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Incidence And Clinical Profile Of Hyponatremia Among Patients Admitted In The Respiratory Care Unit Of A Tertiary Care Hospital In South India

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Abstract

Background:
Hyponatremia is particularly common in the intensive care unit (ICU) where both access to water and renal water handling are impaired in critically ill patients often afflicted with multiorgan system failure

Aim:
To assess the incidence of hyponatremia among the patients admitted in ICU and to study their clinical profile.

Methodology:
A prospective study was conducted in the respiratory care unit of R.G.Kar Medical College, Kolkata for a period of one year. All Adult patients above 18 years of age admitted in Respiratory care unit were included for the study. Patients with serum sodium level less than 135mmol/L were studied for clinical profile and patients with pseudo hyponatremia and hypertonic hyponatremia are excluded in our analysis.

Results:
In our study out of 358 patients admitted in ICU 128 patients had hyponatremia with a incidence rate of 35.7% among which 28.4% had sodium levels between 125 – 135 mmol/L and the remaining 9.4% had the sodium levels <125 mmol/L. Among the various types of hyponatremia euvolemic hypotonic was found to be the most common type of hyponatremia. SIADH (syndrome of inappropriate anti-diuretic hormone) was the most common cause for hyponatremia and pneumonia was found to be the most common cause for SIADH. Increase in age, presence of CNS symptoms, severe hyponatremia cases and increase in the duration of ICU stay are the various factors which influenced in causing death among the hyponatremia patients.

Conclusion:
Evaluating the cause for hyponatremia and treating it would prevent considerable morbidity and mortality associated with this enigmatic electrolyte disorder.

Keywords: hyponatremia, SIADH, respiratory care unit, euvolemic hypotonic

Introduction

Sodium plays a vital role in maintaining cellular homoeostasis and total sodium body content is the key determinant of extracellular fluid volume and, in most circumstances, effective arterial blood volume.[1] Several diseases and conditions can disrupt the delicate balance between intake and output of water and sodium, and serum sodium measurements are therefore among the most commonly performed laboratory tests.[2] Abnormalities in serum sodium, generally defined as hyponatremia if sodium concentration is <135 mmol/l and as hypernatremia if

sodium concentration is >145 mmol/l, virtually always result from disturbances in water balance, with excess or deficit body water relative to body sodium content.[3,4]

Hyponatremia is predominantly accompanied by hypotonicity but can also occur under isotonic or even hypertonic conditions; for example, in the event of elevated glucose, where water is translocated from the intracellular fluid to the extracellular fluid, resulting in hyponatremia without sodium being excreted.[5] Because total body sodium can be decreased, normal, or increased in the presence of hyponatremia, hyponatremia is often classified according to the hydration status of the patient into hypovolemic, euvolemic, or hypervolemic hyponatremia.[3] It occurs in up to 30% of hospitalised patients and can lead to a wide spectrum of clinical symptoms, from subtle to severe or even life threatening.[6,7] It also frequently accompanies pulmonary diseases, both infectious and neoplastic.[8] With respect to pneumonia, a recent single-centre cohort study found the incidence of hyponatremia at hospital admission among CAP patients to be 28%.[9]

Hyponatremia is particularly common in the intensive care unit (ICU) where both access to water and renal water handling are impaired in critically ill patients often afflicted with multiorgan system failure. The incidence of hyponatremia in the ICU has been reported to be about 30%.[10] 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.[11] 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.[12,13]

Early diagnosis and treatment can prevent complications such as worsening condition of the neurological patient, prolonged hospital stay, and rate of mortalities. The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is considered as one of the main causes of hyponatremia among adult neurological patients. Hyponatremia can also be due to the syndrome of cerebral salt wasting (CSW) characterized by polyuria and natriuresis because of intracerebral problems. It seems that higher atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) levels are associated with increased hyponatremia and natriuresis in patients with acute brain injury especially following subarachnoid hemorrhage (SAH).[14] Administration of hypotonic fluids is among the main causes of iatrogenic hyponatremia in hospitalized cases.[15] As very few studies in this part of India were conducted on incidence and clinical profile of hyponatremia among the ICU patients and so this study was ascertained to study the frequency, aetiology and outcome of hyponatremia in critically ill patients admitted to the ICU.

Aim: To assess the incidence of hyponatremia among the patients admitted in ICU and to study their clinical profile.

