



CLINICO-ETIOLOGICAL PROFILE OF HYPONATREMIA AMONG ADMITTED PATIENTS AT DR. RADHA KRISHNAN GOVT. MEDICAL COLLEGE AND HOSPITAL HAMIRPUR HIMACHAL PRADESH

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ABSTRACT

Hyponatremia is a common electrolyte disturbance encountered in hospitals. It is defined as serum concentration <135 meq/l. Various comorbidities predispose to the development of hyponatremia.

Patient has symptoms of both hyponatremia as well as comorbidities. This contributes to increased morbidity and mortality. However early recognition and treatment makes prognosis better.

Aim: To study clinical features of patients admitted with hyponatremia and investigate them to find out various aetiologies.

Methods And Material: Study was conducted at newly opened medical college at Hamirpur in Himachal Pradesh with limited facilities. A total of 50 patients with symptoms and documented hyponatremia were enrolled in study. Detailed history, clinical examination and laboratory investigations were done. Data thus collected was analysed.

Results: Total number of patients was 50. Females were more as compared to males. Mean age of presentation was 67 years and lethargy, nausea and vomiting were the most common symptoms. Diabetes mellitus and hypertension were the most common comorbidities. Among drugs diuretics were the most commonly used causing hyponatremia. Out of 50 patients 45 patients recovered and five patients have to be referred because of comorbidities.

Conclusions: Hyponatremia is a common problem and clinicians need to be aware of it mainly in the elderly patients. A systemic approach and simple diagnostic algorithm can significantly improve the outcome in these patients. Treatment of hyponatremia is governed by levels of hyponatremia not by its etiology along with comorbid conditions.

KEYWORDS : hyponatremia, osmolality, comorbidities.

INTRODUCTION

Disorders of plasma sodium concentration is a common electrolyte abnormality, because of changes in relative ratio of sodium to water in the body.¹ Hyponatremia represents an imbalance in the ratio where total body water is more than body solutes. Based upon the volume of ECF, a patient can be classified into hypovolemic, euvoletic, or hypervolemic.²

Incidence more common in elderly patients due to comorbidities, multiple medications, and a lack of access to food and drinks.³ Early symptoms are nausea, headache and vomiting followed by seizure and even coma⁴. Lab investigations are done to find out serum and urine osmolality.⁵

Early recognition and prompt treatment are important. Prognosis depends upon severity and co morbidities. Prognosis is poor in patients with severe hyponatremia, acute hyponatremia, and elderly.⁶

This study was done at Dr. Radha Krishnan Govt. Medical College and Hospital Hamirpur a budding medical college in the lap of Himalayas to find out various symptoms and causes of hyponatremia depending upon the serum sodium concentration and patient's presentation.

MATERIAL AND METHODS

After obtaining approval from the Institutional Ethical Committee, the study was conducted from April 2020 to June 2021. 50 consenting inpatients in the Department of General Medicine, any age, both sexes with documented hyponatremia, whose serum electrolytes (serum sodium) had been estimated, were identified from the biochemistry laboratory records and were enrolled in the study. Detailed clinical assessment was done and recorded on a predesigned proforma and managed in a Microsoft Excel spreadsheet. Collected data was systematically analyzed and presented as a frequency distribution. Descriptive statistics have been

calculated for the continuous variables and categorical variables are expressed as percentages. For analytical statistics, Chi-square test was used where appropriate. Patients with hyponatremia were classified based on serum sodium levels into mild (130–135 mEq/L), moderate (125–130 mEq/L), and severe (less than 125 meq/l).

Inclusion and exclusion criteria was as follow.

Inclusion Criteria:

All admitted patients with symptoms suggestive of hyponatremia and serum sodium concentration less than 135 meq/l.

Exclusion Criteria:

patients already diagnosed and on sodium replacement therapy were excluded.

