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CLINICO-ETIOLOGICAL PROFILE OF HYPONATREMIA IN HOSPITALISED ADULT PATIENTS - A CROSS- SECTIONAL, OBSERVATIONAL STUDY

General Medicine

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ABSTRACT

Introduction: Hyponatremia is defined as a serum sodium level less than 135meq/L. An abnormal sodium level does not necessarily imply abnormal sodium balance, but can be due to abnormal water balance as well. Serum sodium levels and serum osmolality are normally maintained under precise control by homeostatic mechanisms involving thirst, anti-diuretic hormone and the renal handling of filtered sodium. Hyponatremia occurs in a broad spectrum of patients who are asymptomatic to critically ill patients. The clinical presentation has a wide spectrum, varying from asymptomatic patients to ones having seizures and coma.

Aim: To find out co-relation between grade of hyponatremia with hospital stay, mortality rate and to study whether the primary disease is a cause for hyponatremia and whether other features cause hyponatremia also.

Materials And Methods: A 1 year cross-sectional observational study was conducted, including 100 adult patients admitted in Vivekananda Institute of Medical Sciences, Kolkata with hyponatremia (serum sodium <135 mEq/L) in General Medicine ward and in Orthopedics ward (with fragility fracture).

Results: There was a wide range of etiologies, most common being SIADH (47%), renal disorder (13%), diuretic use (13%), congestive heart failure (8%), and liver disorder (4%). 16% patients had multiple causes. In 5% patients no cause could be found after extensive investigations. Mean duration of hospital stay was 7.04 days, which was significantly higher in patients with severe hyponatremia. Incidence of fragility fracture in our study was 16%.

Conclusion: SIADH was the single most important etiology of hyponatremia. Use of diuretics and chronic kidney disease were also significant cause of hyponatremia in this study. Other major causes of hyponatremia were CHF, acute gastroenteritis and chronic liver disease. A relatively large number of patients had endocrine abnormalities (thyroid, adrenal and pituitary).Hyponatremia was found to be related to multiple etiological factors in a significant number of patients. Neurological symptoms are common in hyponatremia patients. Symptoms of hyponatremia increased with severity of hyponatremia.

KEYWORDS

Hyponatremia, serum sodium, serum osmolality and seizures.

INTRODUCTION

Hyponatremia is defined as a serum sodium level less than 135meq/L. [1,2] An abnormal sodium level does not necessarily imply abnormal sodium balance, but can be due to abnormal water balance as well.

Serum sodium levels and serum osmolality are normally maintained under precise control by homeostatic mechanisms involving thirst, anti-diuretic hormone and the renal handling of filtered sodium. Hyponatremia occurs in a broad spectrum of patients who are asymptomatic to critically ill patients. The clinical presentation has a wide spectrum, varying from asymptomatic patients to ones having seizures and coma.[3]

Patients in whom the serum sodium concentration is greater than 130 meq/L are usually asymptomatic, whereas those in whom these values are lower may have symptoms. Clinical symptoms vary from individual to individual.

The clinical manifestations of hyponatremia are produced by brain swelling and are primarily a function of the rate of fall of serum sodium concentration and not the absolute level. Symptoms occurring early in hyponatremia is usually anorexia, nausea, vomiting. Some patients may have headache and irritability. As serum sodium levels falls further patients develop neuropsychiatry symptoms.

There is a lack of Indian data on clinical spectrum of hyponatremia in hospital setting and treatment strategies to be adapted in various clinical studies; therefore, we planned to undertake this prospective follow up study in hospitalized patients at our tertiary care centre.

I. To study the clinical profile of hospitalized patients with hyponatremia
II. To probe into the causes of hyponatremia
III. To find out co-relation between grade of hyponatremia with hospital stay, mortality rate
IV. To study whether the primary disease is a cause for hyponatremia and whether other features cause hyponatremia also.
V. To find out incidence of hyponatremia in patients with fragility fracture

MATERIALS AND METHODS

Study Population

Patients admitted in Vivekananda Institute of Medical Sciences, Kolkata with hyponatremia (serum sodium <135 mEq/L) in General Medicine ward and in Orthopedics ward (with fragility fracture).

