ORIGINAL ARTICLE

Hyponatraemia: Epidemiology and aetiology in a tertiary care centre in Pakistan

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Abstract

Objective: To determine the incidence, aetiology and epidemiology of hospitalized patients with hyponatraemia.

Methods: Subjects were identified through hospital information system for two consecutive low sodium values (< 130 mEq/L) and charts were reviewed retrospectively. Possible etiologic factors were identified and co-morbidities documented. Management plans were also noted.

Results: Among the hospitalized patients the incidence of hyponatraemia was 6.72%. The mean age was 54.8±14.8 years and there were 50% males. The mean serum sodium at presentation was 122 mEq/L. Most common causes were volume depletion (30.6%) and chronic kidney disease (22.6%). Most of the patients had two or more co morbidities. Hyponatraemia at presentation and improvement or worsening during hospital stay did not affect survival of patients.

Conclusions: Hypervolaemic hyponatraemia was the most common presentation in our study.

Keywords: Hyponatremia, Serum Sodium concentration, Hypovolemic Hyponatremia, SIADH, Hypervolemic Hyponatremia. (JPMA 66: 1436; 2016)

Introduction

Hyponatraemia (serum sodium < 135 mEq/L) is a common electrolyte imbalance, observed in hospitalized patients.[1] It usually results from disturbance in water homoeostasis[2] and is classically divided into: hypervolaemic, euvolaemic and hypovolaemic hyponatraemia.[3] The aetiology of hyponatraemia therefore includes diverse conditions such as cardiac, hepatic, renal, metabolic and medications, besides others.[4]

Mortality rate increases with severity of hyponatraemia ≤130 mEq/L and is therefore a predictor and an independent factor for mortality.[5-10]

We therefore performed a cross sectional study to evaluate the etiology of hyponatraemia in patients hospitalized in a tertiary care setup.

Patients and Methods

This was a retrospective study. With the help of Medical Information System department at our hospital all patients aged 18 years and above admitted from January 1st to April 30th, 2015 (4 months) were included for evaluation. Total of 2248 patients were admitted in the hospital during this time period, out of which 922 patients were admitted under Medicine Service. The inclusion criterion of our study was the presence of hyponatraemia (serum sodium level < 130 mEq/L on at least two consecutive readings). All patients with pseudohyponatraemia secondary to hyperglycaemia, hyperlipidaemia and paraproteinaemia were excluded. Basic demographic data including age, gender, co-morbidities and physical examination details were noted from patient medical records. Aetiology of hyponatraemia was defined as a disease or condition directly responsible for the current episode of hyponatraemia based on estimation of volume status of patient determined by bedside clinical examination for presence or absence of peripheral oedema, jugular venous pressures (JVP), pulmonary rales, postural hypotension, decrease skin turgor and dry mucous membranes thus dividing the whole cohort into three classes: hypervolaemic, euvolaemic and hypovolaemic hyponatraemia. The data review also included input/output fluid balance records and management done (fluid restriction, fluid resuscitation or diuretic use) during the hospital course. Final outcome (death or discharge) was also noted. Co-morbidities were also noted and were defined as presence of coexisting disease or condition not thought to be directly responsible for the current episode of hyponatraemia.

All serial biochemical markers were taken from computerized laboratory records till discharge or death. Serum sodium levels were noted on admission, every 24 hours (where available) and the last value before discharge. Serum creatinine, potassium, uric acid, blood glucose, albumin, serum osmolarity, urine osmolarity, urinary electrolytes, thyroid function tests, cortisol and lipid profile were noted wherever available.

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All the available data was analysed by PSPP online version.[11] Ranges and percentages were calculated for gender, serum sodium at presentation, clinical volume status at presentation, co-morbidities and aetiology of hyponatraemia. Means and standard deviation were calculated for age and serum sodium at presentation and discharge.

Results

Over the study period, 922 patients were admitted under Department of Medicine out of which, 62 (6.72%) patients met the inclusion criteria of our study. Basic demographic data along with clinical diagnoses is presented in Table-1.

