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Research Article

Clinico-etiological profile and outcome of hyponatremia in hospitalised adult patients

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ABSTRACT

Background: Hyponatremia is a common electrolyte abnormality in hospitalised patients. Incidence varies from 1% to 40%. It is common in the elderly, mainly owing to impaired water and electrolyte balance in response to diet, drugs and environmental changes. This study is to evaluate clinical features, aetiologies and outcome in patients with hyponatremia (Sr. Na <120 mmol/L at the time of admission).
Methods: An observational study was conducted in 76 patients admitted in Kamalnayan Bajaj Hospital, Aurangabad from August 2013 to August 2014. All patients having their serum sodium concentration less than 120 mmol/L were included in the study. History, examination and relevant details were taken. Outcome was noted. Student's t-test, chi square test and Fisher's exact test were applied for statistical analysis.
Results: In the present study, mean age of the patients was 59.4% years. 43% patients were euvolemic, 38% hypervolemic and 19% hypovolemic. Nausea (54%) was most common gastrointestinal while drowsiness (42%) was the most common neurological symptom. Etiology of hyponatremia was multifactorial in 76% cases. Use of diuretics (53%) was the most common etiological factor. SIADH was suspected in nine patients. Mortality was 21%. Most common comorbid conditions were hypertension (51%) and diabetes mellitus (42%).
Conclusions: Hyponatremia is a common electrolyte abnormality in hospitalised patients. There is an increasing tendency for it to occur with increasing age, hypertension, diabetes mellitus and use of drugs (diuretics). Nausea, vomiting and drowsiness are the commonest symptoms. Mortality is high, though not directly related to serum sodium levels. Hyponatremia acts as a poor prognostic marker of primary disease.

Keywords: Hyponatremia, SIADH

INTRODUCTION

Hyponatremia is a common electrolyte abnormality in hospitalised patients.[1,2] Incidence varies from 1% to 40%. It is common in the elderly, mainly owing to impaired water and electrolyte balance in response to diet, drugs and environmental changes.[3,4]

It is defined as serum sodium concentration of less than 135mmol/L. It can be broadly categorized as mild hyponatremia (130-134mmol/L), moderate hyponatremia (120-129mmol/L) and severe hyponatremia (<120mmol/L).[6-8] Severe hyponatremia can lead to neurological complications as a result of cerebral oedema.[9,14]

Mild symptoms include anorexia, nausea and vomiting which can progress to severe ones like neuropsychiatric symptoms - restlessness, altered consciousness, lethargy, seizures, coma and death (if untreated).[7,9,10] Hence it is important to recognise hyponatremia early to decrease morbidity and mortality. Rapid correction of serum sodium is not recommended as it can cause severe

neurological deficit and death. Since it is a very vital metabolic problem, we undertook this prospective observational study in hospitalised patients in our tertiary care centre.

Sodium is the most important determinant for maintaining the tonicity of extracellular fluid Sodium and potassium are the major cations in the ECF and ICF, respectively.[11] Osmolality refers to the concentration of all solutes, whereas tonicity refers to the concentration of solutes that are "effective" in eliciting a water shift between body fluid compartments.

Plasma osmolality is calculated by following formula.[12]

Serum osmolality = [2 × (P Na + P K)] + (PBUN / 2.8) + (P Glucose/18) PNa= plasma sodium, PK= plasma potassium, PBUN= plasma BUN level (Glucose in mg/dl, BUN in mg/dl).

METHODS

Patients of age 15 years or more and patients with serum sodium less than 120 mmol/L on admission were included in the study and patients of age less than 15 years and patients with serum sodium more than 120 mmol/L on admission and patients not willing to participate in the study were excluded from study. Detail history including onset, duration and progress of symptoms, history of illnesses such as congestive heart failure, chronic kidney disease, chronic liver disease and hypothyroidism. Drug history causing hyponatremia like diuretics (loop and thiazide), antidepressants (SSRI, TCA), anticonvulsants, chemotherapeutic agents and NSAID's were taken. And detailed physical examination was done in every patient. According to hydration status, patients were divided in hypovolemic, euvolemic and hypervolemic status. Following investigations were done as follows:

a. Serum electrolytes were recorded and successively repeated.
   Normal range of serum sodium – (135-145mmol/L).
b. Serum osmolarity : It is calculated by formula
   [2× (P Na +P K)] + (P BUN/2.8) +
   (P Glucose /18)PNa.
   P Na- Plasma Sodium, P K Plasma potassium.