Type And Duration Of Study

Cross sectional - observational study; period of one year (January 2019 to December 2019).

Inclusion Criteria

1. Patients admitted with hyponatremia (serum sodium <135 mEq/L) in General Medicine ward with age >18 years
2. Patients admitted with fragility fracture and hyponatremia in Orthopedics ward with age > 18 years.

Exclusion Criteria

1. Patients admitted with age <18 years
2. Post-operative patients

Table : Distribution Of Mean K And Serum Uric Acid

		Number	Mean	SD	Minimum	Maximum	Median	P value
K	In non SIADH patients	53	3.7906	0.6140	2.0000	5.2000	3.8000	0.0113
	In patients with SIADH	47	3.5340	0.3123	2.8000	4.3000	3.5000	
serum uric acid	In non SIADH patients	53	4.5683	0.8634	3.2000	7.2000	4.4500	<0.0001
	In patients with SIADH	47	3.2915	0.5290	1.5000	4.0000	3.4000	

Table : Distribution Of Mean Plasma Osmolarity (mOsm/kg H20), Urine Osmolarity (mOsm/kg H20) And Urine Spot Sodium (mmol/L)

	Number	Mean	SD	Minimum	Maximum	Median
Plasma Osmolarity (mOsm/kg H20)	100	264.5000	12.52000	223.8000	279.1000	269.4000
Urine Osmolarity (mOsm/kg H20)	100	334.0000	169.0000	96.0000	1000.0000	309.0000
Urine spot sodium (mmol/L)	100	58.0000	26.0000	10.0000	102.0000	62.0000

RESULT & DISCUSSION

Hyponatremia is the most common electrolyte disturbance seen in hospital practice. It is more common in the elderly patients with multiple medical comorbidities. [4,5]Hyponatremia has been associated with considerable morbidity and mortality in many chronic diseases, most notably in patients with chronic kidney disease, congestive heart failure and chronic liver disease. [6]Hyponatremia also leads to increased health care cost and the majority of these costs are attributable to the incremental resource utilization for patients who were not admitted specifically for hyponatremia, but whose hospitalization was prolonged due to hyponatremia.

This study had included 100 patients of hyponatremia admitted in general medical wards. In previous studies incidence of hyponatremia in hospitalized patients was found to be about 5.2 to 28.8%, with an average of about 25.98% for elderly patients experiencing this disorder. [7,8,9]In this study overall incidence of hyponatremia was 8.2%. Incidence of hyponatremia has been shown to have direct correlation with age. [10] In our study 44% of the patients were 61 to 75 yrs old and mean age was 62.52 years. In the study of Jain AK et al [7] and Thomas Vurgese et al, [11] commonest age group affected was 67–80 years (mean age 73.87 ± 6.54 years) and 45-64 years respectively. Multiple comorbidities like Hypertension and Diabetes Mellitus are present in this age group treatment of which predisposes a patient to hyponatremia. Use of diuretics is also more common among the elderly patients, which has been a major cause of hyponatremia in hospitalized patients. Hawkins et al noted that increasing age, after adjusting for sex, was independently associated with both hyponatremia at presentation and hospital-acquired hyponatremia. [10]

In the present study prevalence of hyponatremia was almost comparable in male and female patients with female and male ratio of 1.08:1 (52 females and 48 males). It is more or less corroborative with the study of Jain AK et al[7] (0.96:1) but not corroborative with other studies.

In our study 12% patients presented with chronic hyponatremia (>48 hours duration of persistent hyponatremia). There was difficulty in assessing the exact duration of hyponatremia as the data of serum sodium prior to the detection of hyponatremia was not available for most patients in this study. SIADH was responsible in 3 patients.

