

Research Article

Syndrome of inappropriate antidiuretic hormone secretion in hospital inpatients: a descriptive study in a tertiary care centre in South India

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ABSTRACT

Background: Hyponatremia is the most common electrolyte abnormality among the patients in medical wards as well as in the intensive care unit contributing to substantial morbidity and mortality. The most common cause of hyponatraemia in hospital inpatients is Syndrome of Inappropriate Anti Diuretic Hormone secretion (SIADH). This prospective observational study was designed to assess the clinical profile of SIADH. Aim: To assess the clinical profile of SIADH in medically ill patients.

Methods: This was an observational study for 24 months conducted in a tertiary care hospital. Patients were assessed clinically to study the volume status, effects of hyponatremia on nervous system and find out various etiologies for SIADH. All patients underwent routine hemogram, blood biochemistry, serum electrolytes, thyroid function tests, morning serum cortisol estimation, plasma and urinary osmolality determination as well as urinary sodium estimation. Patients were diagnosed to have Syndrome of Inappropriate Antidiuretic Hormone secretion (SIADH) if they satisfied the Bartter and Schwartz criteria.

Results: Among the eighty patients with euvolemic, hypoosmolal hyponatremia who were screened for SIADH, seven patients were excluded due to various reasons (hypothyroidism, Sheehan's syndrome, Addison's disease). The mean age of the patients was 64 ± 13 years. Among 73 patients included there were 33 (45.2%) male patients and 40 (54.8%) female patients. Severe hyponatremia ($\text{Na} < 110$ meq/l) was detected in 33 patients (45%). Pulmonary causes were the most common cause of SIADH in this study seen in 25 (34.2%). The other causes were idiopathic in 20 (27.4%), neurological in 17 (23.3%), drug induced in 2 (2.7%), positive pressure ventilation in 5 (6.8%) and other infections in 4 (5.5%). The average rate of correction was $5 \text{ meq} \pm 1.5$ in the first 24 hours. The overall mortality was found to be 7%.

Conclusion: Hyponatremia due to SIADH is common among elderly patients with preponderance for female population. Majority of the patients in the present study were noticed to have an underlying respiratory cause as the etiology. Mortality in SIADH patients was related to the underlying cause rather than the severity of hyponatremia.

Keywords: Euvolemic, Hyponatremia, Syndrome of inappropriate antidiuretic hormone secretion

INTRODUCTION

Hyponatraemia is the commonest electrolyte abnormality found in hospital in-patients with a prevalence of 15% in general hospital population.¹ Patients with symptomatic hyponatraemia have increased mortality when compared with normonatremic controls. Hyponatraemia has many

different pathophysiological causes which need to be managed differently, to reduce morbidity and mortality. The most common cause of hyponatraemia in hospital inpatients is syndrome of inappropriate antidiuretic (SIADH). SIADH is the isoosmotic variant of hyponatremia which was first described by Schwartz and associates in two patients with bronchogenic carcinoma and later further characterized by Bartter and Schwartz.

Where possible, all attempts should be made to identify and rectify the cause of SIADH.

Aim

To assess the clinical profile of SIADH in medically ill patients.

METHODS

This observational study was conducted in the medicine teaching unit of a tertiary care hospital in south India for a period of 24 months. History and clinical examinations were recorded in all patients at admission. Extracellular volume status of all patients was determined clinically and euvolemic patients were identified. For all patients complete hemogram, blood glucose, renal function tests, thyroid function tests, Liver Function Tests (LFTs), serum uric acid, morning serum cortisol, and serum electrolytes, plasma and urinary osmolality determination as well as urinary sodium estimation were done. Serum and urine sodium were estimated by automated analyzer by ion selective electrode s and osmolality by freeze point osmometer. Diagnosis of Syndrome of Inappropriate Antidiuretic Hormone secretion (SIADH) if they satisfied the Bartter and Schwartz criteria which included:

1. Decreased effective osmolality of extracellular fluid.
2. Inappropriate urinary concentration in the presence of hypoosmolality.
3. Clinical signs of euvoemia; absence of signs of hypovolemia (tachycardia, orthostatic changes) or hypervolemia (edema, ascites).
4. Elevated urinary sodium excretion with normal salt and water intake.
5. Absence of other causes of euvolemic hypoosmolality (hypoadrenalism/hypothyroidism).

The normal serum sodium is 136-145 meq/l. Hyponatremia is defined as a decrease in the serum sodium concentration to a level below 136 mmol per liter.² Severe hyponatremia defined as serum Na <110 meq/l. SPSS (Statistical Package for the Social Sciences) were used for data analysis. Chi-square test was applied to find the significance of difference between two proportions and a P value of less than 0.05 was accepted as indicating statistical significance.

