Original Article

Incidence of Hyponatremia in Critically Ill Patients in Intensive Care Unit: Observational Study

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ABSTRACT

Background: Hyponatremia is defined as common electrolyte disturbance or decline blood sodium concentration in critically ill patients. Hyponatremia often results in intensive care unit (ICU) admissions and are also associated with significant mortality and morbidity. The study was undertaken to assess the follows points: (1) To assess the incidence of hyponatremia in patients in ICU. (2) To describe the etiological factors responsible for hyponatremia. (3) To describe clinical manifestations of hyponatremia. (4) To describe treatment modalities for hyponatremia in ICU patients. **Materials and Methods:** (1) Study design - Cross-sectional. (2) Study period - 01/09/2014 to 01/05/2015 data on patients admitted to the hospital in the ICU with hyponatremia were collected. (3) Inclusion criteria - Patients admitted to the ICU with serum sodium levels ≤130 mEq/L, age of patients >18 years. (4) Exclusion criteria - Patients, who did not give consent, age of the patients <18 years, patients admitted to the ICU with serum sodium levels >130 mEq/L, and post-operative patients. (5) Sample size: 100 cases. (6) Sampling type: Purposive. **Results:** A total of 100 hyponatremic and 50 non-hyponatremia critically ill admitted patients in ICU were observed and evaluated out of which 41 (hyponatremic) [Table 2] were males and 59 were females in the study. We have included the non-hyponatremia patients to evaluate with hyponatremia patients. In our study, we observed that in hyponatremic patients, 66% patients had neurological manifestations. These include seizures, reduced consciousness level, confusion, unsteadiness, and falls. **Conclusion:** Hyponatremic patients should be diagnosed early in ICU, and the treatment should be start accordingly. It is frequent finding in critically ill patients admitted to ICU. Most etiological factors involved in it are severe sepsis, renal failure, liver cirrhosis, trauma, hypothyroidism, and hypocortisolism. A patient with hyponatremia needs longer duration stay in ICU with higher mortality rate and longer ventilation days.

Key words: Critically ill, electrolyte disturbance, hyponatremia, intensive care unit, sodium

INTRODUCTION

Hyponatremia is well-known as a decline in plasma sodium level that is <135 mmol/L in blood. Hyponatremia is the most common electrolyte disorder among hospitalized critically ill patients and has been associated with increased mortality ranging from 5% to 50%, depending on severity and acuity of onset. Its prevalence among non-hospitalized elderly patients has been estimated to be between 7% and 11.4%, increasing to 11-22.5% among hospitalized patients. Acute, severe hyponatremia has substantially high morbidity and mortality.[1,2] Rapid correction of chronic hyponatremia can lead to the neurological deficit and even death. Etiology and treatment are not as simple as that of the other electrolyte deficit. Common understanding is that the deficit should be treated with supplementation, e.g. potassium deficit is corrected with K+ supplementation. However, in case of hyponatremia, the treatment may be contrary to this common understanding, thus hyponatremia = sodium deficit, so salt replacement is required in all is a wrong concept. Serum sodium reflects the relative proportion of sodium and water.[3,4] Hyponatremia usually means water overload and not sodium deficit. Hyponatremia can occur with normal, low, or even high total body sodium. Hyponatremia usually means water retention.[5,6]

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Symptoms include:
- Neurological dysfunction
- Associated with cerebral edema
- Nausea
- Headache
- Malaise
- Can also lead to seizures and then death (depending on magnitude and severity of onset).

Hyponatremia can be classified as follows:

A. On the basis of osmolality, volume status and urinary sodium
   - Hypertonic
   - Isotonic
   - Hypotonic.

B. Hypotonic Hyponatremia is again classified as:
   - Hypovolemic hyponatremia
   - Euvolemic hyponatremia
   - Hypervolemic hyponatremia.