Methodology:

A prospective study was conducted in the respiratory care unit of R.G.Kar Medical College, Kolkata for a period of one year. All Adult patients above 18 years of age admitted in Respiratory care unit were included for the study. Patients with serum sodium level less than 135mmol/L were studied for clinical profile and patients with pseudo hyponatremia and hypertonic hyponatremia are excluded in our analysis. The study was started after getting the clearance from the institutional ethical committee and the informed consent was obtained from all the patients involved in the study. A total of 358 patients were admitted in the respiratory care unit during our study period. All patients admitted in RCU are initially evaluated with proper history and clinical examination followed by routine blood investigations along with serum sodium and potassium, serum osmolality, urine osmolality, urine spot sodium, serum cortisol and serum T3, T4, TSH was done wherever indicated, imaging studies was performed as relevant to the admission. Patients with serum sodium level less than 135mmol/L were considered as hyponatremia and levels less than 125 mmol/L are considered as severe hyponatremia. Serum sodium

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estimation was done in the Automated Analyzer by Ion Selective Electrode (ISE) technology. With the clinical evaluation of volume status and other blood investigations reports patients are classified into hypo, iso or hypervolemic hyponatremia. Based on the type of hyponatremia and severity of symptoms patients are treated on by taking into account the guidelines and the formula. Serum sodium levels are checked 4 th hourly during rapid correction, daily and as and when needed. Patients clinical parameters were recorded while treatment. Serum glucose levels were also checked and in patients having hyperglycemia corrected serum Na+ levels were calculated using the standardized formulas. All data are entered and analysed using SPSS version 21. Mean and standard deviation was calculated for all the parametric variables. Chi-square test and student T test was used to derive the statistical inference.

Results:

In our study out of 358 patients admitted in ICU 128 patients had hyponatremia with a incidence rate of 35.7% among which 28.4% had sodium levels between 125 – 135 mmol/L and the remaining 9.4% had the sodium levels <125 mmol/L. The age wise incidence of hyponatremia among the study subjects was shown in table 1 and it is seen from the table that the mean age for mild hyponatremia (125 – 135 mmol/L) was 65.8 and for severe hyponatremia (<125 mmol/L) it was 76.3 years and it proves that as age increases the severity of hyponatremia increases. Among the gender the incidence of hyponatremia is almost similar in both males and females and there is no statistical significant difference between the two (table 2). Among the various types of hyponatremia euvolemic hypotonic was found to be the most common type of hyponatremia followed by hypervolemic and hypovolemic hypotonic hyponatremia, as we excluded hypertonic hyponatremia in our study (table 3). Of the various co-morbidities present in the patients hypertension was found to be the most common co-morbidity which is seen in 66.7% of the patients with hyponatremia followed by diabetes which is seen in 28.9% of the subjects. Lethargy, drowsiness and confusion were the common CNS symptoms present in our patients, seizure was seen in 4% of the patients and only 4 patients were found to be comatose. All the hyponatremia patients were evaluated for identifying the etiology and it was found that SIADH (syndrome of inappropriate anti-diuretic hormone) was the most common cause for hyponatremia followed by other causes like liver disorder, heart disease, kidney disorder, multifactorial causation etc. SIADH had shown a strong significant association for both mild and severe hyponatremia (table 4). Evaluating the various causes for SIADH we found causes related to respiratory system was found to be the most common which includes pneumonia, respiratory failure, asthma and small cell carcinoma of lung and among all these causes pneumonia had shown a statistical significant association for mild and severe hyponatremia (table 5). All the patients with hyponatremia were treated with sodium replacement therapy based on their requirements during their stay in the ICU. The mean stay in ICU for mild hyponatremia was only 5.7 days whereas for severe hyponatremia it is 9.2 days and it shows a statistical significant difference in the ICU stay between mild and severe hyponatremia (table 6). Among the 128 patients with hyponatremia who got admitted in ICU 20 patients had expired and the remaining 108 patients had improvement in their sodium status and got discharged from ICU. The various factors which had influenced death among the hyponatremia patients are increase in age, presence of CNS symptoms, severe hyponatremia cases and increase in the duration of ICU stay, as all these factors had shown a statistical significant association ($p<.05$) (table 7).

