

Original Article

Clinical profile of hyponatremia in tertiary care center in India : retrospective hospital based observational studyAkash Thomas Oommen¹, VS Srikanth², Senthivel Vasudevan³, Ranjitha⁴

Hyponatremia is the most common electrolyte abnormality seen in clinical practice and is associated with altered sensorium, seizures, falls and cognitive dysfunction. Even mild hyponatremia could lead to severe complications and prolonged hospital stays. Understanding the emerging trends in manifestations of hyponatremia will help in efficient management of hyponatremia and its allied co morbidities. This study conducted on 904 patients admitted in AIMS, Kochi. They were categorized, based on serum sodium level under 3 groups (Mild, Moderate and Severe). The data collected were analyzed for Clinical presentations, Severity and Etiology of hyponatremia. Hyponatremia predominantly observed in age group >70 years (37.3%), with male predominance (63%). Altered sensorium is the most common presentation of hyponatremia. Disorientation was observed majorly in moderate hyponatremia (64%) compared to severe hyponatremia (20%). Syndrome of inappropriate Antidiuretic hormone secretion (SIADH) was indicated as main cause of Hyponatremia. Respiratory causes like, pneumonia, asthma, Obstructive Airway Disease (OAD) were the predominant causes of SIADH, Lung and genitourinary cancer were the main causes of SIADH among various carcinoma types. The infections associated with hyponatremia were Urinary tract infection (UTI) (68%), Chest Infection (15%) and Cellulitis (14%). In 42.0% population with hyponatremia had Diabetes Mellitus, of which 64% had peripheral neuropathy and 10% had diabetic foot and necrotizing fasciitis. This study summarizes various presentations of hyponatremia, its causes and co-morbidities which will provide better understanding on hyponatremia and aid physicians in diagnosing the precise cause of hyponatremia and its management.

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Key words : Hospital based study, Hyponatremia, SIADH, UTI.

Hyponatremia, defined as serum sodium concentration of <135 mmol/L, often develops as a consequence of elevated levels of Arginine Vaso Pressin (AVP) hormone. AVP elevation can occur in a number of common clinical conditions, including SIADH, volume depletion, postoperative states, heart failure, cirrhosis, neuroendocrine disorders and trauma. Hyponatremia is the most common electrolyte abnormality seen in clinical practice. Severe hyponatremia can be symptomatic and life threatening¹. Sodium as a major extra cellular ion is of primary importance in reflecting changes of water and electrolytes status in the body². This retrospective study was conducted in our hospital to get the clinical overview of hyponatremia in hospitalized patients and distribution of various symptomatic presentations of Hyponatremia. Symptoms of hyponatremia depend on its severity and the rate of sodium decline. Polydipsia, muscle cramps, headaches, falls, con-

fusion, altered mental status, obtundation, coma, and seizures may indicate the need for acute intervention³. Most patients with hyponatremia are asymptomatic, and hyponatremia is noted incidentally. Understanding the emerging trends in manifestations of hyponatremia will help in efficient management of hyponatremia and its allied co morbidities

MATERIALS AND METHODS

This retrospective observational study was conducted in Amrita Institute of Medical Sciences, Kochi, in the Department of General Medicine. The study included a total of 904 patients who were admitted during January 2016 till June 2017.

Clinical Assessment — This included history of symptoms of hyponatremia, predisposing factors and pre-existing illnesses if present. The definition of symptomatic hyponatremia was based on a clinical assessment of symptomatology including the presence of altered sensorium, lethargy and seizures. Categorization of study population is done based on age, gender, and severity of sodium level, symptoms and causes of hyponatremia.

Lab Investigations — Patients Lab Investigations were studied retrospectively. Serum Sodium levels, Serum Os-

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molarity, Urinary sodium excretion were studied and based on this categorization is done as below :

- Mild hyponatremia (130-135mg/dl).
- Moderate hyponatremia (120-130mg/dl)
- Severe hyponatremia (<120mg/dl)

Data collection — For all the patients clinical and demographic detail and other details of symptom and various presentations, as mentioned above were recorded in a standard data collection sheet as per the study pro-forma and later transferred to a Microsoft Excel spreadsheet for analysis.

