Hyponatremia in a Group of Iraqi Patients with Stroke

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Abstract

Background
Hyponatremia is a common electrolyte disorder encountered in patients of stroke, which is usually either due to inappropriate secretion of antidiuretic hormone (SIADH) or cerebral salt wasting syndrome (CSWS). Making an accurate diagnosis is important because the treatment of each condition is quite different.

Objectives
We conducted this study to determine the incidence and etiology of hyponatremia in patients of stroke.

Methods
A cross sectional study of 100 patients diagnosed to have stroke (50 ischemic, 50 hemorrhagic) based on clinical history, examination and brain images. Patients were evaluated for hyponatremia (serum sodium < 135 mmol/L) during the second week of their admission.

Results
Out of 100 patients, 17 patients had hyponatremia, all Patients with serum sodium level in hyponatremic range were limited to patients with hemorrhagic stroke, while no patients with ischemic stroke had a low serum sodium level, this difference was significantly different, P-value was < 0.001.

Conclusion
Incidence of hyponatremia in our study population was 17%, all Patients with hyponatremia were limited to patients with hemorrhagic stroke, in patients of hyponatremia; 82% were having SIADH and 18% were having CSWS.

Keywords
Hyponatremia, ischemic stroke, hemorrhagic stroke, syndrome of inappropriate antidiuretic hormone, cerebral salt wasting syndrome.

List of Abbreviations: SIADH = syndrome of inappropriate antidiuretic hormone, CSWS = cerebral salt wasting syndrome, ADH = antidiuretic hormone, Na+ = Sodium.

Introduction
Stroke is the third most common cause of death in developed world after cancer and cardiovascular disease; it is the most common cause for severe physical disability (1). Stroke is defined by the World Health Organization as the clinical syndrome of rapid onset (usually seconds or minutes) of focal (or global, as in subarachnoid hemorrhage) cerebral deficit, lasting more than 24 hours or leading to death, with no apparent cause other than a vascular one (2). Strokes can be classified into two major categories: ischemic and hemorrhagic (3).

Hyponatremia is a common electrolyte disorder encountered in patients of neurological disorders such as stroke, subarachnoid hemorrhage, and meningitis, which is usually either due to syndrome of inappropriate secretion of antidiuretic hormone (SIADH) or cerebral salt wasting syndrome (CSWS) (4).

Hyponatremia can be a vexing problem for those who care for critically ill neurologic patients. Although seemingly simple at first glance, the accurate diagnosis and effective treatment can be complex (5).

CSWS first described by Peters et al in 1950, and it is defined by the development of extracellular volume depletion due to a renal sodium transport abnormality in patients with...
intracranial disease and normal adrenal and thyroid function. Complications of CSWS include symptomatic hyponatremia and dehydration; CSWS is considered a definite clinical entity and may be more common than perceived. CSWS usually develops in the first week following a brain insult. Its duration is usually brief (spontaneously resolves in 2-4 weeks), although it can last for several months.

The SIADH is the most common cause of euvoletic hyponatremia in hospitalized patients. The syndrome is defined by the hyponatremia and hypo-osmolality that results from inappropiate, continued secretion and/or action of antidiuretic hormone (ADH) despite normal or increased plasma volume, which results in impaired water excretion.

The ADH promotes the reabsorption of water from the tubular fluid in the collecting duct, the hydro-osmotic effect, and it does not exert a significant effect on the rate of sodium (Na\(^{+}\)) reabsorption.

A second action of ADH is to cause arteriolar vasoconstriction and a rise in arterial blood pressure, hyponatremia in this syndrome is a result of an excess of water and not a deficiency of Na\(^{+}\).

SIADH consists of hyponatremia, inappropriately elevated urine osmolality (>100 mmol/kg), and decreased serum osmolality in a euvoletic patient. SIADH should be diagnosed when these findings occur in the setting of otherwise normal cardiac, renal, adrenal, hepatic, and thyroid function.

In SIADH, there is a persistent production of ADH despite body fluid hypotonicity and an expanded effective circulatory volume so that the negative feedback mechanism that normally controls ADH fails and ADH continues to be released.

Other factors known to stimulate ADH secretion, such as hypotension, severe pain, nausea, and stress. Hyponatremia that meet the criteria for the diagnosis of SIADH develop on an average of seven days following the brain insult.

Neurologic complications in SIADH occur as a result of the brain’s response to changes in osmolality. Hyponatremia and hypo-osmolality lead to acute edema of the brain cells. The rigid calvaria prevent expansion of brain volume beyond a certain point, after which the brain cells must adapt to persistent hypo-osmolality. However, a rapid increase in brain water content of more than 5-10% leads to severe cerebral edema and herniation and is fatal.

