

# Etiology, Clinical Profile and Outcome of Symptomatic Hyponatremia - A Hospital Based Study

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## ABSTRACT

**Background:** Hyponatremia (serum sodium <135 mEq/litre) is one of the most common electrolyte abnormalities in hospitalised patients. It is more common in elderly, multi-morbid patients taking multiple medications and in those having lack of access to food and water. Prognosis in such patients depends upon the severity and underlying condition causing it. It therefore becomes imminent to identify the etiology of hyponatremia and also to correct it at an appropriate pace (10-12mEq/litre/day) such that a drastic neurological outcome is averted.

**Aims and Objectives:** To study the clinico-etiological profile in admitted patients of hyponatremia in a tertiary care hospital of North India and their in-hospital outcome.

**Study Design:** A hospital-based observational study.

**Materials and Methods:** A total of 250 patients were studied over a period of 18 months. Detailed clinical and drug history, physical examination, assessment of volume status, routine baseline biochemical parameters, spot urinary sodium followed by paired urine and serum osmolality was done in all patients.

**Results:** The mean age of patients was 62.4 years with a male to female ratio of 1:1.6. GI symptoms like nausea and vomiting was the most common symptom seen in 60% of patients. Commonest neurological complaints were confusion (52%) followed by lethargy (22%), seizures (18%) and coma (8%). Diuretic use was the most common cause of hyponatremia (36%) followed by SIADH (26%) and GI losses (10%). 52% patients were euvolemic, 40% were

hypervolemic and 8% were hypovolemic. Mortality in our study was 14%.

**Conclusion:** From our study, we concluded that diuretics are the most common cause of hyponatremia followed by SIADH, with a significant mortality in euvolemic type of hyponatremia.

**Keywords:** Hyponatremia, Diuretics, Euvolemic, Hypervolemic, Hypovolemic, SIADH.

## INTRODUCTION

Hyponatremia is the commonest electrolyte abnormality in hospitalised patients (1,2) with incidence varying from 1-40% in different studies. It is more commonly seen in critically ill/ICU patients (3). It is defined as a serum sodium concentration of <135mEq/litre (4). Depending upon severity, it can be classified into mild (130-134mEq/litre), moderate(120-129mEq/litre) and severe(<120mEq/litre) (5,6,7). Serum sodium concentration does not merely depend upon total body sodium, rather it is determined by the ratio of total body solutes to total body water (8). Sodium being the major ECF solute, hyponatremia can be classified into euvolemic, hypervolemic and hypovolemic (9). Many drugs are notorious for causing hyponatremia including vasopressin analogues, tricyclic antidepressants, thiazide diuretics, vincristine, cyclophosphamide, illicit drugs like amphetamines, etc (10). Symptoms can

range from anorexia, nausea/vomiting, fatigue, headache and muscle cramps to altered mental status, agitation, seizures, coma and even death. (11) Early recognition and treatment of hyponatremia to prevent permanent neurological sequelae is of paramount importance, thereby translating directly into morbidity/mortality benefit (12).

Keeping the same in mind, this study was conducted to evaluate for the commoner causes of hyponatremia in our setting and to witness their final outcome in hospital.

### **Aims and Objectives**

1. To study the clinical and etiological profile of admitted patients of hyponatremia.
2. To study their in-hospital outcome.

### **MATERIALS AND METHODS**

After getting clearance from the ethical committee of our hospital, we conducted this study in 250 consecutive admitted patients of symptomatic hyponatremia aged 16 years and above in medicine wards of a 700- bedded tertiary care hospital of North India, over a period of 18 months from October 2020 to April 2022. Symptomatic patients with a serum sodium of  $<125\text{mEq/litre}$  were included. Proper informed consent was taken from all patients. Detailed history including medications, underlying comorbidities, physical examination, volume status and course of symptomatology was sought in every patient. All baseline investigations including chest x-ray and ultrasonography were done. Serum sodium estimation was done using ion selective electrode technology in the automated analysers. A normal serum sodium in our laboratory ranges from  $135\text{--}145\text{mEq/litre}$ . Spot urinary sodium followed by paired urine and serum osmolality was done in all patients via depression in freezing point method. A spot urine sodium  $>40\text{mEq/litre}$  suggests SIADH and  $<20\text{mEq/litre}$  suggests hypovolemia. The reference values for serum and urine osmolality in our lab are  $278\text{--}298\text{mmol/litre}$

and  $300\text{--}900\text{mmol/litre}$  respectively. Furthermore, depending upon the clinical/lab scenario, more tests like serum uric acid, serum cortisol, thyroid function tests, radiological imaging and other investigations deemed necessary were performed. Patients having pseudohyponatremia (those with hyperlipidemia, paraproteinemia, those receiving mannitol) and those who did not give consent to participate were excluded from the study.

Patients were individually managed, depending upon severity and underlying etiology. Most patients with long standing hyponatremia were managed only with dietary modifications like increased salt intake (depending upon sodium deficit) and free water restriction. Those with acute onset, severely symptomatic hyponatremia (including seizures) was given hypertonic (3%) saline after calculating proper dose at an appropriate rate. Patients were followed till the eventual in-hospital outcome.

