

# Clinical Profile of Euvolemic Hyponatremia in Elderly Hospitalized Patients in a Tertiary Care Hospital in India

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## Abstract

**Introduction:** Hyponatremia is common among hospitalized patients and can lead to serious neurological complications. Hyponatremia is especially common in older people owing to impaired ability to maintain water and electrolyte homeostasis in response to diet, drugs, and environmental changes. Even mild, chronic hyponatremia can lead to cognitive impairment, falls, and fractures, the latter being in part due to bone demineralization and reduced bone quality. Hyponatremia is therefore of special significance in frail older people.

**Aim:** The aim of the study is to study the etiology, clinical features of euvolemic hyponatremia in elderly hospitalized individuals and to assess the morbidity and mortality.

**Materials and Methods:** The study was conducted in Government Rajaji Hospital affiliated to Madurai Medical College during the period from April to September 2016. 50 patients aged  $\geq 60$  years admitted with serum sodium  $< 135$  mEq/L were included in the study. Patients with hypovolemic and hypervolemic hyponatremia (congestive cardiac failure, chronic kidney disease, and chronic liver disease) were excluded from the study. Detailed history, clinical examination including meticulous neurological examination, and relevant laboratory investigations and imaging studies were done. Treatment was done with fluid restriction, saline infusion, and other measures as necessary.

**Results:** 58% were asymptomatic at presentation. The most common symptom was lethargy. Syndrome of inappropriate antidiuresis was the most common etiology. One patient died during the study period.

**Conclusion:** Hyponatremia is a potentially lethal disorder which is more harmful in the elderly hospitalized. Proper and meticulous management according to the clinical picture gives a better outcome.

**Key words:** Hyponatremia, Lethargy, Geriatrics

## INTRODUCTION

Hyponatremia is defined as a plasma sodium concentration  $< 135$  mEq/L.<sup>1</sup> Hyponatremia is found in 15-22% of hospitalized patients. Most cases of

hyponatremia arises out of water imbalance rather than sodium imbalance. Sodium is the principal determinant in maintaining extracellular fluid volume and in the regulation of blood pressure and osmotic equilibrium. The plasma sodium concentration is dependent on multiple factors including sodium intake, osmolality and tonicity of plasma, the renin angiotensin system, total body potassium, and water.<sup>2</sup>

Several physiological changes occur in the regulation of water and sodium balance as a part of the normal aging process, such as decreased glomerular filtration rate, decreased renal blood flow, impaired ability to dilute

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urine, and impaired water excretion. These changes result in an increased likelihood of developing hyponatremia with increasing age. The thirst mechanism decreases as age advances which significantly impairs the capacity to maintain homeostasis thereby intensifying the risk for dehydration. Maximal urinary concentrating capacity also diminishes with age. In the aged, there is a five-fold increase in atrial natriuretic peptide (ANP) concentration over the basal levels.<sup>3</sup> Increased ANP leads to direct suppression of renin with a secondary decrease in angiotensin II and in aldosterone, resulting in renal loss of sodium associated with ageing.

The etiology of hyponatremia in older people is predominantly multifactorial. Common causes include drugs (thiazide and loop diuretics, antidepressants, anticonvulsants, non-steroidal anti-inflammatories, and proton pump inhibitors), comorbidities (congestive cardiac failure [CCF], renal failure, cirrhosis, and respiratory infections), fluid overload, and volume depletion.<sup>4</sup>

Symptoms are related largely to dysfunction of the central nervous system (CNS) and are more evident when the decrease in the serum sodium concentration is large or fast. However, patients also present with non-neurologic symptoms, such as fatigue, thirst, weakness, cramping, nausea, vomiting, bloating, swelling, and tightness of the hands and feet. Headache, muscle cramps, reversible ataxia, psychosis, lethargy, restlessness, disorientation, apathy, anorexia, and agitation are symptoms seen in patients with serum sodium levels below 125 mEq/L. Complications of severe and rapidly developing hyponatremia include seizures, coma, brainstem herniation, respiratory arrest, permanent brain damage, and death. These complications result primarily from hyponatremia-induced cerebral edema.<sup>5</sup>

Distinction between acute and chronic hyponatremia is clinically important because chronic hyponatremia is surprisingly well-tolerated, even at very low levels of serum sodium, and overly aggressive treatment may result in serious neurological sequelae. Aggressive initial correction is warranted in patients with acute symptomatic hyponatremia, which can potentially cause irreversible neurological damage and death.