Inclusion criteria —

- Patients aged more than 20 years who were admitted in AIMS with Serum Sodium level less than 135mEq/l

Exclusion criteria —

- Patients aged less than 20 years and admitted in the ward with Sodium level greater than 135mEq/l.
- Pregnant or breast-feeding women

Data and Statistical Analysis — Data were collected and recorded on a pre-designed proforma and complied using Microsoft Excel 2010. Data was systematically analyzed by SPSS 20.0 version. In the statistical analysis, p-value <0.05 was considered as statistically significant.

RESULTS

Out of the total population, 63.3% were males and 36.6% were females. Gender wise presentation of hyponatremia showed male predominance. The prevalence was higher in the age group of above 70 years (37.3%) and lower in the age group of less than 30 years (1.5%) as shown in Table 1. In our

Table 1 — Hyponatremia age wise prevalence in study population

Age group	No of Patients	Percentage
≤ 30	14	1.5%
30 - 40	18	2.0%
41 - 50	45	5.0%
51 - 60	173	19.1%
61 - 70	317	35.1%
>70	337	37.3%

study, the population was categorized based on the sodium level (mild, moderate and severe). The moderate category showed higher presence (64%), followed by severe category (20%) and 17% were categorized as mild, as shown in Fig 1.

Clinical manifestations of Hyponatremia :

Altered sensorium is the most common presentation indicated, followed by seizures and drowsiness, also 3% of the study group reported restlessness as showed in Fig 2. The serum sodium level severity and seizure incidence irrespective of gender as shown in Table 2.

Severity of hyponatremia in relation to sensorium :

The severity of sodium level influencing the altered sensorium and drowsiness is more prevalent in moderate and mild group as compared to the severe category of hyponatremia group as shown in Fig 3.

Results indicated that the cause of hyponatremia can be any of the following condition as shown in Fig 4.

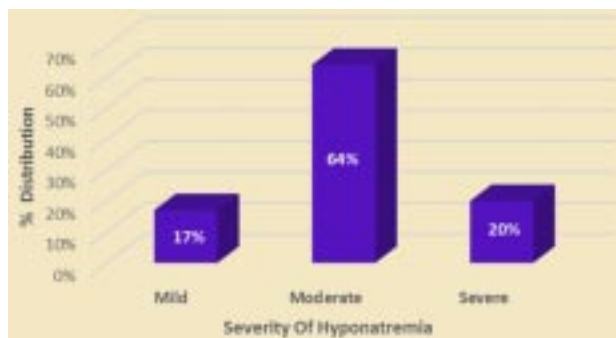


Fig 1 — Distribution of hyponatremia in the study population based on severity

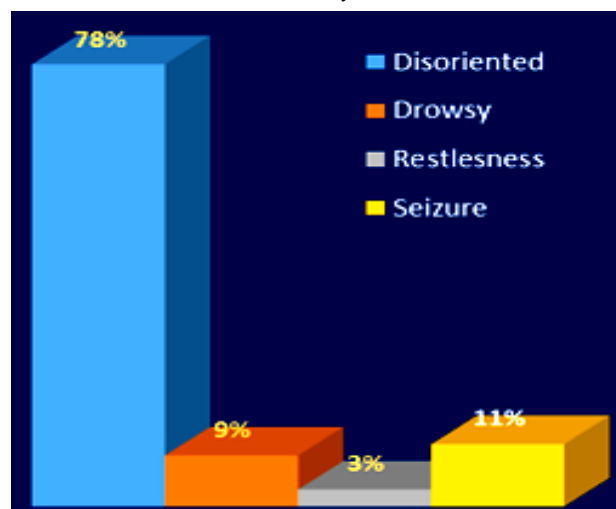


Fig 2 — Distribution of Clinical manifestations of Hyponatremia

- Depletion Hyponatremia : Renal failure, diuretics (except Mannitol), pancreatitis
- Dilutional Hyponatremia : Coronary Artery Disease (CAD), Chronic Kidney Disease (CKD), Chronic Liver Disease (CLD), Nephrotic syndrome