In our study 55% patients were euvolemic, while 25% were hyper and 20% were hypovolemic at presentation. This finding is also corroborative with the study of Babaliche P et al [12] and Chatterjee N et al [13]where euvolemic hyponatremia was 50% and 50.74% respectively. In our study 13 (13%) of the patients had hyponatremia due to renal disorders out of which 11 patients had pre-existing renal disease (chronic kidney disease), one patient had acute renal failure and one patient was diagnosed to have urinary bladder carcinoma. Total 4 (4%) patients had liver disorder (4 patients with pre-existing chronic liver disease and 2 of them developed hepatic encephalopathy) and another 8 (8%) patients had hyponatremia due to heart failure. Thus 23 (23%) of the patients in our study had pre-existing renal disorder, heart failure or chronic liver disease. Sixteen out of these 23 patients were admitted to the hospital due to non-compliance with treatment and inappropriate fluid intake leading to volume expansion and dilutional hyponatremia. In majority of these patients loop diuretics and fluid restriction was sufficient to correct hyponatremia. In study by Saeed et al, 37 % of the patients had hyponatremia due to these disorders (renal disorders 21%, liver disorders 7% and CHF 9%).[14,15]

Nineteen percent patients in our study had pre-existing hypothyroidism. 3 (3%) patients had hyponatremia due to hypothyroid state. In study by Clayton et al hypothyroidism induced hyponatremia occurred in 3.7%. [16]

Forty seven (47%) patients in present study fulfilled the diagnostic criteria for SIADH. The incidence is comparable to the available literature on hyponatremia in hospitalized patients. In study of Babaliche P et al [12] , Jain AK et al [7] and Chatterjee N et al [13] SIADH was responsible for 46%, 36% and 33% respectively.

In our study 3 patients had drug induced SIADH (all due to selective serotonin reuptake inhibitors) 17 patients had SIADH due to pulmonary disease (6 cases of pneumonia, 3 lung abscess, 4 bronchogenic carcinoma and 4 tuberculosis), 18 patients had primary neurological disorders (12 cases of cerebrovascular accident, 4 cases of meningitis, 1 case of chronic subdural haematoma and 1 case of Guillain Barre Syndrome), 2 patient had abdominal Koch's, 1 patient had carcinoma pancreas and 1 had bladder carcinoma. In 5 cases diagnostic criteria for SIADH was fulfilled but cause couldn't be determined even after extensive investigations like CT Thorax, Abdomen etc. Those patients after correction of serum sodium and clinical improvement, were asked to come OPD on regular basis to search for any occult pathology.

Clayton et al had concluded in their study that selective serotonin reuptake inhibitors (SSRIs) were a frequent cause of drug induced hyponatremia. [16] They had 12 (11.1%) patients out of 108 who were taking SSRI while in our study only 3 patients had hyponatremia associated with SSRI use. This is possibly because SSRIs are not usually prescribed for the patients in general medical wards.

Other causes of hyponatremia in this study included Addison's disease (2 cases), Sheehan Syndrome (1 case), diabetic ketoacidosis (1 case), extra-renal losses like acute gastroenteritis (5 cases), Psychogenic polydipsia (2 cases). In the study of Chatterjee N et al[13] cause of hyponatremia due to GI fluid loss was 19.5%. That is not in our case because acute gastroenteritis patients are usually not admitted in our hospital, they are referred to nearby infectious disease hospital.

40 patients in this study had severe hyponatremia. Cerebrovascular accident was the most common etiology associated with severe hyponatremia in 7 patients. Other causes were: chronic kidney disease (5%), thiazide diuretics (4%), pneumonia (3%), meningitis (2%), acute gastroenteritis (2%), chronic liver disease (2%), lung abscess (2%), lung carcinoma(2%), pulmonary tuberculosis (2%), Addison's disease (1%), carcinoma pancreas (1%), chronic diarrhoea (1%), diabetic ketoacidosis (1%), primary hypothyroidism (1%), Sheehan syndrome (1%), SSRI drug (1%), psychogenic polydipsia (1%) and no cause could be identified in 1 case. In study by Clayton et al on severe hyponatremia in a hospitalized patients 25 out of 105 patients had single etiology for severe hyponatremia which included thiazide diuretics in 11 patients, liver disease in 4 patients, CNS lesion/stroke in 2 patients, hypopituitarism/Addison's disease in 2 patients, lower respiratory tract infection in 1 patient, carbamazepine in 1 patient and unknown cause in another 4 patients. [16]

Distribution of serum potassium among SIADH and non-SIADH was statistically significant in our study (p value 0.0113). In non SIADH mean serum potassium was 3.79 while in patients with SIADH it was 3.534. Hypokalemia is rare in SIADH. Serum potassium concentration generally remains unchanged. Changes in potassium balance are rarely mentioned although a reduced total exchangeable potassium was noted in the earliest reported cases (Schwartz et al., 1957) [17]. Movement of potassium from the intracellular space to the extracellular space prevents dilutional hypokalemia.