Hyponatremia associated with adverse outcome and delay in treatment can result in increased adverse events. Hyponatremia can also be associated with the use of hypotonic solutions to the patients with symptomatic benign prostatic hyperplasia which are undergoing transurethral resection of the prostate.[7,8]

MATERIALS AND METHODS

This was an observational prospective study conducted on a series of randomly selected critically ill patients with hyponatremic and non-hyponatremic admitted in intensive care unit (ICU) during 12-month period. The patients were divided into two groups consisting of 150 patients in which 100 patients were diagnosed as hyponatremic (serum sodium level <135 mmol/L), and 50 patients were non-hyponatremic (normal sodium level 135-145 mmol/L). Complete clinical examination and proper details history were recorded in all the critically ill patients at the time of admission in ICU. Detail history included drug history especially about diuretics, thiazides, and selective serotonin reuptake inhibitors. Final the clinical evaluation of volume status was observed and recorded. Parameters for the critically ill patients in ICU include the presence of acute renal failure, ventilator support with days, duration of ICU past and present, and hospital days were recorded as observational data, and other useful parameters such as male:female ratio, complications, morbidity and mortality, etc., were recorded and calculated.

Laboratory investigation includes routine blood investigations in which complete blood count, serum blood glucose level fasting and random, serum potassium (K), serum creatinine, serum urea, liver function test, lipid profile, urine sodium and osmolality with serum osmolality, and serum sodium were analyzed and recorded.

Statistical Analysis

Statistical analysis used was done with unpaired t-tests and Mantel-Cox test. All the *P* values were two-tailed, and $P < 0.05$ was considered to be statistically significant.

RESULTS

The study was conducted at a tertiary care center. Successive patients of hyponatremia who were admitted to the hospital ICU were included in the study. These patients were evaluated for the underlying cause of hyponatremia which included detailed history and physical examination followed by appropriate laboratory investigations based on serum osmolality. 100 patients of hyponatremia were included in the study. 34% of the patients were asymptomatic, and 66% had abnormal behavior. There was a wide range of etiologies, most common being cerebral malaria (15%), sepsis (13%), pneumonia (14%), hypothyroidism (12%), syndrome of inappropriate secretion of antidiuretic hormone (SIADH) (8%), diuretics (9%), heart failure (8%), renal failure (7%), liver disorder (7%), and vomiting (5%) [Table 1]. 14% of the patients received normal saline, 21% of the patients were on fluid restriction, 65% patients were given oral sodium chloride supplementations. The overall mortality among patients hyponatremia in our study was 19%. In the present study, the prevalence of hyponatremia was more in male patients with male:female ratio of 1.4:1 (59 males and 41 females) [Table 2]. Cerebral malaria and sepsis were associated in a large proportion of the patients in this study which have not been considered as etiology of hyponatremia in the available literature. In our study, hypertension was a major risk factor for hyponatremia due to diuretic use in elderly patients. Poor nutritional intake secondary to various other co-morbidities was a major risk factor in this study. Total 49 (49%) patients had history of poor intake which was associated with various other causes. 10 (10%) patients in present study fulfilled the diagnostic criteria for SIADH. The incidence is comparable to the available literature on hyponatremia in hospitalized patients.

Table 1 compares the causes and characteristics of the critically ill patients with hyponatremia to those of the control group. The critically ill patients (Table 2) with hyponatremia were older (58.23 ± 12.5 vs. non-hyponatremic 58.74 ± 14.7 years, $P < 0.001$), predominantly female (59.0% vs. 52.0%, $P = 0.41$). Table 3 shows serum osmolality patients suffering from severe hyponatremia were 246.63 ± 41.57, and mild to moderate were 278.59 ± 12.3, and the $P < 0.001$.