Table 2 — Seizure Incidence across the different Severity conditions of Hyponatremia

Hyponatremia Severity	Frequency of Seizure Incidence Gender	
	Male n (%)	Female n (%)
Mild	3 (42.9)	4 (57.1)
Moderate	17 (81.0)	4 (19.0)
Severe	2 (50.0)	2 (50.0)

Distribution : Chi-Square = 4.29; df = 2; p = 0.117 (>0.05) : Statistically Not Significant

Diuretics usage and SIADH

- Other causes: Mannitol (diuretics), Cancer, Injury, hypothyroidism, surgery Transurethral resection of the prostate (TURP)etc,

Effect of diuretics on Hyponatremia :

It is indicated that Hyponatremia is caused by diuretics usage.

- Furosemide
- Hydrochlorothiazides are major contributors.

Causes of SIADH :

SIADH is caused by various systemic influences as

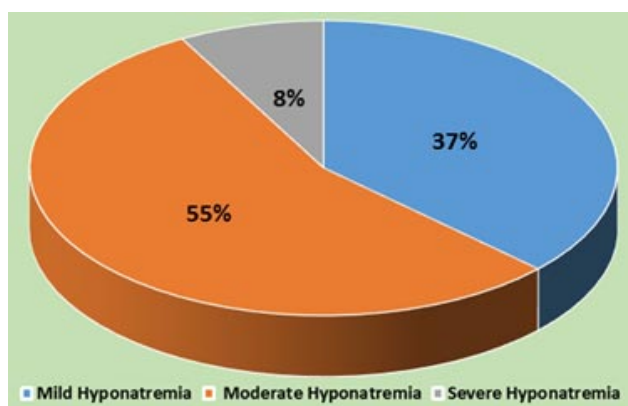


Fig 3 — Altered sensorium presentations in the study population

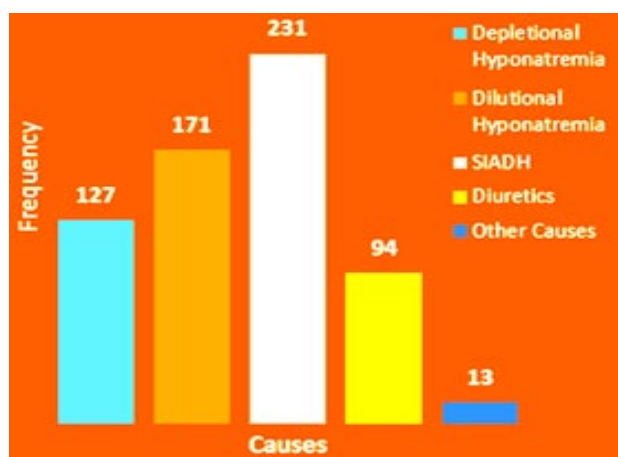


Fig 4 — Distribution of causes of Hyponatremia

follows – The distribution of various causes among the population as observed is shown in Fig 5.

- o Central Nervous System
 - o Meningitis
 - o Encephalitis (Including encephalopathy)
 - o Capsular bleed
 - o Carcinomas
 - Lung cancers (small-cell lung cancer and mesothelioma)
 - Gastrointestinal cancers (stomach, duodenum, pancreas)
 - Genitourinary cancers (bladder, urethral, prostate, endometrial)
 - Lymphoma
 - Sarcomas
- o Respiratory System
 - Lung infections - all Pneumonia
 - Asthma
 - COPD (Chronic obstructive pulmonary disease)
- o Renal System
- o Drug Induced

Observation showed drugs referred here have high potential to cause hyponatremia-SIADH. Drug categories