Mean serum sodium in our cohort at presentation was 122±6.021 mEq/L (Range: 102 - 129) and at discharge was 127±4.684 mEq/L (Range: 104 - 135). Majority of patients (N=43, 69.4%) were symptomatic ranging from headache, nausea, vomiting, hiccoughs and irritability to acute confusional state. The mean serum sodium was lower (mean: 120.04±6.83 mEq/L vs 123.6±4.9 mEq/L) in the age group of more than 60 years. Distribution of serum sodium levels and volume status revealed hypervolaemia as the major clinical presentation at all levels of severity of hyponatraemia (Table-2).

The underlying causes of hypervolaemia were mainly cardiac, renal or hepatic diseases (Table-3).

Table-1: Patient demographics.

Total Patients	922
Patients with Serum Sodium < 130 mEq/L	62(6.72%)
Mean Age (years)	54.8±14.8 (Range 19-81 years)
Age Distribution	
18 - 40 years	43.6%
40 - 60 years	38.7%
>60 years	17.7%
Gender Distribution	31(50%) Males, 31 (50%) Females. Ratio 1:1.
Admitted to ICU	31 (50%)
Volume Status	N (%)
Hypovolaemia	21(33.9)
Euvolemia	9(14.5)
Hypervolaemia	32(51.6)
Clinical Diagnoses	N (%)
Chronic Kidney Disease	14 (22.6)
Chronic Liver Disease	9 (14.5)
Gastrointestinal Fluid Loss	12 (19.3)
Sepsis	4 (6.4)
Decreased Intake.	3 (4.8)
Acute Kidney Injury	7 (11.3)
SIADH*	5 (8.1)
Cardiorenal Syndrome	6 (9.7)
Medications	1 (1.6)
Salt Losing Nephropathy	1 (1.6)

*Syndrome of Inappropriate Antidiuretic Hormone Secretion.

Table-2: Serum sodium distribution and volume status.

Sodium Range (mEq/L)	N (%)	Volume Status N. (%)
126-130	30 (48.4)	Hypervolaemic 14. (46.6%) Euvolaemic 4. (13.3%) Hypovolaemic 12. (40%)
116-125	22 (35.5)	Hypervolaemic 13. (43.3%) Euvolaemic 2. (6.66%) Hypovolaemic 7. (23.3%)
?115	10 (16.1)	Hypervolaemic 5. (16.6%) Euvolaemic 3. (10%) Hypovolaemic 2. (6.66%)

Table-3: Underlying Major Disease contributing to Hyponatraemia.

Aetiology.	N (%)	Volume Status
Gastrointestinal Loss.	12(19.3)	Hypovolaemic: 12.
Sepsis	4(6.4)	Hypovolaemic: 3, Euvolaemic: 1
Decreased Intake	3(4.8)	Hypovolaemic: 2, Euvolaemic: 1
Chronic Kidney Disease	14(22.6)	Hypervoalemic: 13. Euvolaemic: 1
Chronic Liver Disease	9(14.5)	Hypervolaemic: 8, Hypovolaemic: 1
Acute Kidney Injury	7(11.3)	Hypervolaemic: 5 Hypovolaemic: 2
Congestive Heart Failure	6(9.7)	Hypervolaemic: 6
Syndrome of Inappropriate ADH Secretion	5 (8.1)	Euvolaemic: 4 Hypovolaemic: 1
Drugs	1(1.6)	Euvolaemic: 1
Salt Loosing Nephropathy	1(1.6)	Euvolaemic: 1

Being a tertiary care hospital most of our patients had multiple co-morbidities present that were not directly contributing to hyponatraemia including hypertension (n=48, 77.4%) and diabetes (n=38, 61.3%) as the common co-morbidities present in our cohort. Majority of the patients had three or more co-morbidities (n=35, 56.5%). Record charts were reviewed for current or recent medications with hyponatraemia as a documented side effect. Angiotensin receptor blockers (ARB) or angiotensin converting enzyme inhibitors (ACE-I) were being used by 10 (16.1%) and SSRIs by 5(8.1%). None of the medicines were implicated as a direct cause except in one case of thiazide diuretic use. The management of patients was dependent upon symptoms and volume status at presentation. Fluid restriction (n=39, 62.9%) with or without loop diuretics (n=34, 55%) were used in majority of patients whereas intravenous fluids mainly isotonic saline was used for volume depleted patients (n=23, 37.1%).Serum sodium level improved in 41 patients (66.1%), while 13 patients (21.0 %) showed partial

