A comparative study of the clinico-aetiological profile of hyponatremia at presentation with that developing in the hospital

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Background & objectives: Hyponatremia is a common problem encountered in patients presenting with nonspecific symptoms. We undertook this study to investigate the clinical profile of patients with hyponatremia, the precipitating factors, the response to therapy and to compare, using these parameters, hyponatremia at presentation to that developing in the hospital.

Methods: Seventy consecutive patients with serum sodium less than or equal to 125 mmol/l at presentation or at any time during hospital admission were identified and studied using a proforma. The severity of hyponatremia, therapy given and time taken for recovery were analysed.

Results: The mean age of patients was 48.1 ± 16.1 yr. The mean serum sodium was 117.8 ± 6.4 mmol/l. Confusion, headache and malaise were the most common symptoms, two patients had seizures, and 20.0 per cent patients showed no clinical manifestations. Nausea was significantly (P<0.05) more common in patients presenting with hyponatremia. 22 patients (31.4%) developed hyponatremia during their stay in the hospital. 3 patients (4.3%) presented with hyponatremia which got worse during the admission period. Most had multiple precipitating factors, decreased intake being the most common (82.9%), followed by increased losses (65.7%) and miscellaneous factors (70.0%). Drugs, fluid overload and inappropriate Ryle's tube feeds more commonly precipitated hyponatremia in in-hospital patients. Time taken for recovery showed negative correlation with the serum sodium. Patients with in-hospital hyponatremia took significantly longer time to recover (P<0.05).

Interpretation & conclusions: Decreased intake was found to be the commonest cause of hyponatremia, thus, ensuring adequate oral intake, especially in patients on liquid diet and in manual labourers, and correction of hyponatremia as soon as an abnormality is detected is important.

Key words Hyponatremia - in-hospital - serum sodium

Hyponatremia is the most common electrolyte disturbance encountered in clinical practice. Dilutional hyponatremia, diuretics, and prolonged exertion are common causes of hyponatremia. Hyponatremia frequently develops in hospitalized patients, including patients in the pediatric and
elderly\textsuperscript{8} age group. Symptomatology depends more on the rate of development of the electrolyte abnormality than on its severity\textsuperscript{1}. The optimal treatment of hypotonic hyponatremia requires balancing the risks of hypotonicity against those of therapy\textsuperscript{9}.

It was observed that many patients with hyponatremia had been advised low salt intake by the treating physician as a part of the treatment for hypertension or even diabetes, or were on liquid feeds. This preliminary study was planned to investigate the clinical profile, precipitating factors and response to therapy in patients with hyponatremia, and to compare hyponatremia developing after admission in hospital with that at presentation.

\textbf{Material & Methods}

\textit{Inclusion & exclusion criteria:} All patients over 18 years of age with serum sodium less than or equal to 125 mmol/l at admission or at any point during their stay in the Medicine in-patients department, Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER), Puducherry, were included after obtaining an informed written consent. Patients in whom repeat sodium estimation was above 125 mmol/l, were excluded.

The study was conducted over a two month period during April - May, 2007. The study protocol was approved by the Institute Ethics Committee. In 70 consecutive patients satisfying the inclusion criteria, a detailed history was elicited and examination done as per a proforma with emphasis on the aetiological factors, symptoms and signs of hyponatremia. Serum sodium was measured using potentiometric method (with an ion sensitive electrode), in the department of Biochemistry, JIPMER, regularly till it returned to normal. The sodium deficit was calculated using the formula: Deficit = (Normal sodium level – Measured sodium level)/ Total body water. Therapy with salt added diet, normal saline and hypertonic saline was started singly or in combination based on the severity of the patient’s condition, taking care that no more than 1500 meq of sodium was given in a single day. Fluid restriction was started if the patient had fluid overload. Patients’ details were analysed and judgment made regarding the possible precipitating factor(s) for his/her condition. The patients were retrospectively divided into two groups.

\textbf{Group A} - (45 patients): Patients who presented with hyponatremia to the hospital.