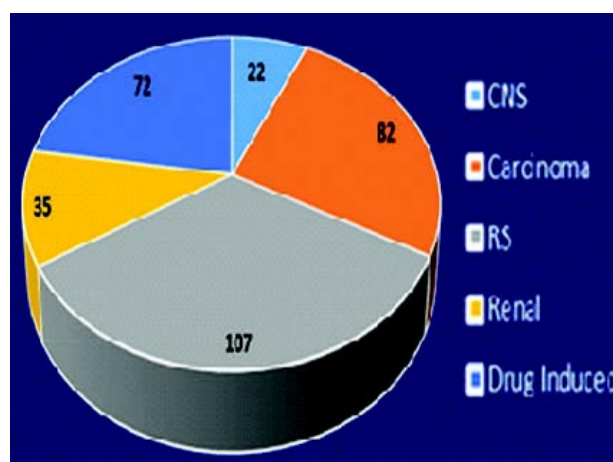


Fig 5 — Distribution of causes of SIADH (N=318)

listed here found to cause drug induced SIADH.

- ANTIPILEPTIC : Carbamazepine, Oxcarbazepine, Phenytoin
- ANTIBIOTIC : Moxifloxacin,
- NSAID : Aceclofenac
- OPIOD : Morphine
- IMMUNOSUPPRESSANT : Cisplatin, Melphalan, Cyclophosphamide

Our study results indicated various carcinomas being causative for manifestation of SIADH. Lung cancer and genitourinary cancer (Prostate and Ovary) had major representation in our sample population as shown in Fig 6.

Common Co-Morbidity in Hyponatremia :

In 42% of the study population had Diabetes Mellitus. Out of them 64% had Peripheral neuropathy and 10% had Diabetic foot or Necrotizing fasciitis leading to severe complications. Other co-morbidities presented include Diabetic Retinopathy 28%, Diabetic Nephropathy 13% and 55% of the population had hypertension. The most common infection associated with hyponatremia patients was Urinary tract Infection (68%), other infectious conditions included Chest Infection (15%) and Cellulitis (14%). Moderate hyponatremia patients were more prone to infections as compared to Mild or Severe hyponatremia patients.

DISCUSSION

Hyponatremia is the most common electrolyte disturbance seen in hospital practice. In previous studies, incidence of hyponatremia in hospitalized patients was found to be about 1% to 6%^{3,4}. Hyponatremia has been associated with considerable morbidity and mortality in many chronic diseases^{5,6}. Hyponatremia leads to increased health care cost due to extension of their hospital stays though they were not admitted specifically for hyponatremia^{7,8}.

Incidence of hyponatremia has been shown to have direct correlation with age in few earlier studies. Our study indicated 37.3% of the patients who had hyponatremia were