RESULTS

This observational study was conducted in the patients who were admitted in medical ward and intensive care unit of a tertiary care hospital in south India for a period of 24 months. Among the eighty patients with euvolemic, hypoosmolal hyponatremia who were screened for

SIADH, seven patients were excluded due to various reasons. Four of them had hypothyroidism, two had Addisons disease one had Sheehans syndrome.

The mean age of the patients was 64 ± 13 years. 48 (66%) patients were in the 61-80 years age group (Figure 1). Among the 73 patients studied 33 (45.2%) were males and 40 (54.8%) female patients. The male to female ratio was 1:1.21.

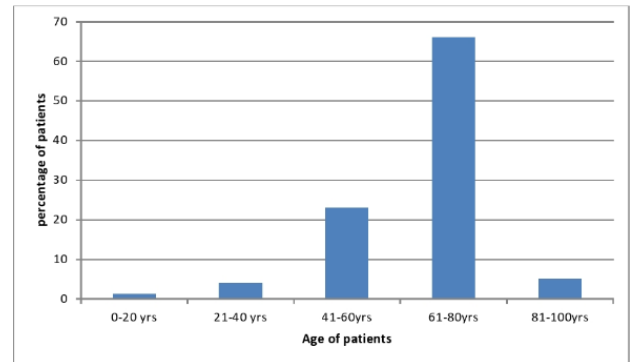


Figure 1: Age distribution of SIADH patients.

15% patients had mild hyponatremia with serum sodium 121-130 mEq/L, 40% patients had moderate hyponatremia with serum sodium between 111-120 mEq/L and 45% patients had severe hyponatremia with serum sodium less than or equal to 110 mEq/L (Figure 2). Severe hyponatremia was more common among females.

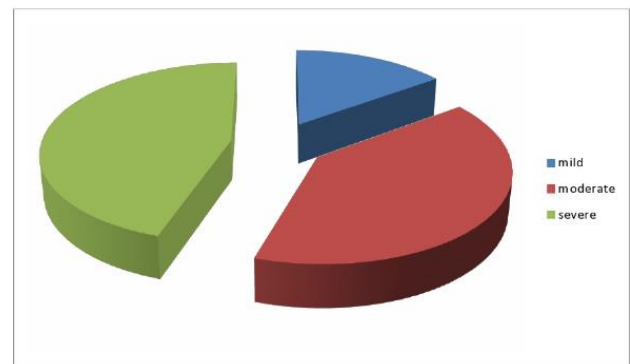


Figure 2: Severity of hyponatremia in SIADH.

The majority patients were symptomatic at presentation. 35 (48%) patients had varying degrees of altered sensorium. The other symptoms were nausea 23 (32%), vomiting 34 (47%), headache 31 (43%), hiccoughs 5 (7%) and seizures 10 (14%).

Pulmonary causes were the most common cause of SIADH in this study seen in 25 (34.2%). The pulmonary causes were infection in 60%, bronchogenic carcinoma in 20% and obstructive airway diseases in 20%. CNS causes were found in 17 (23.3%) patients which included cerebrovascular accidents (41.2%), infections (35.3%), parkinsonism (11.8%), subarachnoid hemorrhage (5.9%)

and psychosis (5.9%). The other causes were idiopathic in 20 (27.4%), drug induced (mirtazapine and resperidone) in 2 (2.7%), positive pressure ventilation in 5(6.8%) and other infections in 4 (5.5%) (Figure 3). Other infections included two patients with urinary tract infection, one each with HIV and herpes zoster.

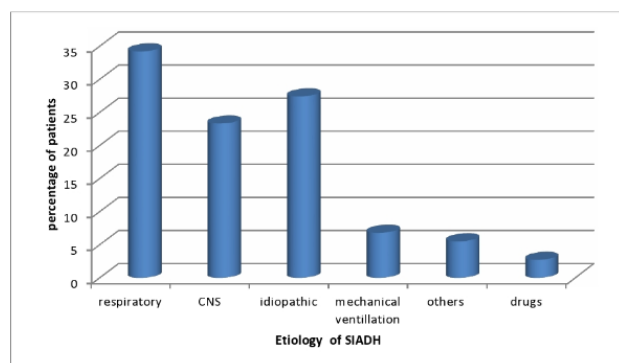


Figure 3: Etiological distribution of SIADH.

The mean serum uric acid levels found was 2.51 ± 0.86 mg%. Fluid restriction was advised for all the patients. Overtly symptomatic patients were treated with hypertonic saline intravenously by proper dose and rate calculation followed by oral salt supplementation. 38 (52%) patients received hypertonic saline. The average rate of correction was $5 \text{ meq} \pm 1.5$ in the first 24 hours. With this rate of correction none of the patients developed any complications.

Among the 73 patients five died and all of the deaths were due to septicaemia from various causes. The overall mortality was found to be 7%. The association of mortality with severity of hyponatremia was not found to be statistically significant (P value 0.631).