Euvolemic hyponatremia is the most common form of asymptomatic hyponatremia. If the underlying cause is syndrome of inappropriate antidiuretic hormone (SIADH) and its etiology is unknown or cannot be effectively treated, therapy should be instituted for the hyponatremia itself. A recent alternative to saline administration in the management of hyponatremia is the use of ADH receptor

antagonists. The most specific treatment for SIADH is to block the V2 receptors in the kidney that mediate the diuretic effect of antidiuretic hormone (ADH). Vasopressin antagonists are currently indicated for the treatment of euvolemic and hypervolemic hyponatremia, and these agents are usually preferred if SIADH or ADH is the cause. Central pontine myelinolysis has traditionally been associated with rapid correction of hyponatremia, but the etiology has not been clearly established.

### Aim

The aim of the study is to study the etiology, clinical features, and to assess the morbidity and mortality of euvolemic hyponatremia in elderly individuals hospitalized in Government Rajaji Hospital.

## MATERIALS AND METHODS

The study was conducted in Department of General Medicine at Government Rajaji Hospital. Individuals aged  $\geq 60$  years with serum sodium  $< 135$  mEq/l (Government of India defines "senior citizen" or "elderly" as a person who is of age 60 years or above) were included in the study. Patients with hypovolemic and hypervolemic hyponatremia (CCF, chronic kidney disease [CKD], and chronic liver disease [CLD]) were excluded from the study. Detailed history was taken. This included symptoms of hyponatremia, predisposing factors, and pre-existing illness if present. Symptomatology included the presence of altered sensorium, postural dizziness, lethargy, and seizures. Sensorium changes included acute confusional states, memory disturbances, stupor, delirium, and coma. Detailed clinical examination was done in every patient. Hydration status of the patient was determined by clinical examination. Accordingly patients were divided into hypervolemic, hypovolemic, and euvolemic. SIADH and cerebral salt wasting were differentiated on the basis of volume status of the patient, urine osmolality after volume expansion, treatment, and response to treatment. At the time of diagnosis of hyponatremia, detailed CNS examination was done to document mental status of the patient and other focal neurological deficit. CNS examination was repeated after the correction of hyponatremia and the presence of symptoms such as dizziness, lethargy, altered sensorium, and seizures were attributed to hyponatremia unless there was a coexisting medical condition or medication effect to account for these symptoms. Complete blood count, serum sodium, osmolality, blood urea nitrogen, glucose; urine osmolality, specific gravity, sodium, microscopic examination; serum proteins, lipid profile, thyroid function tests, brain imaging, and cerebrospinal fluid analysis were done. Treatment included fluid restriction, normal saline, hypertonic saline, loop diuretics, etc.

For all patients clinical and demographic details, final diagnosis, investigations, and management were recorded onto a standard data collection sheet as per the study pro forma and later transferred to Microsoft excel spreadsheet for analysis. Analysis was done using SPSS for windows (version 20.0). Statistical method used was descriptive and analytical statistics. Data are presented as frequency distribution and simple percentages. Analysis was done using probability tests.

## RESULTS

The maximum number of patients were in the age group 60-70 years, i.e., 39 cases (78%), 14% were in 71-80 group and 8% were in >80 group. In the study, out of 50, 60% were males and 40% were females.

The majority of the cases were asymptomatic at time of presentation, 58%. Out the symptomatic cases, 42%, 100% had lethargy, 76% had abnormal behavior, 14% had postural dizziness and 9% (2 cases) had seizures. None of the patients were in coma (Table 1).

Out of 50 cases majority 62% were having severe hyponatremia, 16% were having moderate hyponatremia and 22% were having mild hyponatremia (Table 2).

Out of 29 asymptomatic patients 11 were having mild hyponatremia, 10 were having severe hyponatremia and 8 were having moderate hyponatremia. All the symptomatic patients were having severe hyponatremia. All the mild hyponatremic patients (11) had Glasgow coma scale (GCS)  $\geq 13$ . Out of 8 moderate hyponatremic patients, 7 had GCS  $\geq 13$  and 1 had GCS 8-12. Out of 31 severe hyponatremic patients, 17 had GCS  $\geq 13$  and 14 had GCS 8-12. None of the patients had GCS  $< 8$ .

CNS infections and endocrine causes constitute the major predisposing factors, followed by malignancy and pulmonary diseases.

Out of 50 cases, the most common etiology was SIADH. About 36% had SIADH. 26% had hypothyroidism. 18% were having drug induced hyponatremia. 6% with exercise induced, and other causes like reset osmostat. The days for normalizing sodium were noted during the study. For 17 cases, 1-3 days were needed, 22 cases needed 4-7 days. 2 cases had not recovered (Table 3).

There is significant association between serum sodium values and symptoms (Table 4).

There is significant association between serum sodium values and outcome (Table 5).