\textbf{Group B} - (25 patients): Patients who either developed hyponatremia for the first time in the hospital or whose sodium levels fell further after admission.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|}
\hline
\textbf{Characteristic & clinical features} & \textbf{Overall (n=70) no. (%)} & \textbf{Group A (n= 45) no. (%)} & \textbf{Group B (n=25) no. (%)} & \textbf{Patients with diabetes (n=19) no. (%)} & \textbf{Non-diabetic patients (n=51) no. (%)} \\
\hline
\textbf{Age (yr) Mean ± SD} & 48.1 ± 16.1 & 50.8 ± 14.8 & 43.1 ± 17.5 & 56.3±13.3\textsuperscript{a} & 45.0 ± 16.2 \\
\textbf{Sr. Sodium (meq) Mean ± SD} & 117.8 ± 6.4 & 118.0 ± 6.8 & 117.8 ± 6.2 & 117.5 ± 6.4 & 118.1 ± 6.1 \\
\textbf{No. of diabetics} & 19 (27.1) & 17 (37.8) & 2 (8.0)\textsuperscript{a} & 10 (52.6) & 9 (17.6) \\
\textbf{Nausea} & 21 (30.0) & 16 (35.6) & 5 (20.0)\textsuperscript{a} & 8 (42.1) & 13 (25.5) \\
\textbf{Malaise} & 27 (38.6) & 17 (37.8) & 10 (40.0) & 9 (47.3) & 18 (35.3) \\
\textbf{Headache} & 28 (40.0) & 14 (31.1) & 14 (56.0) & 7 (36.8) & 21 (41.2) \\
\textbf{Lethargy} & 21 (30.0) & 11 (24.4) & 10 (40.0) & 7 (36.8) & 14 (27.5) \\
\textbf{Confusion} & 29 (41.4) & 18 (40.0) & 11 (44.0) & 9 (47.3) & 20 (39.2) \\
\textbf{Seizures} & 2 (2.9) & 2 (4.4) & 0\textsuperscript{a} & 2 (10.5) & 0 (0) \\
\textbf{Altered sensorium} & 12 (17.1) & 10 (22.2) & 2 (8.0) & 1 (5.3) & 11 (21.6) \\
\textbf{Flap} & 5 (7.1) & 3 (6.7) & 2 (8.0) & 0 (0) & 5 (9.8) \\
\textbf{Asymptomatic} & 14 (20.0) & 10 (22.2) & 4 (16.0) & 4 (21.1) & 10 (19.6) \\
\hline
\textsuperscript{a}The difference between groups A and B is statistically significant (P<0.05); \textsuperscript{a}P could not be calculated; \textsuperscript{a}P=0.01 compared to non-diabetic patients. Many patients had more than one clinical feature. Data values rounded off to one place after decimal.
\end{tabular}
\caption{Comparison of demographic and clinical profile between the two groups}
\end{table}
The collected data were analyzed using SPSS 13.0. (SPSS, SPSS Inc., Chicago, IL, USA). Two-tailed unpaired t test, Mann-Whitney test and the chi square test were used for data analysis. \(P<0.05\) was considered significant.

Results

The mean age of patients was 48.1 ± 16.1 yr (15-82 yr) with no significant difference between the two groups. The mean serum sodium was 117.8 ± 6.4 mmol/l, and did not differ significantly between the two groups (Table I).

Confusion (41.4%), headache (40.0%), malaise (38.6%), lethargy and nausea (30.0% each) were the most common features seen in the patients, followed by altered sensorium (17.1%), flap (7.1%, all alcoholics) and seizures (2.9%); 20.0 per cent patients did not have any symptom or sign. Alteration in sensorium was more common in alcoholics (6 out of 13). The clinical profile was similar in group A and B patients (Table I) except nausea which was more common in Group A patients (\(P<0.05\)).

Reduced salt intake was found to be the most important precipitating factor for hyponatremia followed by gastrointestinal and renal losses (Table II).

