Hyponatraemia: Epidemiology and aetiology in a tertiary care centre in Pakistan
Nauman Tarif, Omer Sabir, Azra Niaz, Rizwan Akhtar, Kashif Rafique, Nabiha Rizvi

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 or 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.

Introduction
Hyponatraemia (serum sodium < 135 mEq/L) is a common electrolyte imbalance, observed in hospitalized patients. It usually results from disturbance in water homeostasis and is classically divided into: hypervolaemic, euvoaemic and hypovolaemic hyponatraemia. The aetiology of hyponatraemia therefore includes diverse conditions such as cardiac, hepatic, renal, metabolic and medications, besides others. Mortality rate increases with severity of hyponatraemia <130 mEq/L and is therefore a predictor and an independent factor for mortality.

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, euvoaemic 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. 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±6.83mEq/L vs 123.6±4.9mEq/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.**

<table>
<thead>
<tr>
<th>Total Patients</th>
<th>922</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with Serum Sodium &lt; 130 mEq/L</td>
<td>62(6.72%)</td>
</tr>
<tr>
<td>Mean Age (years)</td>
<td>54.8±14.8 (Range: 19-81 years)</td>
</tr>
</tbody>
</table>

**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**

- Hypovolaemia: 21(33.9)
- Euvolemia: 9(14.5)
- Hypervolaemia: 32(51.6)

**Clinical Diagnoses**

<table>
<thead>
<tr>
<th>N (%)</th>
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<tbody>
<tr>
<td>Chronic Kidney Disease: 14 (22.6)</td>
</tr>
<tr>
<td>Chronic Liver Disease: 9 (14.5)</td>
</tr>
<tr>
<td>Gastrointestinal Fluid Loss: 12 (19.3)</td>
</tr>
<tr>
<td>Sepsis: 4 (6.4)</td>
</tr>
<tr>
<td>Decreased Intake: 3 (4.8)</td>
</tr>
<tr>
<td>Acute Kidney Injury: 7 (11.3)</td>
</tr>
<tr>
<td>SIADH*: 5 (8.1)</td>
</tr>
<tr>
<td>Cardiorenal Syndrome: 6 (9.7)</td>
</tr>
<tr>
<td>Medications: 1 (1.6)</td>
</tr>
<tr>
<td>Salt Losing Nephropathy: 1 (1.6)</td>
</tr>
</tbody>
</table>

**Aetiology.**

<table>
<thead>
<tr>
<th>N (%)</th>
<th>Volume Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal Loss: 12(19.3)</td>
<td>Hypovolaemic: 12</td>
</tr>
<tr>
<td>Sepsis: 4(6.4)</td>
<td>Hypovolaemic: 3, Euvolaemic: 1</td>
</tr>
<tr>
<td>Decreased Intake: 3(4.8)</td>
<td>Hypovolaemic: 2, Euvolaemic: 1</td>
</tr>
<tr>
<td>Chronic Kidney Disease: 14(22.6)</td>
<td>Hypovolaemic: 13, Euvolaemic: 1</td>
</tr>
<tr>
<td>Chronic Liver Disease: 9(14.5)</td>
<td>Hypovolaemic: 8, Euvolaemic: 1</td>
</tr>
<tr>
<td>Acute Kidney Injury: 7(11.3)</td>
<td>Hypovolaemic: 5</td>
</tr>
<tr>
<td>Congestive Heart Failure: 6(9.7)</td>
<td>Hypovolaemic: 6</td>
</tr>
<tr>
<td>Syndrome of Inappropriate ADH Secretion: 5 (8.1)</td>
<td>Euvolaemic: 4</td>
</tr>
<tr>
<td>Drugs: 1(1.6)</td>
<td>Euvolaemic: 1</td>
</tr>
<tr>
<td>Salt Losing Nephropathy: 1(1.6)</td>
<td>Euvolaemic: 1</td>
</tr>
</tbody>
</table>

*Syndrome of Inappropriate Antidiuretic Hormone Secretion.
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%) but less than Chatterjee et al (16%) and Kumar et al (44%). 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 cut-off 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. Physiological decrease in renal reserve and higher prevalence of chronic ailments and poly-pharmacy in the elderly are the likely causes of this observation.

Volume status is very important in judging the cause of hyponatraemia and euvolaemic hyponatraemia is a common presentation. 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). Advanced techniques e.g. inferior vena cava diameter measured by ultrasound Doppler, and Bio-impedance analysis (BIS) 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 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).

**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.

**Disclaimer:** None.

**Conflict of Interest:** None.

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**References**

5. Mohan S, Gu S, Parikh A, Radhakrishnan J. Prevalence of hyponatremia and association with mortality: Results from


