

# Clinical profile of patients with hyponatremia in a tertiary care hospital in the sub-Himalayan region

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## ABSTRACT

**Introduction:** Hyponatremia, defined as a serum sodium concentration ( $[Na^+]$ )  $<135$  mEq/L. It is not a disease but rather a pathophysiologic process indicating disturbed water homeostasis. Hyponatremia should be further classified to provide directions for diagnosis and treatment. It is a heterogeneous disorder. The classifications of hyponatremia are commonly based on tonicity and volume status. The initial differentiation in hypotonic and non-hypotonic hyponatremia is important because management is different. Several studies have been conducted previously to measure the incidence of hyponatremia in medically ill patients. Several studies have demonstrated an increased prevalence of hyponatremia in the presence of co-morbid conditions. We conducted this study to bring out various causes of hyponatremia; their relation with sex, age and outcome and hyponatremia's classification and incidence in our hospitalised population. **Materials and Methods:** This study was conducted to find out etiology, classification, prevalence and outcome and its relation with age and sex in patients of hyponatremia admitted in our institution. A total number of 106 patients were studied. **Results:** Hospital-based incidence of hyponatremia was found to be 1.17%. Mean age of patients in study was  $62.25 \pm 17.7$  years. Male to female ratio was 1.25:1. Altered sensorium was the most common neurological symptom. Ninety-five (90%) patients were hypo-osmolar. Out of ninety four patients, 38 (40%) were euvolemic. Chronic obstructive pulmonary disorder (COPD) with cor pulmonale with right-sided heart failure ( $n = 9$ , 31%) was the most common cause in hyper-volemic hyponatremia. Acute gastroenteritis ( $n = 13$ , 48%) was the most common cause in hypo-volemic hyponatremia. Syndrome of inappropriate anti-diuretic hormone secretion (SIADH) was the most common cause ( $n = 20$ , 53%) of euvolemic hyponatremia. Out of 106 patients, 11 (10.38%) patients expired. **Conclusion:** Hyponatremia acts as a poor prognostic marker of the primary disease. It is important to recognise it early because of the potential morbidity and mortality, economic impact on the patients and health care associated with it. Early management of hyponatremia, which includes determination of the rate of correction, the appropriate interventions and the presence of other underlying disorders, may help in improving the outcome and shortening the hospital stay of the patients.

**Keywords:** Aetiology, hyponatremia, incidence, syndrome of inappropriate anti-diuretic hormone secretio

## Introduction

Hyponatremia, defined as a serum sodium concentration ( $[Na^+]$ )  $<135$  mEq/L, is the most common electrolyte abnormality observed

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in clinical practice and occurs in up to 30% of the hospitalised patients in its mild form (serum  $[Na^+]$  130-135 mEq/L).<sup>[1,2]</sup> It is well-known that acute severe hyponatremia may have severe neurological consequences because of cerebral oedema, and it can be lethal if not diagnosed and effectively treated.<sup>[3]</sup> Recent studies have demonstrated that chronic and mild hyponatremia also may negatively affect health status, with deleterious effects that affect, particularly, the central nervous system (CNS) and the bone,

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causing gait instability, attention deficits, falls, osteoporosis and fractures. Hyponatremia results from the inability of the kidneys to excrete a water load or excess water intake. Acute hyponatremia is characterised by the onset of symptoms in <48 h. Patients with acute hyponatremia develop neurologic symptoms resulting from cerebral oedema induced by water movement into the brain. These may include seizures, impaired mental status or coma and death. Hyponatremia developing over >48 h is considered chronic. The serum sodium concentration is usually above 120 meq/L. The incidence of hyponatremia in hospital-admitted patients, as quoted in various studies, varies between 12 and 14%, with severe symptomatic hyponatremias being 12%.<sup>[4-6]</sup> The identification of risk factors associated with the development of symptomatic hyponatremia is important in determining preventive strategies.<sup>[7]</sup> Data on prevalence and clinical profile of hyponatremia are scarce, to say the least, from the Indian subcontinent. We took up this hospital-based, observational descriptive study as an attempt to evaluate the clinical profile of hyponatremia in medically ill patients in our setting. Primary care physicians encounter numerous cases of altered sensorium in patients who are elderly and on anti-hypertensive medicines. On evaluation, they commonly come up with hyponatremia. This article explicitly explains how to plan workup and how to come up with aetiology in these patients

## Aims and Objectives

### Aim

To assess the incidence of hyponatremia in medically ill patients.

### Objective

To study the clinical profile of such patients.