Serum uric acid was low in patients with SIADH. In our study mean serum uric acid in patients with SIADH was 3.29, while it was 4.56 in patients without SIADH (p value<0.0001). Passamonte PM in their study showed that six of eight patients with SIADH (due to small cell lung CA) had hypouricemia. The coexistence of hypouricemia and hyponatremia predicted SIADH reliably (6/6 patients). [18]

The overall mortality in patients with hyponatremia in the study of Chatterjee N et al [13], Chua M et al [19] and Huda et al [20] were 13.5%, 8% and 27% respectively. However mortality among these patients was not directly related to hyponatremia but to other concomitant severe

comorbidity. Mortality in our study was low. Only 2 patients died. Both had severe hyponatremia. 1 patient had chronic diarrhoea and 1 had chronic liver disease with hepatic encephalopathy. So, we could not analyse category wise mortality in mild, moderate or severe hyponatremia. Papadakis et al had found that hyponatremia is an independent risk factor for mortality in patients with cirrhosis. [21]

In our study incidence of fragility fracture was 16% (considering 5 patients had hyponatremia among 31 patients admitted with fragility fracture). Cumming K, Hoyle GE, Hutchison JD, et al. [22] in their study showed that hyponatremia is highly prevalent in elderly patient with fragility fracture, seen in 26% of cases (Point prevalence of hyponatremia on admission was 13.4% and a further 12.6% developed hyponatremia during admission). In our study mostly serum sodium level at the time of admission was taken. That's why incidence was less. One thing needs to be mentioned that though we found the association with hyponatremia, we didn't elaborate all causes of fragility fracture.

In our study mean duration of hospital stay in moderate hyponatremia was 6.03 days, while it was 7.26 days for severe hyponatremia. Chua M et al. [19] in their study on prognostic implications of hyponatremia in elderly patients found that median length of hospital stay was 13 days. In the study of Rubio Rivas H et al. [23] on hyponatremia in elderly patients in an acute geriatric care unit and assessed its prevalence and prognosis. Mean hospital length of stay was 12.8 days. Duration in these studies were higher because these studies were only on elderly patients.

CONCLUSION

Hyponatremia is a common electrolyte abnormality found in hospitalized patients in general medical and surgical wards. It is more common in elderly patients and critically ill patients. Hypertension and Diabetes Mellitus as pre-existing comorbidity was present in majority of patients and it predisposed the patients to hyponatremia.

SIADH was the single most important etiology of hyponatremia. Use of diuretics and chronic kidney disease were also significant cause of hyponatremia in this study. Other major causes of hyponatremia were CHF, acute gastroenteritis and chronic liver disease. A relatively large number of patients had endocrine abnormalities (thyroid, adrenal and pituitary).Hyponatremia was found to be related to multiple etiological factors in a significant number of patients. Neurological symptoms are common in hyponatremia patients. Symptoms of hyponatremia increased with severity of hyponatremia.

Treatment of hyponatremia with hypertonic saline should be restricted to the patients with severe hyponatremia, patients with rapid decline in serum sodium (in significant amount) and those with neurological symptoms of hyponatremia.

A systematic approach to the diagnosis of hyponatremia with the application of simple diagnostic algorithms, using history, clinical examination and laboratory findings to establish mechanism of hyponatremia can significantly improve the assessment and management of hyponatremia.