Discussion:

Hyponatremia being the most common electrolyte disorder among the hospitalized patients and more so in ICU admitted patients. It is important to recognize hyponatremia at an early stage because of its potential morbidity and mortality and also the economic impact on the patient and the health care. Identifying the etiology and risk factors and targeting it earlier would help in reducing and minimizing the complications associated with hyponatremia. Symptoms of hyponatremia ranges from nausea and malaise associated with mild reduction in sodium, to lethargy, decreased level of consciousness, headache, seizures and coma associated with severe hyponatremia.[16] Particularly in patients with traumatic brain injury the risk of complications like cerebral edema is more within first 48 h of onset due to water shift into brain cells because of low osmolality as compared to chronic hyponatremia

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(onset >48 h), as most of compensatory mechanisms are not fully developed in acute hyponatremia.[17-20] Thus, if hyponatremia is corrected appropriately within this duration, serious complication like malignant brain edema can be prevented. In the present study the incidence of hyponatremia was found to be 35.7% and the results are in par with the study conducted by by Sakr etal and colleagues in which they quoted the incidence of dysnatremia was between 25% - 45% out of which 82% were hyponatremia and only 18% had hypernatremia.[21] In another study done by **R**ajesh Padhi etal found that the frequency of hyponatremia on ICU admission was 34.3% of all ICU admissions and another study done by DeVita *et al reported* hyponatremia to occur in about 30-40% of ICU patients.[22,23] In the present study, unlike many other studies, no association was found between gender and severity of hyponatremia (P = 0.817). The incidence of hyponatremia is higher in the elderly, owing to the impaired water and electrolyte homeostasis due to dietary and environmental variations.[24] In accordance with other reports [25-27] in our study, hyponatremia was more prevalent among the elderly patients than in the younger patients.

Symptoms of hyponatremia range from mild (nausea, headache, and lethargy) to severe (seizures and coma).[28] In our study, symptoms were correlated with severity of hyponatremia, confusion was significantly high in patients with severe hyponatremia. A study by Rahil *et al*. showed CNS involvement in 24.5% of the patients with symptoms that ranged from confusion to coma.[29] Similarly, in our study, majority of the patients had altered sensorium, which was more common with severe hyponatremia. In the present study, nearly half of the study population had a history of hypertension, and nearly one-third had a history of diabetes mellitus. Similar findings were reported in a study by Rao *et al* wherein hypertension and diabetes were the most common comorbid conditions in majority of the patients.[30] Hyponatremic hypertensive syndrome is a well-known entity wherein the most common association is in patients with essential hypertension receiving diuretics, which interfere with the metabolism of a variety of electrolytes and cause electrolyte imbalance.

In the present study euvolemic hyponatremia (47%) was most common type of hyponatremia followed by hypervolemic (33%) and hypovolemic hyponatremia was the least. Similar trend was seen by Patni et al (49%), Bennani *et al*, Rao etal and Prakash Babaliche etal.[30-33] Virtually, an excess of ADH concentration, usually caused by the SIADH or depletion of effective circulating volume, is the main cause of hyponatremia. In the present study, SIADH was the most common cause of hyponatremia noted in nearly half of the study population. Laczi reported that SIADH was the most common cause of euvolemic hyponatremia in their study in Hungary.[34] Another study by Panicker and Joseph on the clinical profile of hyponatremia in ICU hospitalized patients reported SIADH as a predominant cause for hyponatremia.[35] Our study revealed the major cause for SIADH was pneumonia of infective etiology followed by respiratory failure, asthma and small cell carcinoma of lung, similarly Bryant implied SIADH as a cause in patients with infectious pulmonary disease such as pulmonary TB.[36] Cockcroft *et al*. reported severe hyponatremia caused by SIADH which led to miliary TB in a 74-year-old woman.[37] Similarly, Weiss and Katz reported hyponatremia resulting from SIADH in patients with pulmonary TB.[38] In our study, severe hyponatremic patients had longer ICU stay, had longer ventilator days and had an increased mortality, similar to our study Shakhe *et al*. also found an increased mortality and ICU length of stay and increased ventilator days among severe hyponatremic patients admitted to ICU.[39]

Conclusion:

Hyponatremia is a frequent fi nding in the critically ill; most of these patients are euvolumic. SIADH is the most common cause of hyponatremia in critically ill. pneumonia being the leading cause of SIADH. Clinicians need to be aware about the common occurrence of hyponatremia, its early identification, and its association with a large variety of diseases. Evaluating for the cause of hyponatremia is equally important, as treating the underlying cause would prevent considerable morbidity and mortality associated with this enigmatic electrolyte disorder.