Normal range of serum osmolarity is 275 to 295mOsmol/Kg of water. Patients were divided into hypo-osmolar (<275) and hyperosmolar (>295).

c. Blood urea and serum creatinine.
d. Random blood glucose level.
e. Urine osmolality and spot urine sodium.

Outcome assessment was recorded as discharge or death. Serum sodium levels at time of discharge were recorded. Student's t-test and analysis of variance (ANOVA) were statistical methods used to analyse continuous variables. Chi square test and Fisher's exact test were used to analyse categorical variables.

RESULTS

In the present study, the patients were between 28 to 89 years. 63% of the patients belong to the age group of 50 to 69 years; the mean age was 59.4 years. The youngest patient was 28 years and the oldest was 89 years of age (Figure 6).

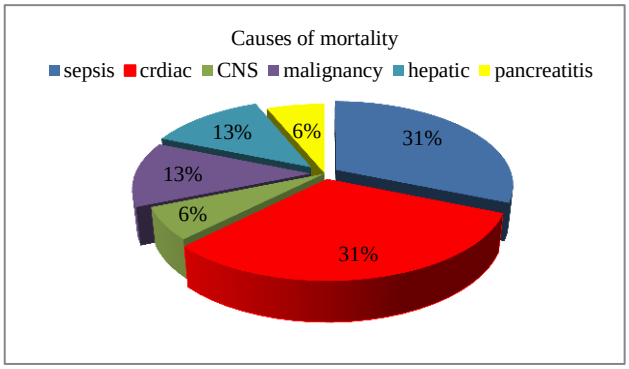

Figure 1: Causes of mortality.

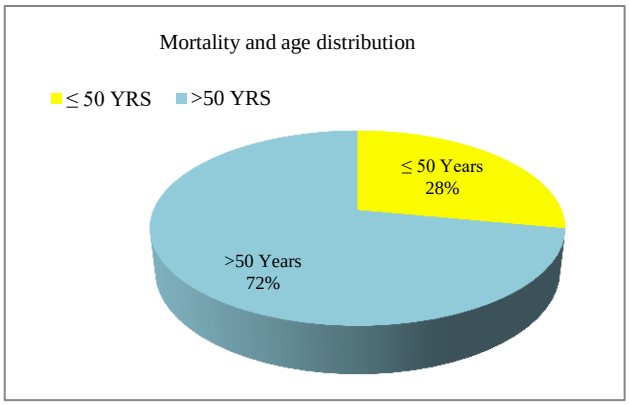

Figure 2: Mortality and age distribution.

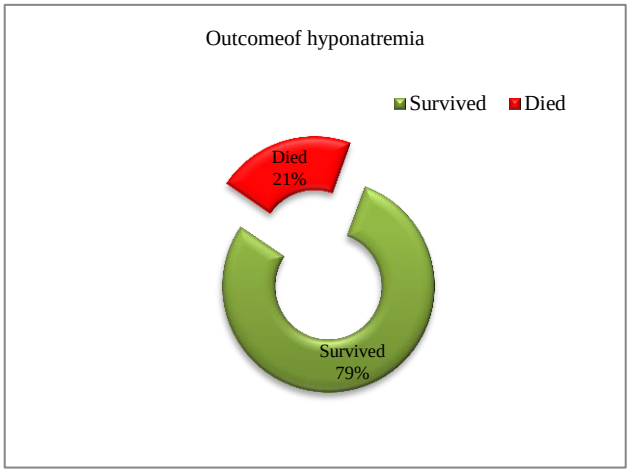

Figure 3: Outcome of hyponatremia.

76% patients were above 50 years and only 24% patients were below 50. This was statistically significant. There

was no statistically significant difference in the age distribution between males and females (Figure 6, 4).