**Table 1: Symptomatology**

Symptoms	Number (%)
Asymptomatic	29 (58)
Lethargy	21 (42)
Postural dizziness	3 (6)
Abnormal behavior	16 (32)
Seizures	2 (4)
Coma	0 (0)

**Table 2: Severity of hyponatremia**

Sodium levels (mmol/L)	Number of patients (%)
130-135 (mild)	11 (22)
125-129 (moderate)	8 (16)
<125 (severe)	31 (62)
Total	50 (100)

**Table 3: Etiology of euvolemic hyponatremia**

Etiology	Number (%)
Hypothyroidism	13 (26)
Adrenal insufficiency	2 (4)
Drugs	9 (18)
Exercise-induced	3 (6)
SIADH	18 (36)
Primary polydipsia	2 (4)
Others	3 (6)

SIADH: Syndrome of inappropriate antidiuretic hormone

**Table 4: Relation between serum sodium level and symptoms**

Symptoms	Sodium level	SD
Asymptomatic	123.55	8.971
Dizziness	112	9.849
Seizure	118	8.485
Lethargy	115	7.475
Abnormal behavior	114.75	7.688
P	0.002 significant	

SD: Standard deviation

## DISCUSSION

This study was undertaken keeping in view of frequent occurrence of hyponatremia in the elderly sick patients who are at higher risk of development of electrolyte disturbance as these people have age-related physiological changes in the function of kidneys and other multiple comorbid conditions.

In the present study, 50 elderly patients ( $\geq 60$  years) were included in the study. Out of 50, 60% (30) were males and 40% (20) were females. In study done by Rao *et al.*,<sup>4</sup> 55 were females and 45 were male. In study by Agarwal *et al.*,<sup>6</sup> 64.3% were males and 53.7% were females.

The majority of the cases were asymptomatic at time of presentation, 58%. Out the symptomatic cases, 42%,

**Table 5: Relation between outcome and serum sodium levels**

Outcome	Sodium level	SD
Complete recovery (38)	121.64	9.506
Residual defects (3)	117.5	5.766
Expired (1)	115	1
Nil (8)	113.64	7.272
<i>P</i> (38/50 vs. 12/50)	0.023 significant	

SD: Standard deviation

100% had lethargy, 76% had abnormal behavior, 14% had postural dizziness and 9% (2 cases) had seizures. In study Rao *et al.*,<sup>4</sup> lethargy, drowsiness with slow response, and irrelevant talk were the common presenting symptoms. 4% had seizures. In study by Agarwal *et al.*,<sup>6</sup> confusion was present in 30% and altered sensorium in 17.1%. 2% had seizures. 14% were asymptomatic.

In the present study, out of 29 asymptomatic patients, 11 were having mild hyponatremia, 10 were having severe hyponatremia, and 8 were having moderate hyponatremia. All the symptomatic patients were having severe hyponatremia. When the GCS score was compared, all the mild hyponatremic patients (11) had GCS  $\geq 13$ . Out of 8 moderate hyponatremic patients, 7 had GCS  $\geq 13$ , 1 had GCS 8-12. Out of 31 severe hyponatremic patients, 17 had GCS  $\geq 13$ , 14 had GCS 8-12. None of the patients had GCS  $< 8$ . However, in studies carried out elsewhere, patients with mild hyponatremia tended to be asymptomatic, while those with moderate hyponatremia tended to have anorexia, nausea, and headache; those with severe hyponatremia had confusion, coma, seizures, or death.<sup>7,8</sup>

In the present study, out of 50 patients, most common predisposing factor was endocrine causes followed by CNS lesions followed by malignancy and pulmonary diseases. In the present study, out of the cases most common etiology was SIADH, about 36% had SIADH. 26% had hypothyroidism. 18% having drug induced hyponatremia, 6% with exercise-induced and other causes. In the study by Rao *et al.*,<sup>4</sup> common causes were SIADH (30%) followed by drugs (24%). In study by Vurghese,<sup>9</sup> the most common etiology was SIADH (34.8%), CKD (19.69%), CCF (18.18%), 6% of diabetes mellitus, hypertension, cirrhosis, and 3% acute gastroenteritis. In the study by Agarwal *et al.*<sup>6</sup> decreased intake (82.9%) was the most common etiology, increased loss (65.7%) was also present as second most common cause.

The days for normalizing sodium were noted during the present study. For 17 cases, 1-3 days were needed, 22 cases needed 4-7 days. 2 cases had not recovered.

## CONCLUSION

Hyponatremia is a common electrolyte abnormality found in hospitalized patients. It is more common in elderly patients. Lethargy was the most common symptom. Other common symptoms were abnormal behavior and postural dizziness. All the symptomatic cases had severe hyponatremia. There is significant association between serum sodium levels and symptoms and with outcome of the patients. Most common etiology was SIADH. Other major causes were hypothyroidism, drugs, and exercise. Hyponatremia was found to be related to multiple etiological factors in a large number of patients. A systematic approach to the diagnosis of hyponatremia with the application of simple diagnostic algorithms, using history, clinical examination, and laboratory findings to establish mechanism of hyponatremia can significantly improve the management and outcome of hyponatremia.

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