improvement. In 8 patients (12.9%) sodium level either did not improve or worsened at the time of discharge or death. Nine (14.5%) patients (mean serum sodium 120.22±4.79, range: 112 - 127) died during the hospitalization. Five (55.5%) of these patients were volume depleted at presentation whereas the other diagnoses were CKD (n=2), CLD (n=1) and acute kidney injury (AKI) (n=1) all with hypervolaemic hyponatraemia. Among these nine patients, 4 patients had improved serum sodium by the time of death, 3 had partially improved whereas 2 failed to improve or got worse prior to death.

Discussion

In our cross sectional study, the frequency of moderate to severe hyponatraemia in patients admitted in medicine wards was 6.7% which was comparable to Al Barqawi et al (6%)[12] but lessthan Chatterjee et al (16%)[13] and Kumar et al (44%).[14] The latter study from Pakistan was a smaller study over a shorter period of time (2 months) and probably over estimates the prevalence of hyponatraemia. Furthermore, their cutoff value of 135 is much higher than ours (130 mEq/L). It was not clear in their study that how many of 72 (85% of total cohort with serum sodium of 128 to 135 mmol/L) patients had actually serum sodium less than 130 mmol/L. Hyponatraemia was evenly distributed among males and females whereas the severity of hyponatraemia increased with increasing age and is similar to the previous studies.[5] Physiological decrease in renal reserve and higher prevalence of chronic ailments and poly-pharmacy in the elderly are the likely causes of this observation.[15]

Volume status is very important in judging the cause of hyponatraemia and euvolaemic hyponatraemia is a common presentation.[16,17] The most common presentation of hyponatraemia (at all levels of serum sodium) in our study was volume overload. (Table-2, 3) It may be a center bias as we have a significant referral for renal and hepatic diseases, nevertheless, physical examination alone for judging fluid status is also fraught with inaccuracies (especially in critically ill patients).[18] Advanced techniques e.g. inferior vena cava diameter measured by ultrasound Doppler,[19] and Bio-impedance analysis (BIS)[20] have been recommended as a means to supplement or replace physical examination. CKD, AKI and CLD cause hyponatraemia by free water retention due to complex neuro-hormonal compensatory mechanism[17] and loss of renal function. In 10% of the patients, cardio-renal syndrome was the cause of hyponatraemia presenting with worsening renal function in face of increasing circulatory congestion and responded well to diuresis.

As one would expect the most common etiology of hyponatraemia in volume depleted patients in our study was gastrointestinal loss (65%) whereas sepsis and decreased intake accounted for the rest. Five cases (8.1%) were diagnosed to have SIADH (malignancy n=2, chest infection n=2, CVA n=1) one of these patients had also underlying hypovolaemia (Table-3).

Yawar A et al[16] in their study of 200 patients from a tertiary care hospital in Pakistan have mentioned euvolemic hyponatraemia as the most common presentation possibly because of the high frequency of medication induced hyponatraemia in their study. Many of our patients were on medications that could have caused hyponatraemia (ARBs/ACE-I, SSRIs) however we, in contrast to Yawar et al found no direct causal role other than a single patient taking hydrochlothiazide usually implicated in hyponatraemia.[4,21]

Nine (14.5%) patients (mean age: 61.77±16.00, range: 31 - 76 years; mean serum sodium 120.22±4.79, range: 112 - 127) died during the same hospitalization. This is in agreement with previous studies (6.7-51%). Studies suggest that there is significant increase in mortality even with mild to moderate hyponatraemia in hospitalized patients[6,7,22] however our study population was not strong enough to attribute any causative role of hyponatraemia to mortality. Still, our study does show important clinical presentations observed with hyponatraemia in a tertiary care centre.

Conclusions

Our retrospective study shows hypervolaemia with underlying CKD and CLD are the commonest presentations of hyponatraemia. Since only two other studies exist from Pakistan on this subject, we suggest that a large multicentre study is needed to highlight the true prevalence of hyponatraemia and its effect on mortality.

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Conflict of Interest: None.

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