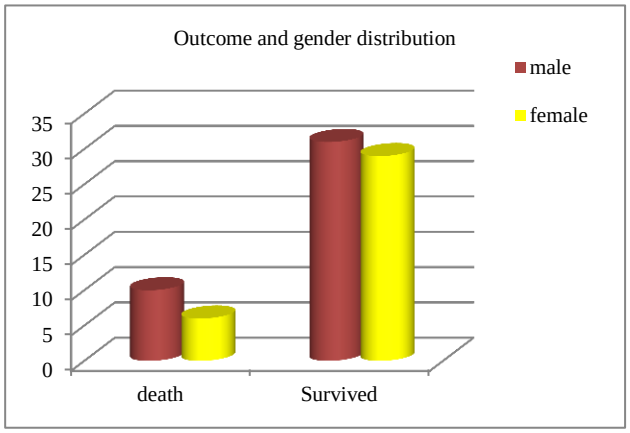

Figure 4: Outcome and gender distribution.

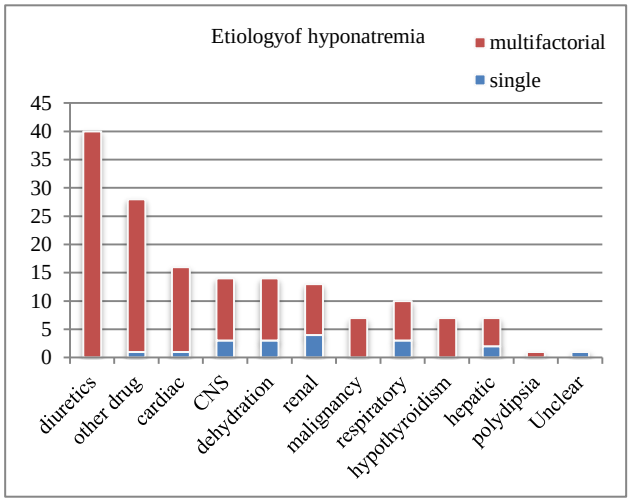

Figure 5: Etiology of hyponatremia.

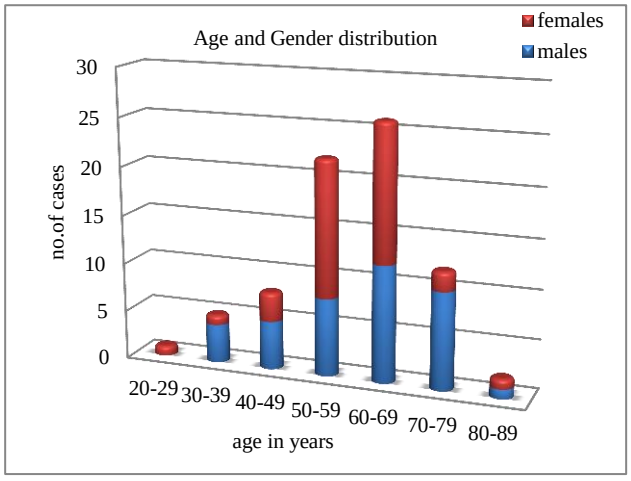

Figure 6: Age and gender distribution.

57% patients were admitted in ICU and 43% patients were admitted in wards. 43% patients had euvolemic hyponatremia, 38%patients had hypervolemic hyponatremia and 19% patients had hypovolemic hyponatremia, 92% patients were hypo-osmolar and 8% patients were hyperosmolar. No patient was normo-osmolar.

Severe neurological symptoms like seizures were present in 11% and coma in 5% cases (Figure 5).

Commonest gastrointestinal symptom was nausea (54%) while commonest neurological symptom was drowsiness (42%) (Figure 5).

Most common comorbid conditions were hypertension (51%) and diabetes mellitus (42%) (Figure 5).

The mean (± SD) serum sodium on admission was 113.4(±4.8) mmol/L. Difference between sodium levels on admission in hypo, eu or hypervolemic groups was not statistically significant.

Use of diuretics was most common drug group associated with hyponatremia (53%).

Etiology of hyponatremia was predominantly multifactorial (76%). Single etiology was found in 24% patients.

In the present study, there were 9 patients of suspected SIADH. Of these, malignancy was present in 45%, CNS lesions in 33% and LRTI in 22%; however we could not do their hormonal studies.