**Material and Methods:** This was a descriptive hospital-based study conducted at the Department of Medicine, Dr Rajendra Prasad Government Medical Hospital, Tanda (Kangra), Himachal Pradesh (HP), India. The study was carried out for 1 year from April 1 2018-31<sup>st</sup> March 2019 after obtaining approval from institutional ethics committee (27/10/2017). All admitted patients (106) of hyponatremia during this period, fulfilling inclusion criteria, were included.

### Inclusion criteria

1. Patients of age 18 years or more.
2. Patients with serum sodium <135 meq/L on admission.

### Exclusion criteria

1. Patients aged below 18 years.
2. Unwilling to give consent.

The socio-demographic parameters of the patients were noted. A detailed history and physical examinations were also noted. Other laboratory investigations included complete hemogram, liver function test (LFT), renal function test, serum electrolytes, serum uric acid, fasting blood sugar/random blood sugar, thyroid

function test (TFT), serum cortisol levels, urine spot sodium, urine urea, urine creatinine, urine uric acid, and imaging studies as required.

## Statistical analysis

Data were presented as frequency and percentages.

## Results

A total 106 patients of hyponatremia admitted in medicine wards were included in the study having patient characteristics and percentages as shown in the Table 1. In the present study, the hospital-based incidence of hyponatremia during the study period was 1.17% among the patients admitted in the department of medicine wards. The patients' age ranged from 20 to 95 years with a mean age of  $62.25 \pm 17.77$  years. Sixty patients (57%) aged more than 60 years and 46 (43%) patients' age was below 60 years. There were more males than females in the present study. The male to female ratio was 1.25:1.

Fifty-one patients (48%) got admitted during the summer season. Thirty-four (32%) and 21 (20%) patients admitted during rainy and winter season, respectively.

Anorexia was the most common general symptom in 29 (27%) patients. Vomiting was the most common gastrointestinal (GI) symptom in 18 (17%) patients. Altered sensorium was the most common neurological symptom in 36 (34%) patients.

Forty-nine (46%) patients had co-morbidities of diabetes or hypertension, 25 (24%) patients had hypertension and 12 (11%) patients had diabetes. Twelve (11%) patients had both diabetes and hypertension.

In the present study, 95 (90%) patients were hypo-osmolar, 10 (9%) patients were hyper-osmolar and one patient (1%) was iso-osmolar. Volume status was available for 94 patients. Out of these 94 patients, 38 (40%) patients were euvolemic, 29 (31%) patients were hyper-volemic and 27 (29%) patients were hypo-volemic. Out of 106 patients, the severity of hyponatremia was severe in 44 (42%) patients, moderate in 51 (48%) patients and mild in 11 (10%) patients.

Chronic obstructive pulmonary disorder (COPD) with cor pulmonale with right-sided heart failure ( $n = 9$ , 31%) was the most common cause in hyper-volemic hyponatremia. Acute gastroenteritis ( $n = 13$ , 48%) was the most common cause in hypo-volemic hyponatremia. Syndrome of inappropriate anti-diuretic hormone secretion (SIADH) was the most common cause ( $n = 20$ , 53%) of euvolemic hyponatremia [Figure 1]. Stroke was the most common cause of SIADH ( $n = 6$ , 30%) in euvolemic hyponatremia followed by pneumonia ( $n = 4$ , 20%). Out of 106 patients, 11 (10.38%) patients expired. In 11 expired patients, 6 (55%) patients aged more than 60 years while 5 (45%) patients aged below 60 years. Male to female ratio was 4.5:1 in expired patients. Serum sodium levels were <125

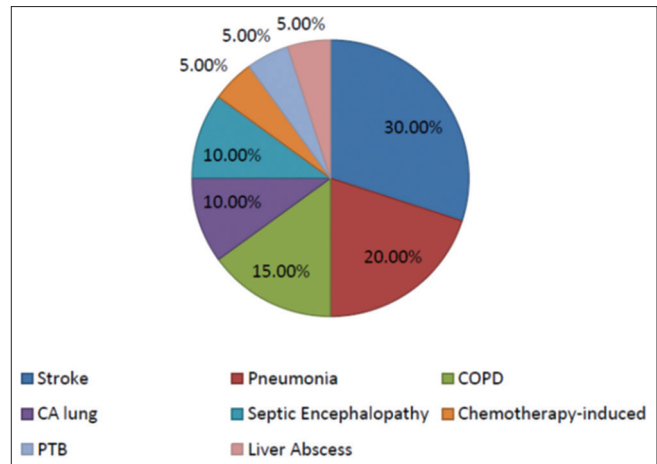
**Table 1: Patient characteristics and percentage of patients**