All patients with serum sodium concentration less than 135 were called as hyponatremic patients. Detailed history regarding comorbidities, intake of any drugs was taken. Complete haemogram, electrolytes, BUN, urinary sodium of all patients was done. Urine osmolality as well as serum osmolality of these patients was calculated using formula $2([Na^+] + [K^+]) + RBS/18 + BUN/2.8$ mOsm/L. Depending upon the serum osmolality patients were divided into Normal osmolality - 280-295mOsm/L, Hyperosmolar - >295 mOsm/L, Hypoosmolar - <280 mOsm/kg). Depending upon the volume status of the individual patients were divided into euvoletic, hypovolemic and hypervolemic. Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) was diagnosed using Schwartz diagnostic criteria as follow: Decreased measured serum osmolality <275 mOsm/l

Clinical euvoletmia

Urinary osmolality >100 mOsm/l

Urinary sodium >40 mmol/l with normal dietary sodium intake.

Normal thyroid, adrenal and renal functions.

Patients were also investigated for any adrenal, thyroid, pituitary or renal insufficiency. USG abdomen , X- ray chest and CT head of selected patients was done depending upon the presentation.. Daily follow up was done and response to treatment, survival at discharge and in hospital mortality was studied.

RESULTS

In the present study, age of the patients was between 31 to 81 years. Only 2 patients were below the age of 50 years. Maximum number of patients were between the age group of 50 -70 yrs. the mean age was 67 years. The youngest patient was 31 years and the oldest was 83 years of age. Maximum number of patients were females as compared to males with ratio of 1.77:1. Mean age of male patients was 62.61 years and mean age of females was 69.61 years. (Table 1)

Table I: Age And Sex Distribution

Age Group	Male (n)	Female (n)	Grand Total (n)
30-60	8	8	16
61-70	4	10	14
71-80	5	9	14
81-90	1	5	6
91-100	0	0	0
Total	18	32	50

Forty one patients were having severe hyponatremia i.e. Na level less than 125 meq/l. Nine patients were having Na between 125-130 meq/l i.e. moderate hyponatremia ,none of patient was having mild hyponatremia.(Table 2)

Table : 2 Severity of Hyponatremia

Severity of Hyponatremia	Patients
Mild	0
Moderate	9
Severe	41
Total	50

Most common symptoms for presentation to hospital were nausea (35 patients) ,vomiting (33 patients) ,lethargy (30 patients) ,confusion (23 patients), muscle cramps (15 patients) , seizure (14 patients) ,headache (5 patients) and decreased oral intake was present in (26 patients) of patients. Most of the patients were having more than one symptoms. Seizures and confusion was seen mainly in severe hyponatremia. (Table 3 &4)

Table : 3 Symptoms of Hyponatremia

Symptoms	No. Of patients
LETHARGY	30
SEIZURE	14
HEADACHE	5
CONFUSION	23
NAUSEA	35
VOMITTING	33
MS. CRAMPS	15
DECREASED ORAL INTAKE	26

Table : 4 Association of symptoms with severity of Hyponatremia

Symptoms	Moderate	Severe
LETHARGY	7	23
SEIZURE	0	14
HEADACHE	2	3
CONFUSION	0	23
NAUSEA	7	28
VOMITTING	7	26
MS. CRAMPS	3	12
DECREASED ORAL INTAKE	5	21

Predisposing factors and comorbidities were present in 42 patients among, Eight patients were not having any predisposing factor. Hypertension was present in 31 patients,

diabetes mellitus was present in 14 patients, Three patients were having CAD and three patients were on treatment for chronic kidney disease. Two patients were having CHF. Six patients were having thyroid disorders four of these were newly diagnosed and two were already on treatment for thyroid disorders. Chronic liver disorders were seen in two patients.(Table 5).

Table : 5 Association of Hyponatremia with Pre-existing illnesses

Pre-existing illnesses	Mild	Moderate	Severe	Total
HTN	0	6	25	31
DM	0	5	9	14
LIVER DS	0	2	0	2
RENAL DS	0	2	1	3
CHF	0	0	2	2
CAD	0	0	3	3
HYPOTHYROIDISM	0	2	4	6

History of drugs which may have cause hyponatremia was present in 14 patients and diuretic intake was present in eight patients, two patients were taking amitryptiline, two patients were taking prochlorperazine and one patient was taking cyclophosphamide for multiple myeloma. One patient was on antiepileptic drugs.(Table 6)

Table : 6 Drugs Causing Hyponatremia

Diuretics	8
Amitryptiline	2
Prochlorperazine	2
Cyclophosphamide	1
Antiepileptic	1
Total	14

Serum osmolality was calculated in all 50 patients and urine osmolality was calculated in 33 patients. and depending upon serum osmolality patients were divided into hypo-osmolar ;iso-osmolar and hyper-osmolar. Two patients were having serum osmolality between 280-295 mosm/l and 44 patients were having serum osmolality less than 280 mosm/l and four patients were having serum osmolality more than 295 called as hyperosmolar they were described as pseudohyponatremia due to hyperglycemia.