Table 4 Shows the mortality level based on serum sodium level. In less than 120 serum sodium the percentage of mortality was 16.6% while in more than 125 it was 27.3%. Table 5 shows overall mortality rates during the treatment of hyponatremia was 57% in 0.9% isotonic solution infusion in which death was 14.04%. In treatment with fluid restriction was around 9.76% death, in demeclocycline was 18.75%, in

Table 1: Causes of hypernatremia

Causes of hypernatremia	Number of cases (%)
Congestive cardiac failure	19
Chronic kidney disease	17
Dehydration	18
Cerebral malaria	15
Bronchopneumonia	14
Neurological diseases including stroke	11
Hypothyroidism	12
Diuretics Like thiazide use	8
Heart failure	8
Renal Failure	7
Selective serotonin reuptake inhibitors use	7
Liver disorder	7
Malignancy	5
Vomiting	5
Carbamazepine use	3
Difficulty in imbibing fluids	3
Decreased glomerular filtration rate	2

Table 2: Comparison of demographic profiles and clinical features between hyponatremic cases and non-hyponatremic subjects

Demographic variables and clinical features	Hyponatremia cases *n*=100 (%)	Non-hyponatremia subjects *n*=50 (%)	*P* value
Age (mean±SD)	58.23±12.5	58.74±14.7	0.87
Sex - Male	41 (41.0)	24 (48.0)	0.41
Nausea	34 (34.0)	12 (24.0)	0.21
Vomiting	50 (50.0)	16 (32.0)	0.036*
Headache	17 (17.0)	4 (8.0)	0.13
Fatigue	63 (63.0)	27 (54.0)	0.28
Irritability	59 (59.0)	16 (32.0)	0.001*
Seizures	23 (23.0)	6 (12.0)	0.038*
Cramps	4 (4.0)	3 (6.0)	0.58
Drowsy	57 (57.0)	18 (36.0)	0.015*
Diarrhea	10 (10.0)	6 (12.0)	0.71

* is significant, SD: Standard deviation

Table 3: Parameters compared between severe and non-severe hyponatremic cases

Parameters (mean±SD)	Severe (≤120)	Mild-Moderate (>120)	*P* value
S. OSM	246.63±41.57	278.59±12.3	<0.001*
U. OSM	319.44±131.34	291±131.5	0.22
U. NA	72.52±39.28	87.5±42.7	0.041*

*Significant difference. S. OSM: Serum osmolality, U. OSM: Urea osmolality, U. NA: Urea sodium, SD: Standard deviation

Table 4: Correlation of mortality with level of hyponatremia

Serum sodium levels	Number of death *n*=19 (%)	Number of discharged *n*=81 (%)
≤120 (*n*=72)	12 (16.6)	60 (83.3)
121-125 (*n*=6)	1 (16.6)	5 (83.3)
>125 (*n*=22)	6 (27.3)	16 (72.7)

P=0.34, No significant difference in the mortality rate

hypertonic solutions (3% or 5%) was 18.18%, in salt tables it was found 14.29%, in furosemide it was around 20.00%, and

Table 5: Treatments used and mortality

Treatment used	Number of cases (%)	Number of deaths (%)
Isotonic saline (0.9%) infusion	57 (57.0)	8 (14.04)
Fluid restriction	41 (41.0)	4 (9.76)
Demeclocycline	16 (16.0)	3 (18.75)
Hypertonic saline (3% or 5%)	11 (11.0)	2 (18.18)
Salt tablets	7 (7.0)	1 (14.29)
Furosemide	5 (5.0)	1 (20.00)
Vasopressin receptor antagonists	3 (3.0)	0 (0.00)

in vasopressin receptor antagonist, it was around 0% means no death was found in this treatment.

DISCUSSION

Hyponatremia is the most common electrolyte disorder in hospitalized patients. Hyponatremia is important to recognize because of the potential morbidity, mortality, and the economic impact on the patient and the health care. Studying the etiology, risk factors, and management of hyponatremia in hospitalized patients will help in reducing its incidence and minimize the complications associated with hyponatremia. Symptoms range from nausea and malaise, with mild reduction in sodium, to lethargy, decreased level of consciousness, headache [Table 2] and if severe seizures and coma. Overt neurological symptoms most often are due to very low serum sodium levels usually <115 mEq/L, resulting in intracerebral osmotic fluid shifts, and brain edema.