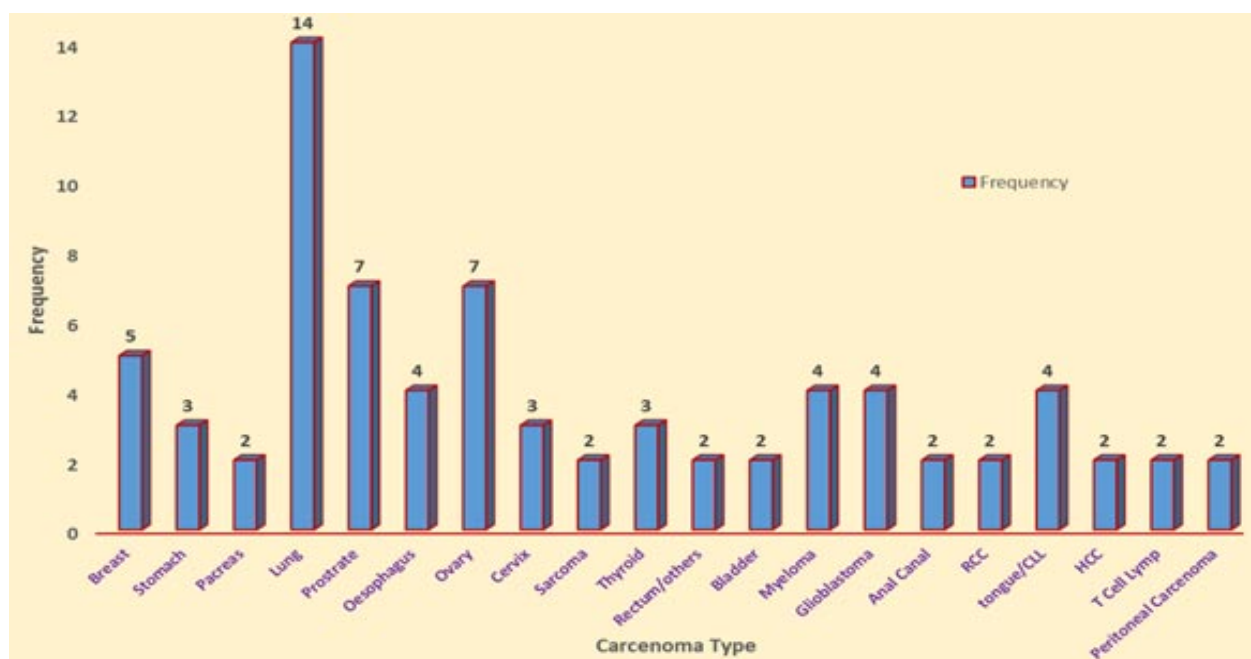


Fig 6 — Distribution of Carcinoma triggering SIADH

in the age group of more than 70 years. The presentation was as low as 1.5% in the age group of less than 30 years. It showed 8 times high in age group of 70 + years. This differs from the study by Hawkins *et al*, that noted that increasing age, after adjusting for sex, was independently associated with both hyponatremia at presentation and hospital-acquired hyponatremia⁹. In the present study prevalence of hyponatremia was more in male patients with male: female ratio of 1.7:1. The male predominance of hyponatremia prevalence is clearly indicated with 63% of hyponatremia cases being male. This observation is markedly different from previous studies by Nidhi Kaeley¹⁰ which showed female predominance of 56% and another study by Amay Parkin & Sumit Mohan showed female predominance of hyponatremia by 2% more than male population^{6,11,12}. In our study presentation of hyponatremia in male population is more than in female population by 30%.

Out of various manifestations that are associated with Hyponatremia, Altered Sensorium is the most common presentation (78% of population)¹³. The frequency of altered sensorium observed in our study is almost double as compared to the study by Clayton *et al*¹⁴, in a study of severe hyponatremia in Queen's Medical Centre, UK, which showed only 36.2% patients had neurological symptoms attributable to the hyponatremia. High presentation of this correlation in our analysis reinforces that altered sensorium is most common indicator for hyponatremia. In addition, it is observed that altered sensorium was most commonly seen in patients with Mild and Moderate hyponatremia³. The distribution showed more than half of the population with altered sensorium being in Moderate hyponatremia group

(55%) as compared to patients in Mild hyponatremia (37%) and in severe (8%) hyponatremia groups.

Drowsiness (11%) and Seizures (9%) observed as major presentations associated with hyponatremia in our study. In further analysis of presentation of Seizures in hyponatremia revealed that Seizure incidence is majorly observed in the population with serum sodium level in the range of 121mM–130mM (Moderate category) as compared to Severe & Mild hyponatremia category. This result is interestingly deviating from the findings in the study by Imad *et al*¹⁵, which was indicating Seizure presentation was reported mainly from Severe hyponatremia (<115mM of serum sodium level) and only one incidence was reported from Moderate hyponatremia (Serum sodium level 121mM-130mM). In addition, it is observed that 62% of the patients presented with seizure events were “oriented” and seizure episode was associated with hyponatremia more in male patients as compared to female study population similar in lines with study results by Sherlock¹⁶. Normally Cutaneous loss of sodium occurs due to excessive sweating in Indian climatic condition. Further addition of diuretics as a part of treatment protocol in patients will contribute to further loss of sodium, eventually causing hyponatremia. Diuretics are recommended as first-line anti-hypertensive treatment in elderly patients. Although attention is usually paid to prevent hypokalemia with diuretic therapy, risk of hyponatremia is often ignored.