Depending upon serum osmolality ,urine osmolality and urine sodim conc. SIADH was diagnosed in 19 patients. Causes of SIADH were infections in nine patients, drugs in six patients ,cerebrovascular lesions in six patients and malignancy was seen in two patients.(Table 7)

Table : 7 Causes of SIADH

Infection	9
Drugs	6
Cerebrovascular lesions	2
Malignancy	2
Total	19

SIADH was found in 19 of patients, drugs were causing hyponatremia in 14 ,hypothyroidism was present in ten patients , CHF and liver disorders were seen in two each ,renal losses in three patients. Maximum number of patients were having more than one aetiology. (Table 8)

Table : 8 Etiology of Hyponatremia

SIADH	19
Drugs	14
Thyroid disorder	10
Renal disorder	3
CHF	2
Liver disorder	2
Total	50

Out of 50 patients 5 patients were referred to higher centre for treatment of comorbidities after treatment of hyponatremia ,no patient died due to hyponatremia. Maximum number of patients were treated with hypertonic saline and no patient

developed any complication due to treatment.

DISCUSSION

This is a clinical study on hyponatremia designed to study symptoms and causes of hyponatremia. Hyponatremia leads to increased health care cost along with utilisation of resources for patients whose hospitalisation was prolonged due to hyponatremia.

Out of 50 patients included in our study, maximum number of patients were more than 50 years of age, mean age was 67.28 years, in various studies done maximum number of patients are elderly. Thomas A Vurgese et al.⁷ from Kuwait reported commonest age group of 45-64 years and mean age was 57 years. Amit et al.⁸ reported mean age of patients 73.8 years where as mean age of patients was 72 years in study done by Rao et al.⁹ Elderly people have more comorbid conditions like diabetes mellitus, hypertension and coronary artery disease for which they are on drugs like ACE-I, diuretics that predispose them to develop hyponatremia. Increased release of anti-diuretic hormone to a given stimulus, impaired ability to conserve sodium by kidneys and decreased glomerular filtration rate are independent risk factors for development of hyponatremia among elderly. In our study number of patients increased with increasing age similar was also observed in another study done by Hawkins et al.¹⁰, that increasing age is independently associated with hyponatremia.

In our study 64% of patients were females, similar increased prevalence of hyponatremia among females were observed by Cumming K and Wagner S 78% and 66% respectively.^{11,12} in some studies there is male predominance which may be because of males usually outnumber hospital admissions as compared to females. Jalan et al.¹⁰ from Singapore have reported that gender is not an important risk factor for serum sodium concentration abnormalities.

18% of our patients were having moderate hyponatremia and 82% of our patients were having severe hyponatremia. None of our patients was having mild hyponatremia. It may be because of mild nature of symptoms which patients could not recognise. Severe hyponatremia was found distributed among all age groups.

Nausea and vomiting were the most common gastrointestinal symptoms present in 70% and 66% of patients. Drowsiness followed by seizures were the most common neurological symptoms present in 60% and 24% of patients. Baji et al.¹³ reported that drowsiness was the most common neurological symptom. Out of 12 patients who presented with seizures 10 were having their sodium conc. less than 115 meq/l. These findings are consistent with various studies done.^{14,15,16} in one study done by Nandakumar et. al. seizures were seen in patients with severe hyponatremia.¹⁷ Headache was present in ten % of patients whereas 30% patients reported muscle cramps and 52 % of patients were not able to accept food. Lethargy, nausea, vomiting and decreased oral intake were the most common symptoms present in majority of patients. Nausea and vomiting were most common in patients with sodium conc. between 125-130 meq/l.