Among 76 patients, 16 (21%) died while 60 (79%) survived. Survival was 76% in males and 83% in females (not statistically significant). Mortality in hyponatremia was not in direct relation with their sodium levels and related more to their primary disease. Cardiac failure was the most common etiological factor of hyponatremia associated with mortality. Sepsis was the most common diagnosis in the hyponatremic patients who died (Figure 3, 6).

DISCUSSION

Hyponatremia is a common electrolyte abnormality seen in various settings and various degrees in adult hospitalised patients. Patients are more prone to develop hyponatremia with increase in age due to development of co morbidities like hypertension, diabetes mellitus, cardiac failure/shock, liver cirrhosis and use of drugs like diuretics, antidepressants which are known to cause or aggravate hyponatremia. Nausea, vomiting are most common gastrointestinal symptoms and headache, giddiness, slurred speech and drowsiness are most common neurological symptoms of hyponatremia. Euvolemic hyponatremia (43%) is the most common type of hyponatremia followed by hypervolemic (38%) and hypovolemic hyponatremia (19%). Hyponatremia is often multifactorial. Diuretic use is the most common aetiology

of hyponatremia. Mortality in diseases associated with hyponatremia is high and it may not be related directly to serum sodium concentration.

There are many causes of hyponatremia as mentioned below

Hypervolemic hyponatremia - There is decreased effective circulatory volume. Both sodium & water content increase: Increase in sodium content leads to hypervolemia and water content to hyponatremia. Total body water and sodium are regulated independently. Examples are cirrhosis of the liver, congestive heart failure, nephrotic syndrome in the kidneys, massive edema of any cause.[13,14] In our study, we found 31% of cardiac cause, 31% hepatic cause, 6% pancreatic cause, 13% malignancy and 31% cases due to sepsis.

Euvolemic hyponatremia - There is volume expansion in the body, no edema, but hyponatremia occurs.[12] Examples are SIADH (and its many causes), hypothyroidism, glucocorticoid (steroid) deficiency.

Hypovolemic hyponatremia - The hypovolemia (extracellular volume loss) is due to total body sodium loss. The hyponatremia is caused by a relatively smaller loss in total body water.

Examples are:

- Any cause of hypovolemia such as prolonged vomiting, decreased oral intake, severe diarrhoea
- Diuretic use (due to the diuretic causing a volume depleted state and thence ADH release, and not a direct result of diuretic-induced urine sodium loss)
- Addison's disease and congenital adrenal hyperplasia in which the adrenal glands do not produce enough steroid hormones (combined glucocorticoid and mineralocorticoid deficiency)

Miscellaneous causes of hyponatremia that are not included under the above classification scheme include the following:

- Fictitious hyponatremia (due to massive increases in blood triglyceride levels, extreme elevation of immunoglobulin as may occur in multiple myeloma, and very high level of blood glucose). In our study, we did not find any patient of this type of hyponatremia.
- Hypothyroidism and adrenal insufficiency (both thyroid hormone and cortisol are required to excrete free water).
- Poor dietary protein intake leads to inadequate urine solute formation thereby impeding the kidney's ability to excrete free water. In our study, we did not find any patient of this type of hyponatremia.
- Primary polydipsia (where the amount of urine solute required to excrete huge quantities of ingested water exceeds the body's ability to produce it; this typically occurs when 12 or more liters of water are ingested per day). In our study, we did not find any patient of this type of hyponatremia.

This study of 76 patients was conducted at Kamalnayan Bajaj Hospital, Aurangabad from August 2013 to August 2014. All these patients had hyponatremia (Sr. Na< 120 mmol/L).

In the present study, incidence of the patients admitted with Sr. Na less than 120 mmol/L was 0.7% of hospital administration. Laczi F[14] in his study reported that hyponatremia with Sr. Na < 120 mmol/L was present in 1% to 4% patients.

The mean age of the patients was 59.4 years. Compared to other studies,[26] 6, patients in the present study were younger. The incidence of hyponatremia in patients above 50 years (76%) and below 50 years (24%) when compared was found to be statistically significant (p <0.0001). Similar trend was observed by Hochman[27] and Vurgese[28] in their study and they had shown that elderly patients were more prone to hyponatremia.

