanisms that contribute to hyponatremia.⁽⁸⁾ Amongst the potential causes of hyponatremia, the most common cause is reported to be syndrome of inappropriate antidiuretic hormone (SIADH).⁽⁹⁾ As the studies on hyponatremia in elderly population is sparse, given the high prevalence of this condition in this group, SIADH should also be highly prevalent in this age group. However, a recent publication from Israel have reported that hyponatremia in elderly is often multifactorial rather than a single entity.⁽¹⁰⁾

Hyponatremia can be mild (130-135 mmol/L), moderate (125-129 mmol/L) and severe (< 125 mmol/L) and clinical manifestation ranges from mild, nonspecific form to more severe, life threatening symptoms eg. seizures, coma and even death in persons developing rapid onset hyponatremia.⁽¹¹⁾ Studies have shown that rapidity of drop in serum sodium level had a greater effect than severity of hyponatremia on key clinical outcomes, such as institutionalization,

duration of stay in hospital and mortality.⁽¹²⁾ Paradoxically, evidences suggest that even mild chronic hyponatremia can lead to cognitive impairment, falls and fractures and even increased mortality.^(6,13) Evidence also suggests that active measures to prevent or minimize hyponatremia in hospital set up can improve outcomes and probably reduce mortality.^(12,13)

There are very few studies in our country, and no such studies from our state evaluating the etiological factors, clinical manifestations, severity and out come following treatment of hyponatremia in elderly patients for which this study was taken up.

AIM AND OBJECTIVES:

The present study was undertaken to investigate the clinical manifestations, severity, etiological factors, comorbid conditions and out come following treatment of hyponatremia in elderly patients.

MATERIALS AND METHODS

This study was a prospective hospital based study conducted in the Post Graduate department of Medicine, S.C.B. Medical College and Hospital, Cuttack, Odisha, India. A total of 50 patients, aged ≥ 60 years⁽¹⁴⁾ of both gender who had serum sodium below 135 mmol/L at the time they presented to the hospital or dropped below 135 mmol/L during the hospital stay were included in the study during the period September 2015 to September 2016. Patients having hypernatremia, of age less than 60 years, postoperative patients, patient with colonoscopy preparation, hyperlipidemia and macroglobulinemia, receiving radio contrast agents were excluded from the study.

Each patient underwent detailed history taking and complete clinical examination. Details regarding age, sex, urban or rural and socio-economic status were recorded. Drugs that can increase the non-osmotic release of antidiuretic hormone (ADH) or potentiate its

renal action (ADH-stimulating drugs) were recorded. History of pre-existing illness causing hyponatremia such as congestive heart failure (CHF), Chronic Kidney disease (CKD), Chronic liver disease (CLD), hypothyroidism and other conditions which are associated with SIADH such as small cell lung carcinoma, CNS diseases including stroke, pulmonary disease were noted. History of precipitating factors such as vomiting, diarrhoea and excessive sweating was taken in all patients.

Detailed clinical evaluation was done in all patients. Classification of symptoms of hyponatremia was done as per clinical practice guideline on diagnosis and treatment of hyponatremia : (1) moderately severe - Nausea without vomiting, confusion, headache, (2) Severe: Vomiting, cardiorespiratory distress, abnormal and deep somnolence, seizures, coma (Glasgow coma scale <8).⁽¹¹⁾

Further, patients were classified based on their volume status as hypovolemic, euvolemic or hypervolemic.^(1,15)

Laboratory investigations included complete blood count (CBC), urine routine / microscopic, blood glucose, serum potassium (K), blood urea, serum creatinine, serum uric acid, liver function tests, lipid profile, morning serum cortisol, thyroid function tests. Urine sodium, urine osmolality, serum osmolality, serum sodium were analysed directly with an iron specific electrode (Cobas 121 POC system). Patients were diagnosed as SIADH if they met the criteria proposed by Bartter and Schwartz in 1967.⁽¹⁶⁾ Computerised tomography(CT) scan of brain, ultrasonography of abdomen and pelvis, chest X-ray (Postero Antero) view, high resolution CT thorax were done as and when required. Patients were divided into three categories according biochemical severity¹.

- (i) Mild hyponatremia: Biochemical finding of serum sodium concentration between 130 - 135 mmol/L as measured by ion specific electrode (ISE).
- (ii) Moderate hyponatremia: Biochemical finding of serum sodium concentration between 125 - 129 mmol/L as measured by ISE.
- (iii) Profound hyponatremia: Biochemical finding of serum sodium concentration <125 mmol/L as measured by ISE.

In all patients the possibility of pseudo-hyponatremia was excluded through analysis of plasma osmolality, total protein, triglyceride and cholesterol concentration.

Management of hyponatremia was done based on the cause, severity of hyponatremia and symptoms according to standard protocol.⁽¹¹⁾

Statistical analysis was done using SPSS statistical package version 20.0. Quantitative variables were described as mean ± standard deviation (SD) unless otherwise indicated. Qualitative variables were described by percentage. For all statistical tests, p value <0.05 was considered significant.