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Table 1: Age wise incidence of hyponatermia among the study subjects

Age group	Sodium level 125 – 135 mmol/L	Sodium level <125 mmol/L	P value
40 – 50 (n=88)	11 (12.5%)	3 (3.4%)	<.0001
51 – 60 (n=74)	15 (20.2%)	6 (8.1%)	
61 – 70 (n=91)	36 (39.5%)	8 (8.7%)	
71 – 80 (n=74)	19 (21.6%)	11 (14.8%)	
81 – 90 (n=31)	13 (41.9%)	6 (19.3%)	
Total (n=358)	94 (28.4%)	34 (9.4%)	
Mean ± SD	65.8 ± 9.1	76.3 ± 7.8	

percentage indicates row percentage

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Table 2: Gender wise incidence of hyponatremia among the study subjects

Age group	Sodium level 125 – 135 mmol/L	Sodium level <125 mmol/L	P value
Male (n=198)	51 (25.7%)	19 (9.5%)	0.817
Female (n=160)	43 (26.8%)	15 (9.3%)	
Total (n=358)	94 (28.4%)	34 (9.4%)	

percentage indicates row percentage

Table 3: Distribution of the study subjects based on the type of hyponatremia

Type of hyponatremia	Frequency	Percentage
Euvolemic hypotonic	72	56.2%
Hypervolemic hypotonic	35	27.3%
Hypovolemic hypotonic	21	16.4%
Total	128	100%

Table 4: Various etiologies for hyponatremia among the study subjects

Etiology	Sodium level 125 – 135 mmol/L	Sodium level <125 mmol/L	P value
SIADH	30 (31.9%)	13 (38.2%)	<.001
Heart failure	10 (10.6%)	5 (14.7%)	
Multifactorial	15 (15.9%)	4(11.7%)	
G I loss	5 (5.3%)	3 (8.8%)	
Renal disorders	8 (8.5%)	4 (11.7%)	
Chronic liver disease	14 (14.8%)	3 (8.8%)	
Hypothyroidism	7 (7.4%)	2 (5.8%)	
Drugs	5 (5.3%)	0	
Total	94 (100%)	34 (100%)	

percentage indicates column percentage

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Table 5: Causes for SIADH among the study subjects

Causes for SIADH	Sodium level 125 – 135 mmol/L (n=30)	Sodium level <125 mmol/L (n=13)	P value
Pneumonia	12 (40%)	6 (46.1%)	<.05
Respiratory failure	6 (20%)	2 (15.3%)	
Asthma	5 (16.6%)	3 (23%)	
Small cell carcinoma of lung	2 (6.6%)	2 (15.3%)	
Meningitis	5 (16.6%)	0	

percentage indicates column percentage

Table 6: Distribution of the study subjects based on the duration of stay in ICU

Duration of stay in ICU	Sodium level 125 – 135 mmol/L (n=94)	Sodium level <125 mmol/L (n=34)	P value
<5 days	25 (26.6%)	3 (7.6%)	<.01
5 – 7 days	50 (53.3%)	8 (23%)	
7 – 10 days	19 (20%)	18 (53.8%)	
>10 days	0	5 (14.7%)	
Mean ± SD	5.7 ± 2.2	9.2 ± 2.6	

percentage indicates column percentage

Table 7: Various factors influencing the outcome of the study subjects

Factors		Patient status		P value
		Improved (n=108)	Expired (n=20)	
Age	**<70 (n=79)**	74 (68.5%)	5 (25%)	**<.001**
	>70 (n=49)	34 (31.4%)	15 (75%)	
Gender	**Male (n=70)**	58 (53.7%)	12 (60%)	0.318
	Female (n=58)	50(46.2%)	8 (40%)	
Type of hyponatremia	**Euvolemic hypotonic (n=72)**	66 (61.1%)	6 (30%)	0.0814
	Hypervolemic	25 (23.1%)	10 (50%)	

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	hypotonic (n=35)			
	Hypovolemic hypotonic (n=21)	17 (15.7%)	4 (20%)	
CNS symptoms	**Present (n=98)**	82 (75.9%)	16 (80%)	**<.001**
	Absent (n=30)	26 (24%)	4 (20%)	
Serum sodium levels	**125 – 135 mmol/l (n=94)**	86 (79.6%)	8 (40%)	**<.01**
	<125 mmol/l (n=34)	22 (20.3%)	12 (60%)	
SIADH status	**Present (n=43)**	34 (31.4%)	9 (45%)	0.0718
	Absent (n=85)	74 (68.5%)	11(55%)	
ICU stay	**<7 days (n=86)**	79 (73.1%)	7 (35%)	**<.01**
	>7 days (n=42)	29 (26.8%)	13 (65%)	

percentage indicates column percentage

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