### **Statistical Analysis**

When analysing statistics, continuous variables were summarised as mean and standard deviation. Categorical variables were summarised as frequency and percentages. Chi-square test was used to test the independence between two categorical variables. P-value of  $<0.05$  was considered as statistically significant.

### **RESULTS**

A total of 250 admitted patients with symptomatic hyponatremia were included in the study. Most of the patients were in age group of 56-65 years accounting for 52% of patients with a mean age of 62.4 years. Out of 250 studied patients, 155(62%) were females with a male to female ratio of 1:1.6. Diuretic use accounted for 38% of total patients with hydrochlorothiazide being the most common offending drug. Patients on Chlorthalidone and combination of diuretic and SSRI had profound hyponatremia with increased mortality. SIADH accounted for 26% patients of hyponatremia with stroke being the commonest cause of SIADH.

Other causes of hyponatremia are discussed in detail in table 1. Regarding symptomatology GI symptoms like nausea and vomiting was seen in 60% of patients. Among neurological symptoms, confusion was seen in 52% of patients followed by

lethargy (22%), seizures (18%) and Coma in 8% patients. 52% patients had euvolemic hyponatremia, 40% patients had hypervolemic hyponatremia and 8% patients had hypovolemic hyponatremia. (table 1).

**Table 1. Demography, etiology and Clinical Characteristics of Study Population:**

Parameter	No. Of Patients	Frequency (%)
Age (Years)	16-25	5
	26-35	7
	36-45	30
	46-55	32
	56-65	130
>65	46	18.4
Gender	Males	95
	Females	155
Etiology	Diuretics	95
	Hydrochlorothiazide	60
	Chlorthalidone	20
	Metolazone	10
	HCTZ+Metolazone	5
	SIADH	65
	Stroke	50
	SSRI# intake	8
	Meningo-encephalitis	7
	Gastrointestinal losses	25
	Chronic Liver Disease	20
	Chronic Heart Failure	20
	Chronic Kidney Disease	15
	Hypothyroidism	5
	Primary Adrenal Failure	2
	Primary Polydipsia	2
Beer Potomania	1	
Symptoms	Nausea/Vomiting	150
	Confusion	130
	Lethargy	55
	Seizures	45
	Coma	20
Type of Hyponatremia	Euvolemic	130
	Hypervolemic	100
	Hypovolemic	20

\*Hydrochlorothiazide# Selective serotonin reuptake inhibitors

Out of 250 studied patients, 35 patients died. Majority of patients who expired had euvolemic hyponatremia (27 patients), 7 had hypervolemic hyponatremia and 1 patient had hypovolemic hyponatremia. (table 2)

**Table 2: Outcome with respect to type of hyponatremia.**

Type of Hyponatremia	Died(n=35)	Survived(n=215)	p-Value
Euvolemic	27	103	.005
Hypervolemic	7	93	
Hypovolemic	1	19	

## DISCUSSION

Hyponatremia is not a disease in itself rather it is an important over manifestation of an underlying disease process which should be identified at an earliest and treated with

In our study, we found that there is a female preponderance with regard to hyponatremia and it is more common in elderly patients. Similar inferences were drawn in previous studies by Hochman (13) and Vurgese (14).

We found that euvolemic hyponatremia is more common in our setting (52%), as also seen in a study by Schwartz WB et al (15).

Confusion (52%) followed by lethargy (22%) were the most common symptoms in our studied subset of patients. It is also in accordance with previous studies done by Rao MY (16) and Nandkumar (17). Seizures were found in 18% of our patients all of whom had severe

hyponatremia. Similar results were found by Halawa I et al (18).

The most common cause of hyponatremia was found to be diuretic related (36%) with Hydrochlorothiazide being the commonest causative agent and Chlorthalidone being the cause behind more severe hyponatremia. Similar results were obtained by Spital (19) in his study.

The second most common cause found in our study was SIADH (26%) with stroke being the main contributing cause. Similar results were seen by Lockett J et al (20) and Liamis G et al (21) in their studies.

Mortality was 14% in our study, most of which was contributed by SIADH. 12% mortality was seen in severe hyponatremia group and 2% in moderate group. Similar mortality data was seen in a study by Ewout J et al. (22)

Main factors contributing to mortality in our study population were elderly patients with underlying comorbidities, SIADH and severe hyponatremia.

## CONCLUSION

Hyponatremia being the most common electrolyte abnormality in hospitalised patients should be sought at the very first encounter for its underlying cause and also for appropriate correction.

It is worthwhile mentioning here that one should be very cautious about prescribing diuretics as anti-hypertensives in elderly patients unless absolutely necessary, in lowest possible doses with careful monitoring of serum sodium levels especially during first week of initiation of therapy. This is because, it is an important cause associated with falls in them, directly contributing to morbidity and mortality.

## Limitations:

1. Smaller sample size of study population remains a drawback of this study.
2. The study was conducted in general medicine wards of a tertiary care hospitals. It would have been worthwhile to include patients admitted in ICU as well where hyponatremia is

common and a defining prognosticating factor.

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