Results:

Our study is a hospital based study and reflects the prevalence of etiological factors, clinical features, severity and outcome following treatment in the in-patient setting. Table-1 shows the baseline characteristics of the patients. Of the total 50 elderly hyponatremia patients recruited majority were male (58%, no = 29), female (42%, no = 21), M: F-1.38:1 (p value 0.08). The age of the patients studied ranged between 61 - 94 years with a mean age of 68.64 ± 7.88 years. The importance of age on prevalence of hyponatremia shows that majority of patients were from age group of 61 - 70 years (68%, no = 34) followed by in the age group of 71 - 80 years (26%, no = 13).

Mild hyponatremia was found in 11 (22%) cases, moderate hyponatremia in 14 (28%) cases and profound hyponatremia in 25 (50%) cases.

With regard to symptoms, 36 (72%) patients had symptoms related

to Hyponatremia as shown in Table-2, out of which nausea was presenting feature in 7 (19.4%), vomiting in 7 (19.4%), seizure 5 (13.8), lethargy 2 (5.5%), altered sensorium which includes confusion, somnolence, coma in 15 (41.6%) of cases (no = 36). Of the symptomatic patients 22(61.2) were severely symptomatic and the rest 14(38.8%) were moderately symptomatic .Fourteen patients (28%) were asymptomatic.

The symptoms among various grades of hyponatremia was as follows(Table-2): mild hyponatremia (no= 11): only nausea in 3 (27.3%) cases and rest were asymptomatic; moderate hyponatremia (no = 14):nausea in 4(28.5%),vomiting in 2 (14.2%), seizure 1 (7.1%), altered sensorium in 1 (7.1%) cases and no symptoms attributable to hyponatremia in 6(42.8%) cases, profound hyponatremia (no = 25), altered sensorium 14 (56%), vomiting 5(20%), seizure 4 (16%) and lethargy in 2 (8%) cases. Table 2 indicates that maximum no of patients of mild and moderate hyponatremia were asymptomatic and all patients of profound hyponatremia were symptomatic.

Table – 1:Baseline characteristics of the patients (n=50)

Variables	Mean ± SD
Age (years)	68.64 ± 7.8
Female (age/years)	67.29 ± 6.2
Male (age / years)	69.62 ± 8.89
Blood glucose (mg/dL)	158.96 ± 90.11
Sodium (mmol/L)	123.22 ± 9.20
Potassium (mmol/L)	4.05 ± 0.80
Urea (mg/dL)	55.48 ± 41.30
Creatinine (mg/dL)	1.59 ± 1.24
Serum Osmolality (mOsm/L)	274.98 ± 28.30

Table 2:Showing different symptoms in all grades of hyponatremia (Total no = 50)

Symptoms	Mild hyponatremia no = 11	Moderate hyponatremia no = 14	Profound hyponatremia no = 25
Nausea	03 (27.3%)	04(28.5)	-
Vomiting	-	02 (14.2%)	05 (20%)
Seizure	-	01 (7.1%)	04 (16%)
Altered Sensorium	-	01 (7.1%)	14 (56%)
Lethargy	-	-	02 (08%)
Asymptomatic	08 (72.7%)	06 (42.8%)	-

Table 3:Showing Etiology in Hyponatremia (no = 50)

Etiology	No (Percentage)
Drugs	23 (46%)
SIADH	18 (36%)
Renal diseases	10 (20%)
Gastro-intestinal loss	05 (10%)
Chronic liver disease	03 (06%)
CCF	02 (04%)
hypothyroidism	02 (04%)
Sheehan's syndrome	01 (02%)

Table-4:Showing associated comorbid diseases in hyponatremia (no = 50)

Comorbid conditions	Percentage
Hypertension	36
Diabetes mellitus	30
CVA,COPD,CKD	12 each
CLD,DCM	6 each
CAD,Hypothyroid	4 each
Gastric ulcer,parkinsonism,psychiatric illness, Atrial septal defect, Sheehan's	2 each
Multiple comorbidities	34

Analysing the volume status of the patients, euvolemia was found in 27 (54%) cases, followed by hypervolemia in 12 (24%) and hypovolemia in 11 (22%) of cases.

The prevalence of aetiology of hyponatremia are shown in table-3, drugs was the most common aetiology in 23 (46%) cases followed by SIADH in 18(36%), renal diseases 10 (20%), gastrointestinal loss 5 (10%), liver disease 3 (6%), CCF and hypothyroidism in 2 (4%) each, and Sheehan's syndrome 1 (2%).

Of the total 23 cases of drug induced hyponatremia, the drugs responsible for hyponatremia were loop diuretics in 14 (60.8%) cases followed by thiazide diuretics in 6 (26%), angiotensin converting enzyme inhibitors (ACEI) in 2 (8.6%) and SSRI in 01 (4.3%) case.

The comorbidities associated with hyponatremia are shown in Table-4, hypertension was the most common disease followed by DM, CVA/CKD/COPD in 12% each, CLD and DCM in 6% each. Multiple comorbidities were found in 17 (34%) cases.