REFERENCES

1. Janicic N, Verbalis JG. Evaluation and management of hypoosmolality in hospitalized patients. Endocrinol Metab Clin North Am 2003;32:459–481.
2. Schrier R. The patient with hyponatremia or hypernatremia. In: Schrier RW, ed. Manual of Nephrology. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2000:21–36.
3. Laczi F. Etiology, diagnostics, and therapy of hyponatremias. Orv Hetil. 2008;149:1347–54.
4. Berl T. An elderly patient with chronic hyponatremia. *Clin J Am Soc Nephrol*. 2013;8(3):469-475.
5. Filippatos TD, Makri A, Elisaf MS, Liamis G. Hyponatremia in the elderly: challenges and solutions. Clinical Interventions in Aging. 2017 ;12:1957-1965.
6. Corona G, Giuliani C, Parenti G, et al. Moderate hyponatremia is associated with increased risk of mortality: evidence from a meta-analysis. *PLoS One*. 2013;8(12):e80451. Published 2013 Dec 18.
7. Jain AK and Nandy P. Clinico-etiological profile of hyponatremia among elderly age group patients in a tertiary care hospital in Sikkim. J Family Med Prim Care 2019;8:988-94.
8. Pillai KS, Trivedi TH, Moulick ND. Hyponatremia in ICU. J Assoc Physicians India 2018;66:48-52.
9. Nair S, Mary TR, Tarey SD, Daniel SP, Austine J. Prevalence of hyponatremia in palliative care patients. Indian J Palliat Care 2016;22:33-7.
10. Hawkins RC. Age and gender as risk factors for hyponatremia and hypernatremia. Clin Chim Acta. 2003;337:169 –172.
11. Vurgese TA, Radhakrishan SB, Mapkar OA. Frequency and etiology of hyponatremia in adult hospitalized patients in medical wards of a general hospital in Kuwait. Kuwait Med J. 2006;38:211–3.
12. Babaliche P, Madnani S, Kamat S. Clinical Profile of Patients Admitted with Hyponatremia in the Medical Intensive Care Unit. *Indian J Crit Care Med*. 2017;21(12):819-824. doi:10.4103/ijccm.IJCCM_257_17
13. Chatterjee N, Sengupta N, Das C, Chowdhuri AR, Basu AK, Pal SK. A descriptive study of hyponatremia in a tertiary care hospital of Eastern India. *Indian J Endocrinol Metab*. 2012;16(2):288-291.
14. Ali K, Workicho A, Gudina EK. Hyponatremia in patients hospitalized with heart failure: a condition often overlooked in low-income settings. *Int J Gen Med*. 2016;9:267-273. Published 2016 Aug 1.
15. Saeed B O, Beaumont D, Handley G H, Weaver J U. Severe hyponatremia: investigation and management in a district general hospital.J Clin Pathol 2002;55:893–896
16. Clayton J.A., le Jeune I.R. and Hall I.P. Severe hyponatraemia in medical in patients:aetiology, assessment and outcome. Q J Med 2006; 99:505–511
17. SCHWARTZ, W.B., BENNETT, W., CURELOP, S. & BARTTER, F.C. (1957) A syndrome of renal sodium loss and hypernatremia probably resulting from inappropriate secretion of antidiuretic hormone. American Journal of Medicine, 23, 529.
18. Passamonte PM. Hypouricemia, Inappropriate Secretion of Antidiuretic Hormone, and Small Cell Carcinoma of the Lung. *Arch Intern Med.* 1984;144(8):1569–1570.
19. Chua M, Hoyle GE, Soiza RL. Prognostic implications of hyponatremia in elderly hospitalized patients. Arch Gerontol Geriatr. 2007 Nov-Dec;45(3):253-8.
20. Huda M S B, Boyd A, Skagen K, Wile D, Heyningen C van, Watson I, Wong S, Gill G Investigation and management of severe hyponatraemia in a hospital setting Postgrad Med J 2006;82:216–219.
21. Papadakis MA, Fraser CL, Arieff AI. Hyponatraemia in patients with cirrhosis. Q J Med 1990; 76:675–88.
22. Cumming K, Hoyle GE, Hutchison JD, et al. Prevalence, incidence and etiology of hyponatremia in elderly patients with fragility fractures. PLoS One. 2014;9:e88272.
23. Rubio-Rivas M, Formiga F, Cuerpo S, Franco J, di Yacovo S, Martínez C, Pujol R. Hyponatremia in elderly patients admitted in an acute geriatric care unit prevalence and prognosis. Med Clin (Barc). 2012 Jun 30;139(3):93-7.