Various factors lead to hyponatremia in the elderly patients like decreased glomerular filtration rate, impaired ability of kidney to conserve sodium, increased release of vasopressin and arginine to given osmotic stimulus and increased comorbidities leading to intake of various drugs causing hyponatremia e.g. diuretics, antidepressants.

In the present study, there were 54% males and 46% females with a ratio of 1.17:1, probably because there were more total male admissions (41/7040) compared to total female admissions (35/3527).

43% patients were euvolemic, 38% patients were hypervolemic and 19% patients were hypovolemic. Similar trend (euvolemic, hypervolemic and hypovolemic) was observed in most of the studies except in the study by Hochman[27] where hypovolemic hyponatremia was more common than hypervolemic.

Nausea and vomiting were the most common gastrointestinal symptoms present in 54% and 48% of patients respectively, similar to other studies.18, 20. Like other studies,[19,21] drowsiness was the most common neurological symptom (42%). Seizures were present in 9 (11%) patients. Higher number of patients with seizures in the present study was probably due to more underlying neurological problems e.g. seizure disorder (n=3), neurological infections (n=1), brain metastasis (n=2) and intracranial haemorrhage (n=2) together present in 90% of patients.

80% of patients had one or more co morbid condition, commonest being hypertension (51%) and diabetes mellitus (42%). Cause of hyponatremia in diabetes mellitus was probably due to hyperglycemia, which

induces fall in serum sodium levels by shifting water from intracellular to extracellular compartments, glucose being an osmotically active molecule. It has been calculated that serum sodium falls by 1.6 to 2.4 mmol/L for every 5 mmol/L rise in serum glucose levels.[29]

In the present study, among 39 hypertensive patients, 29 were on diuretics. Most of the studies on hyponatremia had not demonstrated direct correlation between hypertension and hyponatremia, although correlation of hyponatremia and diuretic use was evident.[30]

In 58 (76%) patients, multiple etiologies were present that caused hyponatremia, while in 18 (24%) patients, etiology was single. Many drugs especially diuretics (53%), antidepressants/antipsychotics (13%), anticonvulsants (8%) and chemotherapeutic agents (9%) have contributed to hyponatremia. They may induce hyponatremia by affecting either sodium and water homeostasis (diuretics), or the water homeostasis due to syndrome of inappropriate syndrome (SIADH) e.g. antidepressants, antiepileptics.[31,32] In the present study use of drugs was the most common aetiology of hyponatremia;

The diagnosis of Syndrome of Inappropriate Secretion of Antidiuretic hormone (SIADH) was suspected in nine patients. These features include inappropriately raised urine osmolality and natriuresis; Clayton et al[12] reported that the diagnosis of SIADH was often presumptive and practicing clinicians did not observe all stringent criteria required to make definitive diagnosis.

In our study the most common diagnosis in patients having possible SIADH was malignancy (45%).

The mortality in this study was 21%. All the patients suffered from serious primary illnesses. Other studies report mortality of 9 - 30%.[12, 15] There is no statistical difference between the serum sodium of those who survived and those who died. (p= 0.715); those who succumbed had severe sepsis, congestive heart failure and other conditions like malignancies, liver cirrhosis. Mortality was related more to the primary cause of illness. Our data support that hyponatremia appears to be marker of underlying disease which carries poor prognosis and association of hyponatremia with outcome was probably not directly related.[6,10,12,19,33]

In the present study mortality of patients with cardiac failure/shock was 33.3% which was comparable to the study done by Clayton et al[12] which was 29.6%, while Rawal JR et al[33] in their study of hyponatremia in heart failure patients, reported very high mortality rate (57.14%). The probable reason was that they studied mortality in patients with very low serum sodium concentration (Sr. Na< 105 mmol/L).

CONCLUSION

Hyponatremia is a common electrolyte abnormality in hospitalised patients. There is an increasing tendency for it to occur with increasing age, hypertension, diabetes mellitus and use of drugs (diuretics). Nausea, vomiting and drowsiness are the commonest symptoms. Mortality is high, though not directly related to serum sodium levels. Hyponatremia acts as a poor prognostic marker of primary disease.

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