Mortality: out of 50 cases, 3 patients died. Mortality rate was 6%, out of which, one patient had mild hyponatremia (Case Fatality Rate : 9.09%) and was associated with comorbid conditions like CVA and CKD. Rest 2 cases belonged to profound hyponatremia group (Case Fatality Rate:8%). There was no mortality in moderate hyponatremic group (p value 0.08).

DISCUSSION

Hyponatremia is the most common electrolyte abnormality, particularly in the elderly population and in-hospital settings.

In the present study hyponatremia was more common in males as compared to females though statistically not significant (P value 0.08). This is in contrast to major studies which have reported increased prevalence of hyponatremia in female elderly patients. Post menopausal stage as well as hyponatremia related to diuretic and psychotropic drug was given the lower body weight as a characteristic of the gender.⁽¹⁷⁾ Clayton *et al.*, Kayar *et al.* and Padhi *et al.* reported the female prevalences as 60%, 61.6% and 56.5% respectively.^(18, 19,20) Kayar *et al.* reported a higher mean age of 76.1±7.2 years than our study of 68.6±7.8 years.

Worldwide there is a lack of consensus regarding severity of hyponatremia and different studies adopted different ranges. The Singapore study, reported mild hyponatremia (126-135mmol/l), moderate hyponatremia (116-125 mmol/l) and severe hyponatremia (<116mmol/L) in 36%,5% and 1.2% patients respectively but in contrast our study showed profound hyponatremia as most common followed by moderate and mild hyponatremia respectively, which was similar to observations by Kayar *et al.*^(21,19)

In this study 72% patients were symptomatic. Rest 28% were asymptomatic which may be due to chronic hyponatremia (developed over >48 hours duration).^(1,11)

The major clinical manifestations in our study amongst symptomatic (no:36) were altered sensorium was the commonest (41.6%) followed by vomiting and nausea in (19.4%) cases each, seizure in 13.8% and lethargy in 5.5% cases. This is at par with the observations by Nzerue *et al.* who reported 52.9% patients had neurological manifestations.

The symptoms among various grades of good no. hyponatremia revealed maximum number of patients of mild and that moderate hyponatremia were asymptomatic possibly due to slowly developed hyponatremia. All cases of profound hyponatremia group were symptomatic.

Our study found euvolemic status in maximum cases followed by hypervolemic and hypovolemic status respectively which in contrast to observation by Kayar *et al.* who reported hypervolemic in 58.5% cases, hypovolemia in 24.5% cases and euvolemia in 17% cases which can be explained due to difference in associated comorbid conditions.⁽¹⁹⁾

Though many studies have reported SIADH as the most common cause of hyponatremia,⁽¹⁰⁾ present study revealed drug induced hyponatremia as the commonest cause followed by SIADH and renal diseases. This is in accordance with the findings of Kayar *et al.* who reported iatrogenic causes as the commonest (72.7%) followed by acute renal failure (47.7%) and infections (23.3%). Rao *et al.* from India reported SIADH (30%) as the commonest cause followed by medications and renal losses in 24% and 21% cases respectively.⁽²³⁾

Among the drugs used by the patients of our series the most common ones were loop diuretics followed by thiazides, ACE inhibitors and SSRI. Rao *et al.* reported Frusemide (Loop diuretic) as the commonest cause (17%) in his series.⁽²³⁾ Huda *et al.* found thiazide diuretics as the commonest (63.6% of drug induced hyponatremia) offending drug in their series.⁽²⁴⁾ The reason behind higher number of patients using loop diuretics in our series is associated comorbidities like CCF, CLD and CKD.

Analyzing the associated co-morbid conditions, it was found in 44(88%) patients, 6(12%) patients didn't have any comorbid conditions. Mohan *et al.* identified comorbidities in 73% patients of their series which tallies with our finding.⁽²⁵⁾ Hypertension was the most common cause followed by diabetes mellitus as comorbid condition found in our study. Mohan *et al.* also reported hypertension as most common (51%) followed by DM (16%).⁽²⁵⁾ Kayar *et al.* also reported comorbid conditions as follows : hypertension (73.8%), DM (52.2%), CKD (49.4%), CHF (34%) cases.⁽¹⁹⁾

Mortality depends on the severity of hyponatremia and can approach 50% when severe.⁽¹⁸⁾ Low mortality rate in our series may be due to the fact that hyponatremia may be chronic, and developed slowly and also prompt attention and appropriate management of the critical cases had saved many lives.⁽¹²⁾ The death of the patient of mild hyponatremia group could be attributed to associated lethal comorbid conditions like CVA and CKD. Rao *et al.* and Kayar *et al.* reported mortality in 20% and 17.6% cases respectively.^(23,19)

Conclusion:

Hyponatremia in elderly is a common yet neglected area in clinical practice. It is multifactorial rather than attributable to a single cause. Because of increasing life span and growing elderly population, There is a higher risk of dyselectrolytemia leading to increased morbidity and mortality. Simultaneously associated comorbidities and polypharmacy add fuel to this. Diuretics should be used with caution in elderly. Meticulous monitoring against hyponatremia at the time of hospitalization as well as during the hospital stay is required to reduce morbidity and mortality significantly. Further, large scale multicentric studies are required to throw more light on this global issue.

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Conflicts of interest:None declared

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