Patient characteristic	n	Percentage
Age		
>60 yrs	60	60
<60 yrs	46	46
Sex		
M	59	56
F	47	44
Season		
Summer	51	48
Rainy	34	32
Winter	21	20
Symptom		
Altered sensorium	36	34
Vomiting	18	17
Anorexia	29	27
Comorbidities		
Hypertension	25	24
Diabetes	12	11
Both	12	11
None	57	57
Osmolality		
Hypo-osmolar	95	90
Hyper-osmolar	10	9
Iso-osmolar	1	1
Volume Status		
Hyper-volemic	27	29
Hypo-volemic	29	31
Euvolemic	38	40
Severity		
Mild	11	11
Moderate	54	45
Severe	44	51
Outcome		
Improved	11	10
Discharged	95	90
Serum Sodium in Expired Patients		
>125	3	27
<125	8	73

in 8 patients of the 11 expired patients. SIADH because of various underlying disorders was the most common aetiology in 8 (73%) patients of the 11 expired patients followed by chronic liver disease (CLD) in 2 (20%) patients and congestive cardiac failure (CCF) in 1 patient.

## Discussion

In the present study, the incidence of hyponatremia was 1.17%. In a hospital-based study conducted in elderly patients (>60 years) in HP, hyponatremia was observed in 84% of the patients.<sup>[8]</sup> The incidence of hyponatremia is found to vary. Hyponatremia also depends upon associated pre-disposing conditions and adverse outcomes.<sup>[9]</sup> Chatterjee *et al.* studied the incidence and clinical profile of hyponatremia in medically ill patients and found the incidence to be 16.4%.<sup>[10]</sup> DeVita *et al.* reported a 29.6% incidence of hyponatremia in critically ill patients. Mittal *et al.* reported the incidence of hyponatremia to be 4% per cent in hospitalised patients.<sup>[11]</sup> In our study, 60% of the patients with hyponatremia were elderly (>60 years). Mittal *et al.* observed that



**Figure 1: Etiology of SIADH in euvolemic hyponatremia.** SIADH = Syndrome of inappropriate anti-diuretic hormone secretion

hyponatremia was seen more commonly in patients >50 years than in younger patients. The various factors responsible for hyponatremia in the elderly may be a decrease in the glomerular filtration rate, an increase in the kidney's ability to conserve sodium and increased release of arginine. Similar findings were also observed by Babaliche *et al.*<sup>[12]</sup> In our study, 55.66% of the patients with hyponatremia were males. Babaliche *et al.* reported male predominance (59%) in the incidence of hyponatremia.<sup>[12]</sup> A similar gender distribution pattern was reported by Rahil *et al.*, wherein 33 (62.3%) patients with hyponatremia were males and 20 (37.7%) were females.<sup>[13]</sup> Male predominance was also reported by Bakhtar *et al.*<sup>[14]</sup> The incidence of hyponatremia is also strongly affected by the temperature and is higher during the summer. Incidence of hyponatremia was higher (48.11%) during the summer season in our study followed by rainy season (32.07%). An Indian study by Chakrapani *et al.* conducted for 2 years found an increased incidence of hyponatremia in the monsoon season.<sup>[15]</sup> An increased incidence of hyponatremia during hot seasons has been reported by Pformueller *et al.*<sup>[16]</sup>

Altered sensorium was the most common general symptom in the patients with hyponatremia in our study followed by anorexia and vomiting. Pillai *et al.* observed that among the intensive care unit (ICU) admissions, the different symptoms attributed to hyponatremia included nausea (69.3%), malaise (80%), drowsiness (61.3%), confusion (41.3%), lethargy (24%), frequent falls (1.3%), convulsions (2.7%), altered sensorium (41.3%) and delirium (9.3%).<sup>[17]</sup> Krishnamurthy and Srinivas observed that the symptoms found hyponatremia patients were vomiting (29.6%), giddiness (2.4%), altered sensorium (8.5%), headache (9.2%), chest pain (6.4%), generalised weakness (8.4%), fever (12.3%), cough (15.2%), loss of consciousness (0.7%), nausea (22.5%), loose stools (5%), easy fatiguability (10.4%), breathlessness (17.8%), abdominal pain (8.8%), difficulty in micturition (0.9%), lower limb swelling (3.6%) and seizures (6.4%).<sup>[18]</sup> Hypertension (23.58%) was the most common associated co-morbidity in the patients followed by diabetes (11.32%). Krishnamurthy and Srinivas found that