<table>
<thead>
<tr>
<th>Precipitating factor</th>
<th>Number of patients</th>
<th>Patients with diabetes (n=19)</th>
<th>Non-diabetic patients (n=51)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall (n=70)</td>
<td>Group A (n=45)</td>
<td>Group B (n=25)</td>
</tr>
<tr>
<td></td>
<td>no. (%)</td>
<td>no. (%)</td>
<td>no. (%)</td>
</tr>
<tr>
<td>Decreased Intake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Decreased appetite</td>
<td>42 (60.0)</td>
<td>29 (64.4)</td>
<td>13 (52.0)</td>
</tr>
<tr>
<td>2. Advised salt restricted diet</td>
<td>29 (41.4)</td>
<td>21 (46.7)</td>
<td>8 (32.0)</td>
</tr>
<tr>
<td>3. Ryle’s Tube feeds</td>
<td>17 (24.3)</td>
<td>4 (8.9)</td>
<td>13(52.0)*</td>
</tr>
<tr>
<td>4. Only liquid intake</td>
<td>5 (7.1)</td>
<td>1 (2.2)</td>
<td>4 (20.0)</td>
</tr>
<tr>
<td>Increased Loss</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Vomiting</td>
<td>26 (37.1)</td>
<td>28 (40.0)</td>
<td>8 (32.0)</td>
</tr>
<tr>
<td>2. Renal disease</td>
<td>21 (25.7)</td>
<td>12 (26.7)</td>
<td>7 (28.0)</td>
</tr>
<tr>
<td>3. Diarrhoea</td>
<td>9 (12.9)</td>
<td>6 (13.3)</td>
<td>3 (12.0)</td>
</tr>
<tr>
<td>4. Cutaneous</td>
<td>6 (8.6)</td>
<td>6 (13.3)</td>
<td>0*</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Dilutional</td>
<td>34 (48.6)</td>
<td>17 (35.6)</td>
<td>17 (68.0)*</td>
</tr>
<tr>
<td>2. Diuretics</td>
<td>26 (37.1)</td>
<td>11 (24.4)</td>
<td>15 (60.0)*</td>
</tr>
<tr>
<td>3. Alcohol</td>
<td>13 (18.6)</td>
<td>10 (22.2)</td>
<td>3 (12.0)</td>
</tr>
<tr>
<td>4. Cerebral causes</td>
<td>9 (12.9)</td>
<td>7 (15.6)</td>
<td>2 (8.0)</td>
</tr>
<tr>
<td>5. Hypothyroidism</td>
<td>1 (1.4)</td>
<td>0</td>
<td>1 (4.0)**</td>
</tr>
</tbody>
</table>

*The difference between groups A and B is statistically significant (\(P<0.05\)); ""P could not be calculated. *\(P<0.01\) compared to non-diabetic patients. Many patients had more than one precipitating factor. Data values rounded off to one place after decimal.
group B took 4.3 ± 2.4 days to recover while patients in group A took 3.4 ± 2.5 days, a significant difference if one tailed t test is used ($P$ <0.05) (Table III). Of the 70 patients, 19 had diabetes. These 19 patients were significantly older ($P$ <0.05) than nondiabetic patients (Table I). Of these, 17 belonged to group A. The blood sugar ranged between 86 - 600 mg/dl with a median of 155 mg/dl and mean of 208.11 ± 132.13 mg/dl. They were advised salt restriction significantly ($P$ <0.01) more often compared to nondiabetic patients (Table II). Other than that they did not differ significantly from non-diabetics with respect to clinical features, precipitating factors or response to therapy.

**Discussion**

Our patients were younger than those in other studies\textsuperscript{10-12}. Since we did not have a control group, it cannot be said whether hyponatremia occurs more commonly in the elderly.

Our patients were predominantly (64.3%) males. This is contrary to the literature report where females have outnumbered males in the hyponatremic group (52-70%)\textsuperscript{10-12}. This is probably because we have a larger number of male admissions in the medical wards of our hospital. Again in the absence of a control group, it is not possible to comment on the relative predilection of females to hyponatremia.

Confusion was seen in 30 per cent of the patients and altered sensorium in 17.1 per cent. This is less than that reported by Ellis in his study\textsuperscript{9} where 76 per cent of the patients were found to have clouding of consciousness with 11 per cent in coma. None of the patients in our study were in coma. This is probably because Ellis has included patients with more severe hyponatremia (sodium <120 mmol/l).

In our study 64.3 per cent patients had hyponatremia at presentation while 35.7 per cent developed it in the hospital (in 4.3% hyponatremia worsened) compared to 63.5 and 36.2 per cent reported by Erasmus and Matsa\textsuperscript{13} (worsening reported in 3 patients), 51 and 49 per cent by Hoorn et al\textsuperscript{14} and 78.3 and 21.7 per cent by Hochman et al\textsuperscript{15}. No mortality was observed among our patients. Other studies have reported mortality ranging from 4.3 to as high as 50 per cent with cut-off criteria for inclusion ranging from 120 to 132 mmol/l\textsuperscript{9,12,14-17}.