DISCUSSION

Hyponatraemia is the commonest electrolyte abnormality found in hospital in-patients with a prevalence of 15% in general hospital population.¹ Hyponatraemia is defined as a decrease in the serum sodium concentration to a level below 136 mmol per liter. Euvolaemic hyponatraemia is the commonest cause of hyponatraemia in hospitalised patients. Although experimental models of SIADH show that blood volume is slightly expanded in SIADH with suppression of plasma renin and elevation of plasma natriuretic peptides, the expanded extracellular volume is not detectable clinically and does not cause oedema. SIADH is a clinical manifestation of a wide range of clinical disorders and drug therapies, and is the most common cause of euvolaemic hyponatraemia in modern clinical practice. Proper evaluation of hyponatremic patients is prudent for accurate management.

The mean age of the patients in the present study was 64 ± 13 years. The average age was 77 ± 8.3 in a study by Hirshberg et al.³ Among the 73 patients studied 33

(45.2%) were males and 40 (54.8%) female patients. The male to female ratio was 1:1.21. Male to female ratio showed a female preponderance in other studies as well.^{4,5}

Pulmonary causes were the most common cause of SIADH in this study seen in 25 (34.2%). CNS causes were found in 17 (23.3%) patients and the other causes were idiopathic in 20 (27.4%), drug induced (mirtazapine and resperidone) in 2 (2.7%), positive pressure ventilation in 5(6.8%) and other infections in 4 (5.5%). Hirshberg et al. found that the cause for SIADH in most of the patients (60%) remained obscure, pneumonia was diagnosed in 9 cases (18%) and drugs accounted for hyponatremia in 12% of the cases (4 secondary to carbamazepine therapy, 1 secondary to paroxetine and 1 attributed to fluoxetine). Other infections included two patients with urinary tract infection, one each with HIV and herpes zoster. HIV infection can cause hyponatremia due to various reasons including SIADH.⁶ Herpes zoster infection associated SIADH was reported previously also. Two cases with herpes zoster ophthalmicus contributing to SIADH were reported by Wang et al.⁷ Localised herpes zoster infection with SIADH was also reported by O'Rourke et al.⁸ Although hyponatremia in febrile UTI can occur in association with other underlying disorders, SIADH is also considered to lead hyponatremia in the condition of more severe inflammation by reducing the expression and inhibiting the function of the apical epithelial sodium channel and/or sodium potassium adenosine triphosphatase at the basolateral membrane of renal epithelial cells through inflammatory cytokines such as IL-1 β and tumor necrosis factor. We found that 20 (27.4%) patient in our study had idiopathic SIADH. Miller et al. reported 27 ambulatory patients with hyponatremia due to the SIADH secretion, of which 26% were of idiopathic etiology.⁹ Hochman¹⁰ documented 13 patients defined as SIADH hyponatremia; in 39% of these cases, the underlying cause was considered to be idiopathic. Many drugs have been reported to produce SIADH, most published reports concern vasopressin and its analogues, thiazide and thiazide-like diuretics, chlorpropamide, carbamazepine, antipsychotics, antidepressants and nonsteroidal anti-inflammatory drugs.¹¹ Old age is a risk factor for SIADH following the use of many of these drugs. In a study of the syndrome of Inappropriate Secretion of Antidiuretic Hormone (SIADH) associated with the use of selective serotonin reuptake inhibitors fluoxetine was involved in 75.3% of the cases and paroxetine in 12.4%.¹²

In the study by Hirshberg et al. majority of the patients (68%) regained normal serum sodium concentrations following simple measures such as fluid restriction. Hypertonic saline was needed in only 10% of the patients, and the rest managed on the combination of saline infusion and diuretics. Most of the patients survived the event and only two patients died, both due to sepsis. In our series 38 (52%) patients received hypertonic saline since 45% patients had severe

hyponatremia with serum sodium less than or equal to 110 mEq/L. The average rate of correction was $5 \text{ meq} \pm 1.5$ in the first 24 hours. With this rate of correction none of the patients developed any complications. The duration of correction of hyponatremia ranged from 2 days to 11 days and mean duration of correction was 6.5 days. There were no cases of osmotic demyelination syndrome following correction of hyponatremia in the present study possibly due to the slower rate of correction.

Five patients died and all of the deaths were due to septicaemia from various causes. The overall mortality was found to be 7%. The prognosis of patients having SIADH is dependent on the underlying cause rather than the severity of hyponatremia.¹³ The association of mortality with severity of hyponatremia was not found to be statistically significant (P value 0.631) in present study.

We conclude that SIADH is a common cause for hyponatremia in hospital inpatients and is common among elderly patients with preponderance for female population. Majority of the patients in the present study were noticed to have an underlying respiratory cause as the etiology. Mortality in SIADH patients was related to the underlying cause rather than the severity of hyponatremia.

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