84% of patients were having pre-existing co morbid illnesses, commonest being hypertension in 62% of patients followed by diabetes mellitus 28%, hypothyroid in 20% of patients, chronic kidney disease and coronary artery disease six % each followed by congestive failure which was present in four % of patients.

Study by Shanmugasundaram et al.¹⁸ reported that Hypertension followed by diabetes mellitus was the most common pre-existing illness present among the patients. The studies on hyponatremia have not demonstrated a direct

correlation between hyponatremia and hypertension, although the correlation of hyponatremia with the age and diuretic use is evident.^{19,20}

Thyroid disorders are seen in ten patients in our study 6 were already on treatment and 4 new cases of hypothyroidism were diagnosed. Thyroid disorders are in patients of hyponatremia by Clayton et al.²¹ but no correlation was found between two in study done by.²²

Poor nutritional intake secondary to various other comorbidities was a major risk factor in this study. Total 52% of patients had a history of poor intake, which was associated with various causes, such as anorexia which may be due to uremia, malignancy and acute illnesses. The conventionally fed fluids in India, orally or through Ryle's tube, are sugar based, such as fresh fruit juices, milk, tea and coffee, glucose water, and tender coconut water. Soups and canned juices with salt are not a part of our traditional meal, which may lead to the development of hyponatremia. This is in line with the causes of hospital-acquired hyponatremia as reported earlier.²³

Hypotonic hyponatremia was present in 44 of patients, isotonic hyponatremia was present in two of patients. Four of our patients were having hypertonic hyponatremia i.e serum osmolality more than 295 meq/l which is seen in hyperglycemia and mannitol use. This was comparable to the study done by Baji and Borker, in which 92% of patients were hypo-osmolar.²⁴ In the study by Baji and Borkar, 92% of patients were hypo-osmolar and 8% of patients were hyper-osmolar. Hyponatremia in diabetic patients was probably due to uncontrolled hyperglycemia, which induces fall in serum sodium levels by shifting water from intracellular to extracellular compartments, glucose being an osmotically active molecule. every 5 mmol/l rise in serum glucose causes 1.6-2.4 meq/l of sodium fall.²⁵

28% of our patients were on various drugs that predisposes to hyponatremia, diuretics being most common followed by antipsychotics. Diuretic use was the most common cause under drugs for hyponatremia. Though JNC 8 recommends diuretics as the first-line drug for treatment of hypertension but caution should be maintained while prescribing diuretics in the elderly and dose should be used according to body weight and lowest possible dose should be started first.

Diuretics as cause of hyponatremia was also studied by Saeed et al. reported 33.3% while Huda et al. reported 63.6% hyponatremia cases associated with diuretic usage.^{26,27}

SIADH is the commonest cause of hyponatremia.²⁸ In our study SIADH was diagnosed in 38% of patients. In other studies by Hochman²⁹, SIADH represented 28.3% of cases, 34% in the study by Anderson³⁰ in this study, we evaluated the cause of SIADH as treating underlying etiology may affect morbidity and mortality. Main cause of SIADH was infections, drugs and CNS disturbances. Malignancies were found in two of our patients. two of our patients were using amitriptyline and one patient was on cyclophosphamide for multiple myeloma. ICSOL was found in one patient and one postoperative patient was there for pituitary macroadenoma.

Vomiting is one of the strongest stimulus for release of ADH³¹. Nausea and vomiting was present in 66% of our patients. Vomiting in association with other causes is the major contributing factor for hyponatremia.

In our study 90% of patients improved with conservative management and 5 of our patients were referred to higher centre due to comorbidities after correction of hyponatremia. These findings are in consistent with another study conducted by Joseph and Panicker where mortality was noted in 7% of patients and 93% of patients improved.³²

CONCLUSION:

Hyponatremia is one of the common electrolyte abnormalities encountered in our day to day clinical practice. There is an increasing tendency for it to occur with increasing age, hypertension, diabetes mellitus and use of drugs. It is important to recognize it much early because of its reversibility with treatment and potential morbidity and mortality causing economic impact on the patient and health care system. Studying the symptoms, aetiology, risk factors and management of hyponatremia in admitted patients will help in reducing its incidence and minimize the complications associated with hyponatremia. Caution should be exercised in prescribing drugs to aged patients.

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