the main comorbid conditions with hyponatremia found were hypertension (8.53%), diabetes mellitus (DM) (9.95%), chronic alcohol intake (6.63%), ischemic heart disease (2.13%), HIV positive with AIDS-related complex (1.18%), COPD (2.6%) and thyroid illness in three cases.<sup>[19]</sup> Pillai *et al.* observed that 28% of the patients had systolic blood pressure (SBP) <100 mmHg on admission, 63.3% had SBP between 100 and 140 mmHg and 18.6% had SBP ≥140 mm Hg. Glasgow Coma Scale (GCS) score of ≤10 was seen in 36% of patients. In a prospective study conducted in a general medical-surgical setting, 66 patients (34%) had euvolemic hyponatremia, 38 (19%) had hyper-volemic hyponatremia associated with oedematous disorders and 33 (17%) had hypo-volemic conditions, chiefly related to GI fluid loss or diuretic use.<sup>[20]</sup> In our study, 89.62% had hypo-osmolar hyponatremia, 9.43% had hyper-osmolar hyponatremia and 0.94% had iso-osmolar hyponatremia. In the study by Bajji and Borkar, 92% of patients were hypo-osmolar and 8% of patients were hyper-osmolar. No patient was iso-osmolar.<sup>[21]</sup> COPD with cor pulmonale with right-sided heart failure was the most common cause in hyper-volemic hyponatremia in our study. Acute gastroenteritis (AGE) was the most common cause in hypo-volemic hyponatremia. SIADH was the most common cause of euvolemic hyponatremia. Stroke was the most common cause of SIADH ( $n = 6$ ) in euvolemic hyponatremia, followed by pneumonia ( $n = 4$ ). Pillai *et al.* reported that all the patients with euvolemic hyponatremia had SIADH, except one, who had psychogenic polydipsia. The commonest cause of SIADH was pulmonary pathology (17 patients). Two patients had CNS infection. Other causes included Guillain–Barré syndrome (GBS) (3 patients), N-methyl-d-aspartate (NMDA) receptor encephalitis (1 patient) and idiopathic SIADH (1 patient). Of the 27 patients with hyper-volemic hyponatremia, 14 had an acute kidney injury (AKI), 6 had chronic kidney disease (CKD), 5 had congestive heart failure (CHF) and 2 had cirrhosis of the liver. Of the 23 patients with hypo-volemic hyponatremia, 8 had cerebral salt wasting, 4 had AKI, 8 had dehydration because of different causes, 2 had diuretic-induced hyponatremia and one had salt-losing nephropathy (SLN).<sup>[17]</sup> Babaliche *et al.* reported SIADH as the most common cause of hyponatremia noted in nearly half of the study population. In a study by Rai *et al.*, the most common cause of hyponatremia was SIADH (67%) followed by renal failure (17%).<sup>[22]</sup> In a study by Rahil *et al.*, extra-renal fluid loss, including vomiting, diarrhoea or diaphoresis, was the most frequent cause of hyponatremia, which was found in 33.9% of the patients. SIADH was considered to be the cause in 20.7% of the patients.<sup>[13]</sup> Laczi reported that SIADH was the most common cause of euvolemic hyponatremia in their study in Hungary.<sup>[19]</sup> Another study by Panicker and Joseph on the clinical profile of hyponatremia in ICU hospitalised patients reported SIADH as a predominant cause for hyponatremia.<sup>[7]</sup> Using a large administrative database of hospitalised patients with pneumonia, Zilberberg also found no increased risk of death with hyponatremia (serum sodium concentration <135 mEq/L) compared with normonatremia,<sup>[23]</sup> whereas Nair *et al.* reported a 7% increased risk of death in a single-centre study.<sup>[24]</sup> Waikar

*et al.* found no increased risk of death in any category of hyponatremia in sepsis, pneumonia or medical admissions for respiratory diseases, but an increased risk of death in liver disease with more severe hyponatremia (serum sodium concentration 120–124 mEq/L).<sup>[25]</sup> Previous studies in cirrhosis have yielded conflicting reports, with several reports<sup>[26]</sup> of an increased risk of death with hyponatremia and one study showing no association after multivariable adjustment for disease severity.<sup>[27]</sup>

## Conclusion

There is an increasing tendency for hyponatremia to occur with increased age, use of drugs (diuretics) and co-morbidities like hypertension and diabetes. Vomiting and altered consciousness are amongst the commonest symptoms. Hyponatremia acts as a poor prognostic marker of the primary disease. Early management of hyponatremia, including determination of the rate of correction, the appropriate interventions and the presence of other underlying disorders, may help in improving the outcome and shortening the hospital stay of the patients.

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## Conflicts of interest

There are no conflicts of interest.

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