Hyponatremia can be aggravated by the hospitalization and may be secondary to the administration of hypotonic intravenous fluids.

Irreversible neurologic damage and death may occur when the rate of correction of Na\(^{+}\) exceeds 0.5 mmol/L/hr for patients with severe hyponatremia. At this rate of correction, osmolytes that have been lost in defense against brain edema during the development of hyponatremia cannot be restored as rapidly when hyponatremia is rapidly corrected. The brain cells are thus subject to osmotic injury, a condition termed osmotic demyelination.

Certain factors such as hypokalemia, severe malnutrition, and advanced liver disease predispose patients to this devastating complication.

Differentiation of SIADH from CSWS can be difficult because both can present with hyponatremia and concentrated urine with natururesis. Making an accurate diagnosis is important because the treatment of each condition is quite different.

Vigorous salt replacement is required in patients with CSWS, whereas fluid restriction is the treatment of choice in patients with SIADH. Although most physicians are familiar with SIADH, they are much less familiar with CSWS. This review emphasizes the need for CSWS to be included in the differential diagnosis of hyponatremia in a patient with central nervous system disease. Distinguishing between these two disorders is of crucial importance because therapy indicated for one disorder but used in the other can result in negative clinical consequences. The aim of this study is to...
determine the frequency of hyponatremia in patients of stroke admitted in the hospital.

Methods
This study was a cross-sectional survey on the patients who admitted to the Neurology Ward of Al-Imamain Al-Kadhîmain Medical City from January 2012 to April 2012. The study included 100 patients diagnosed to have stroke (50 patients diagnosed to have ischemic stroke and 50 patients diagnosed to have hemorrhagic stroke) on the basis of clinical history, examination and brain image. A questionnaire was prepared to collect data from the patients it included information about the age, sex, presentation, past medical history, brain image findings, and this information was obtained from the patients themselves or from their relatives. All the patients were assessed for hyponatremia (serum sodium < 135 mmol/L) volume status, packed cell volume, blood urea/serum creatinine ratio, urinary sodium was also measured during the second week of their admission. All those patients who had a history of intake of drugs that can cause hyponatremia, gastroenteritis, head trauma, brain tumor, hemorrhagic infarction, bronchogenic carcinoma, leukemia, lymphoma and recent surgery were excluded from this study. SIADH was differentiated from CSWS by intravascular volume depletion in CSWS (elevated packed cell volume and possibly increased blood urea/serum creatinine ratio) despite a urine sodium concentration that is not low. The data was analyzed using Statistical package for social science (SSPS) software. Data were presented as frequency and percentage. Comparison between groups using Chi-square test.

Results
The study conducted on 100 patients, 50 patients with ischemic and 50 patients with hemorrhagic stroke their ages ranged from 42 to 83 years. Mean of patients’ age with hemorrhagic stroke was not significantly different from that of patients with ischemic stroke. It was 63.4±9.92 years in patients with hemorrhagic stroke while it was 60.94 ± 6.42 years in patients with ischemic stroke (Fig. 1).

Although patients younger than 55 years of age were more frequent in patients with ischemic stroke, 26% versus 16%, there was no statistical significance. Both types of strokes were more frequent in male patients than female patients. Male to female ratio was 1.08:1 in hemorrhagic patients and 1.27:1 in ischemic patients. Hypertension was the main risk factor in hemorrhagic group, accounting for 72%. It was significantly more frequent in hemorrhagic group than ischemic group, 72% versus 40% respectively. This difference was significant with a P-value of 0.001. Other risk factors, diabetes mellitus, structural cardiac disease and/or arrhythmia, previous stroke, smoking, and alcoholism, were not significantly different (Table 1).
Table 1. Risk factors in stroke patients

<table>
<thead>
<tr>
<th>Basic Characteristic and risk factors</th>
<th>Hemorrhagic stroke</th>
<th>Ischemic stroke</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M:F)</td>
<td>No. 26:24 % 52:48</td>
<td>No. 28:22 % 56:44</td>
<td>0.688</td>
</tr>
<tr>
<td>Hypertension</td>
<td>36 % 72</td>
<td>20 % 40</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>12 % 24</td>
<td>13 % 26</td>
<td>0.817</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>3 % 6</td>
<td>5 % 10</td>
<td>0.461</td>
</tr>
<tr>
<td>Structural cardiac disease and/or arrhythmias</td>
<td>6 % 12</td>
<td>8 % 16</td>
<td>0.695</td>
</tr>
<tr>
<td>Smoking</td>
<td>10 % 20</td>
<td>11 % 22</td>
<td>0.806</td>
</tr>
<tr>
<td>Alcoholic</td>
<td>1 % 2</td>
<td>1 % 2</td>
<td>1.000</td>
</tr>
</tbody>
</table>