In the our study, diuretics was found to cause 12.4% of hyponatremia of which, 54.25% diuretic induced hyponatremia was due to loop diuretics and 22.34% diuretic induced hyponatremia was due to thiazide diuretics. This

revelation in our study is quite different from other previous studies where Thiazide diuretics influenced hyponatremia was on high percentage of presentation¹⁷⁻¹⁹. In our study loop diuretics usage is the leading factor and showed as higher percentage of trigger for hyponatremia presentation. According to study, Sonnenblick *et al*²⁰. Thiazides were responsible for severe diuretic-induced hyponatremia in 94 percent of 129 cases reported in the literature. In another study by Sunderam SG^{21,22}, 53% patients on thiazide diuretics developed hyponatremia compared to 21% patients who were on loop diuretics. Our study indicate loop diuretics should also be used with caution while considering a long term maintenance therapy by regular monitoring of electrolyte levels to avoid hyponatremia. While analyzing the causes for hyponatremia, based on our study results SIADH is found to be prime cause standing at 42% followed by Dilutional hyponatremia 22%. Other significant cause factors are from Depletional hyponatremia 16% and Drug induced (12%) and this trend is reflective of the results from a study by Sandez *et al*^{11,23}.

SIADH being the foremost leading cause of hyponatremia in our study. This study revealed us "Pulmonary" causes were prime triggering incidences for hyponatremia 34% of the population. This is substantiated by results from study by Mansoor *et al*²⁴. Next immediate causative factor for SIADH in our study is "Carcinoma", out of the different carcinomas presented in our population, carcinoma of Lung is found be the major contributor. Third line of cause next to Carcinoma for SIADH is found to be Drug induced SIADH. Similar observation was noted in a study by Irish National Neurosciences Centre M Sherlock *et al*¹⁸. The most common class of drug that induced SIADH being antiepileptic²⁵, and followed by Opioid, NASID and Osmotic agents²⁶. Analysis of the data related to Diabetes Mellitus in our study, revealed that 42% of the population with hyponatremia had Diabetes Mellitus. Out of them 64% had Peripheral Neuropathy and 10% of them had Diabetic foot, Gangrene of the lower limb and necrotizing fasciitis. Our study indicated of high possibility of hyponatremia coexisting with Diabetes and its associated complication like peripheral neuropathy which is similar to the results indicated from another study by McNair *et al*²⁷.

In our study, 51% of the population had Hypertension. Results from a study (Prevalence of Hyponatremia and Association with Mortality) by Sumit Mohan *et al*¹¹, - conducted over 14,697 adults indicated that hyponatremia was found to be common in subjects with hypertension, diabetes, CAD, infections, cancer and just 1.04% had no co-morbidities. Our observations about Infection associated with hyponatremia showed UTI (68%), Chest Infection and Cellulitis (14%) as major cause, in similar lines to other studies^{28,29}. There is indication of strong correla-

tion between UTI and hyponatremia but further studies need to be conducted to confirm the degree of correlation. Results showed Chest infection is associated with Moderate hyponatremia cases in higher percentage (72%) as compared to Severe hyponatremia (16%) whereas Thomas *et al*³⁰ and Kennedy *et al*^{31,32} found that chest infection was caused in severe hyponatremia cases only in their study.

CONCLUSION

Elderly Males were majorly affected and presented with altered sensorium in the range of mild-moderate hyponatremia. Seizures could also be a manifestation even in mild and moderate hyponatremia. Loop diuretics should be cautiously prescribed as it was the major class of diuretic which induced hyponatremia. Hyponatremia should be ruled out as primary electrolyte imbalance in diabetic and hypertension patients. Among patients reported with hyponatremia, when respiratory system is involved SIADH should be ruled out first as cause of hyponatremia. There is a correlation between hyponatremia and urinary tract infection and cellulitis as noted in our study. Hyponatremia is common electrolyte imbalance but may lead to serious complications if not identified at an early stage and promptly managed.

Conflict of Interest : None


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