In a study done by Hoffman *et al.*,[8] in year 2015, stated that exercise-associated muscle cramping, dehydration, hyponatremia, and nausea or vomiting during exercise up to 30 h in hot environments are unrelated to total sodium intake, despite a common belief among ultramarathon runners that sodium is important for the prevention of these problems.

Cumming *et al.*[9] in his study on hyponatremia found in 26% of patients and were highly prevalent while in our study it is 15% with $P < 0.001$. They found that dehydration and prescription of thiazide diuretics and proton pump inhibitors were the potential causative factors and not SIADH. In our study, we also found the mortality rate during or while treatments of hyponatremia [Table 5].

Hypovolemic causes of hyponatremia include acute corticosteroid withdrawal, cerebral salt wasting, diuretic use, gastrointestinal loss, iatrogenic (insufficient volume, use of hypotonic solutions), and skin loss. Normovolemic causes include adrenal insufficiency, drug-induced: Selective serotonin reuptake inhibitors, opioids, and oxytocin. Opioids are a group of drugs that are regularly prescribed for palliative care patients. Hypothyroidism and SIADH are other important causes of normovolemic hyponatremia. Hypervolemic causes of hyponatremia include acute renal failure, cirrhosis, and congestive heart failure. In cancer patients, who form a

majority of palliative care patients, hyponatremia is caused mainly by SIADH and salt wasting. Cancers of the lung, breast, head, and neck are the ones commonly associated with hyponatremia caused mostly by SIADH. Among these, lung cancer has the worst prognosis which can be compounded by the increase in mortality caused by hyponatremia.

Clinical parameters that have been previously found to be associated with thiazide-induced hyponatremia are age,[10,11] female sex,[12,13] lower body weight,[10,11] hypokalemia,[11-14] and concurrent use of other medications that impair water excretion.[12] However, these reported findings remain controversial because they were derived from case reports or case series that were limited by small sample sizes and lack of comparison groups.

Potts *et al.* suggested that vasopressin 2 receptor antagonists might be effective against hyponatremia in neurosurgical patients.[15,16] Further studies about the optimal treatment for hyponatremia in traumatic brain injury patients, e.g., studies examining the use of active sodium supplementation, mineralocorticoids, and/or vasopressin 2 receptor antagonists, are needed.

CONCLUSION

Hyponatremia is a common electrolyte abnormality found in hospitalized patients in general medical and surgical wards. It is more common in elderly critically ill patients admitted to the ICU. Hypertension and diabetes mellitus as pre-existing co-morbidity were present in the majority of patients and it predisposed the patients to hyponatremia. Thiazide diuretics were the single most important etiology of hyponatremia. Vomiting and poor intake were also a significant cause of hyponatremia in this study. Other major causes of hyponatremia were renal disorders, SIADH, congestive heart failure, and chronic liver disease. Hyponatremia was found to be related to multiple etiological factors in a large number of patients. Treatment of hyponatremia with hypertonic saline should be restricted to the patients with severe hyponatremia and those with neurological symptoms of hyponatremia. Treatment with hypertonic saline is safe provided gradual correction of hyponatremia is followed. Osmotic demyelination syndrome is a rare complication related to the treatment of hyponatremia and should be suspected in a case of hyponatremia who develop fresh neurological deficits while on treatment or after treatment with hypertonic saline. Severe hyponatremia is associated with considerable mortality in patients with underlying medical diseases as advanced cirrhosis. A systematic approach to the diagnosis of hyponatremia with the application of simple diagnostic algorithms using history, clinical examination, and laboratory findings to establish the mechanism of hyponatremia can significantly improve the assessment and management of hyponatremia.

This study had several limitations. First, it was a single-center retrospective study involving a small population of critically ill patients admitted to ICU. Second, no information was obtained about the patient's daily fluid and sodium balance. In addition, the patient's long-term outcomes were not evaluated.

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