The presentation of patients was the same in both groups, in form of disturbed level of consciousness, focal neurologic deficit, headache and visual disturbances. Convulsion was encountered only in hemorrhagic group. None of presentation was significantly different when compared in both groups. Mean serum sodium was significantly lower in hemorrhagic stroke than in ischemic stroke. It was $134.56 \pm 5.77$ mmol/L in hemorrhagic group, while it was $139.7 \pm 3.16$ mmol/L in ischemic group ($P < 0.001$) as shown in fig. 2.

![Fig. 2. Comparison of mean serum sodium between patients with hemorrhagic stroke and patients with ischemic stroke](image)

Seventeen patients with serum sodium level in hyponatremic range (< 135 mmol/L) were limited to patients with hemorrhagic stroke, while no patients with ischemic stroke had a low serum sodium level. This difference was significantly different ($P < 0.001$) as shown in table 2. Out of 17 Patients with serum sodium level in hyponatremic range 14 patients (82%) had SIADH and 3 patients (18%) had CSWS. This difference was significant ($P < 0.001$) as shown in table 3.

**Discussion**

Hyponatremia in patients with an acute CNS disease is the most common electrolyte disturbance encountered in neurological wards. Hyponatremia in stroke is usually of the hypoosmolal type caused either by SIADH or CSWS.

Out of 100, 17% of the patients who included in this study found to be hyponatremic, about 70% of the hyponatremic patient presented with disturbed consciousness, and 47% have CT scan showing intraventricular extension of the intracranial hemorrhage, this fact may be related to the severity of hemorrhage and increased intracranial pressure that in turns increase the release of ADH. (22,23)

17 Patients with serum sodium level in hyponatremic range (< 135 mmol/L) were limited to patients with hemorrhagic stroke, while no patients with ischemic stroke had a low serum sodium level, this difference was significantly different. Out of 17 Patients with serum sodium level in hyponatremic range 14 patients (82%) had SIADH and 3 patients (18%) had CSWS. This difference was significant.
Table 2. Frequency of patients with hyponatremia in hemorrhagic and ischemic groups

<table>
<thead>
<tr>
<th>Hyponatremia</th>
<th>Hemorrhagic stroke</th>
<th>Ischemic stroke</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>34</td>
<td>0</td>
</tr>
<tr>
<td>No</td>
<td>33</td>
<td>66</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100</td>
<td>50</td>
</tr>
</tbody>
</table>

Table 3. Frequency of hyponatremia according to the cause

<table>
<thead>
<tr>
<th>Hyponatremia</th>
<th>No.</th>
<th>%</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIADH</td>
<td>14</td>
<td>82</td>
<td></td>
</tr>
<tr>
<td>CSWS</td>
<td>3</td>
<td>18</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

This is compatible with the study in Brussels, Belgium, 131 patients were studied retrospectively during 2008-2009, patients developed CSWS in 12.7%, of whom 7.9% within 1 week from admission and 4.8% after one week (24).

Another study, out of 1000 patients, 353 had hyponatremia. Out of this 353 patients, 238 (67%) had SIADH and 115 (33%) had CSWS. SIADH was seen in 83 patients who had an ischemic stroke and 155 patients of hemorrhagic type. CSWS was found in 38 patients with ischemic stroke and 77 patients with hemorrhagic ones (25). This may be due to small sample size this current study.

In one study; hyponatremia in the acute stroke stage was seen in 11.6% of cases and has been found to be a predictor of 3-year mortality in patients with acute first-ever ischemic stroke (25).

Another study in Stanford University School of Medicine, Kao and Vavao included 316 patients from 2004 to 2007, they found that 59% of patients were hyponatremic, 35.4% were categorized with SIADH and 22.9% with CSWS (26).

One study performed previously in critically ill adult neurological patients found hyponatremia in 1-15% of the patients, which was associated with a mortality increase of 7-60% (27).

Therefore close monitoring of serum sodium must be done in all hospitalized stroke patients especially those with hemorrhagic stroke and it is of paramount importance that the physician differentiates between SIADH and CSWS because of the disparate nature of the treatments of these two entities. Improper treatment can worsen the underlying condition and may result in poor neurological outcomes.

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Conflict of Interest
The authors disclose no any financial and personal relationships with other people or organizations that inappropriately influence (bias) outwork.

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