Analysis of the causes of hyponatremia in our patients revealed that most patients (94.3%) had multiple precipitating factors compared to 51 per cent reported by Shapiro et al\textsuperscript{8}, in elderly patients with hyponatremia. Other factors found to reduce dietary salt intake were intake of only liquid feeds and patients put on Ryle’s tube feeds. The conventionally fed fluids in our country, orally or through Ryle’s tube are sugar based like 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. This has made inappropriate feeds an important factor responsible for the development of in-hospital hyponatremia. This agrees with the causes of hospital-acquired hyponatremia as reported earlier\textsuperscript{12,14}.

Increased loss of sodium from the body was seen in 65.7 per cent patients, most commonly via gastrointestinal route, same as that reported by Lee et al\textsuperscript{18} (65%). Cutaneous loss due to excessive sweating in manual labourers is an important cause in our country, as seen in four of our patients. Among the miscellaneous causes, volume overload due to cardiac, renal and hepatic disease was a factor in 48 per cent patients. Only 2 per cent of patients in the study by Huda et al\textsuperscript{10} had renal failure, while none had cardiac disease, 5 per cent of the patients in the study by Gill

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**Table III.** Comparison of time taken for recovery and treatment of hyponatremia between the two groups

<table>
<thead>
<tr>
<th>Mode of correction</th>
<th>Overall (n=70) no. (%)</th>
<th>Group A (n=45) no. (%)</th>
<th>Group B (n=25) no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased oral salt intake</td>
<td>26 (37.1)</td>
<td>17 (37.8)</td>
<td>9 (36.0)</td>
</tr>
<tr>
<td>Fluid restriction</td>
<td>28 (40.0)</td>
<td>17 (37.8)</td>
<td>11 (44.0)</td>
</tr>
<tr>
<td>Normal saline</td>
<td>39 (55.7)</td>
<td>23 (51.1)</td>
<td>16 (64.0)</td>
</tr>
<tr>
<td>3% saline</td>
<td>34 (48.6)</td>
<td>20 (44.4)</td>
<td>14 (56.0)</td>
</tr>
<tr>
<td>Time taken for recovery (days)</td>
<td>3.7 ± 2.4</td>
<td>3.4 ± 2.5*</td>
<td>4.3 ± 2.4</td>
</tr>
</tbody>
</table>

*P*<0.05 compared to group B (one tailed t test)
et al\textsuperscript{12} had liver disease. Diuretics as a precipitating factor for hyponatremia was found in 37.1 per cent of our patients compared to 37 per cent\textsuperscript{12} and 21 per cent\textsuperscript{10} earlier. The differences between the two groups with regard to miscellaneous causes emphasizes iatrogenic causation of hyponatremia in Group B. Care while using fluid therapy or diuretics, is therefore, necessary to bring down adverse events associated with these therapeutic steps.

The time taken for recovery, as expected, was found to vary inversely with the severity of hyponatremia. Patients in group B took longer to recover compared to group A which may be because of the delay in recognizing the condition and starting therapy. This is also corroborated by Hoorn et al\textsuperscript{14} who found a significant delay in starting treatment in hospital acquired hyponatremia and a longer period of hospitalization. Urinary sodium and osmolality and plasma osmolality could not be determined in our study. Another important limitation of our study was the lack of controls.

In conclusion, hyponatremia must be actively looked for and corrected early as delay in starting treatment worsens the hyponatremia and prolongs the hospital stay. Decreased intake especially in patients on liquid diet or Ryle’s tube feeds, a totally preventable cause, was found to be a more common cause of hyponatremia in our setup as compared to excessive loss. Another preventable contributory factor was the advice of ‘salt restricted diet’ to hypertensives and diabetics. Care must be exercised while using diuretics and intravenous fluids, and such patients must be monitored closely, and any abnormality detected should be promptly corrected. A larger study with controls needs to be done to establish the effect of salt restriction and inappropriate Ryle’s tube feeds in patients. Urine sodium and osmolality measurement will help in correctly delineating the type of hyponatremia.

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References


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