A prospective study on clinical profile of hyponatremia in ICU hospitalized patients

Paniker G.I.* and Joseph S.

Department of Medicine, Yenepoya Medical College, Yenepoya University, University Road, Mangalore, Karnataka State, South India 575018

*Correspondence Info:
Dr. Georgy Itty Panicker MD,
Assistant Professor,
Department of Medicine, Yenepoya Medical College, Yenepoya University
University Road, Mangalore, Karnataka State, South India 575018
E-mail: georgy.doc@gmail.com

Abstract
Background: Hyponatremia is the commonest electrolyte abnormality noticed in the ICU which has a diverse variety of manifestations.
Aims: To determine the incidence, etiology and profile of clinical features for varying degrees of hyponatremia in 100 adult patients admitted to Yenepoya Medical College Hospital, Mangalore during the study period September’ 2012 to October’ 2012.
Methods: A prospective cross-sectional study on Clinical Profile of Hyponatremia of 100 patients was undertaken after institutional clearance and with informed consent at Yenepoya Medical College Hospital to study 100 patients of hyponatremia.
Results: Severe hyponatremia was noticed in 13% of study population. The commonest manifestation was confusion and the commonest etiology was SIADH, pneumonia being the most significant reason. Mortality was seen in 4%, all secondary to carcinoma.
Conclusion: Hyponatremia occurs in association with a wide variety of systemic conditions and with treatment with accompanying variety of clinical manifestations. Hyponatremia also is influenced by seasonal variations and occurs more often during the monsoon season.
Keywords: Hyponatremia, pneumonia,

1. Introduction
The incidence of hyponatremia is roughly 12% in ICU hospitalized patients. The precise incidence of hyponatremia varies depending on the conditions leading to and the criteria used to define it. Hyponatremia represents excess of body water relative to body sodium content and is frequently referred to as a serum sodium concentration of less than 135 mEq/L.1, 2

Hyponatremia is the most common electrolyte disorder, reported to occur in up to 6% of hospitalized patients.3 Mild hyponatremia plasma sodium 130 - 135 mmol / l is found in as many as 15 - 30% of hospitalized patients or in the institutionalized elderly.4 Clinically hyponatremia is often unrecognized when it is mild or when it develops slowly. But severe hyponatremia (plasma sodium < 120 mmol / l), particularly of rapid onset, is associated with substantial morbidity and can be life threatening.5 Also moderate to severe hyponatremia bears a substantial associated morbidity and mortality.6

Hyponatremia is associated with varying morbidity. Morbidity varies widely in severity; serious complications can arise from the disturbances itself as well as from the underlying causative conditions. Errors in assessment and management play to a significant extent. Hyponatremia is also an important predictor of mortality in heart failure, cirrhosis and acute pancreatitis. Unfortunately, hyponatremia is more often iatrogenic. Traditional therapies have significant limitations. Newer agents especially those that antagonize arginine vasopressin at V2 receptor or both the V1a and V1b receptors show promise for treating hypervolemic and euvolemic hyponatremia, as they induce desired free water diuresis without inducing sodium excretion. Management of hyponatremia depends upon speed of recognition, its onset, magnitude and severity and associated risk factors especially for neurological complications.

1.1 Effects of Hyponatremia on the Brain and Adaptive Responses
Within minutes after the development of the hypotonicity, water gain causes swelling of the brain and a decrease in osmolarity of the brain cells. Partial restoration of brain volume occurs within a few hours as a result of cellular loss of electrolytes (rapid adaptation). The normalization of brain volume is completed within several days through loss of organic osmolytes from brain cells (slow adaptation). Low osmolarity in the brain persists despite the normalization of brain volume. Proper correction of hyponatricity reestablishes normal osmolarity without risking damage to the brain. Overly aggressive correction of hyponatremia can lead to irreversible brain damage. Therefore correction of hyponatremia must take into account the chronicity of the condition. Acute hyponatremia (duration less than 48h) can be safely corrected more quickly than chronic hyponatremia.11

1.2 Etiology
Based on the initial assessment of volume status, medical history and laboratory measurements of urine osmolarity and sodium, patients with hypotonic hyponatremia can have their hyponatremia classified into one of the three main categories: i) Hypovolemic, ii) Hypervolemic, iii) Euvolemic. On the basis of volume status, urine osmolarity and urine sodium, patients with hyponatremia can be categorized into one of three clinically important classes of hyponatremia: hypovolemic, euvolemic, or hypervolemic.

1.3 Clinical Features
Although most patients with hyponatremia may appear asymptomatic, severe symptomatic hyponatremia is a medical emergency that calls for immediate treatment. Signs and symptoms depend on several factors and vary by patient. The rate of decline in serum sodium concentration, the patient’s age, and the volume of extracellular fluid (ECF) all affect the clinical presentation.9 The clinical manifestations of hyponatremia are related to osmotic water shift leading to increased ICF volume, specifically brain cell swelling or cerebral edema. Patients may be asymptomatic or complain of nausea and malaise. As the plasma Na+ concentration falls, the symptoms progress to include headache, lethargy, confusion and obtundation. Stupor, seizures and coma do not usually occur unless the plasma Na+ concentration falls acutely below 120 mmol/L or decreases rapidly. As described above, adaptive mechanisms designed to protect cell volume occur in chronic hyponatremia. When assessing a patient with hyponatremia, the aim is to determine the probable cause of the hyponatremia and decide the best...
way to treat it. Extracellular fluid volume status, symptoms and signs, the rate at which hyponatremia developed and the severity of the hyponatremia are assessed.

An accurate history and physical examination can help determine evidence of underlying illness such as congestive cardiac failure, cirrhosis or nephrotic syndrome, Addison’s disease (pigmentation), hypopituitarism and hypothyroidism. In practice, evaluation of volume status may be challenging but it should be estimated by skin turgor, pulse rate, postural blood pressure difference and jugular venous pressure, together with examination of fluid balance charts. Measurement of central venous pressure may also be necessary. The symptoms of hyponatremia are primarily neurological and are related both to the severity and, particularly to the rapidity of fall in the plasma sodium concentration.

Patients with mild hyponatremia (plasma sodium 130-135 mmol/L) of any duration are usually asymptomatic. Nausea and malaise are the earliest symptoms typically seen when the plasma sodium concentration falls below 125-130 mmol/L. Headache, lethargy, restlessness and disorientation may follow as the sodium concentration falls below 115-120 mmol/L. With severe and rapidly evolving hyponatremia, seizure, coma, permanent brain damage, respiratory arrest, brain stem herniation and death may occur. 46,47

Concomitant metabolic disturbances (acidosis, hypoxia) usually compound the symptomatic severity. Gastrointestinal symptoms, such as nausea and vomiting, are more common in patients with serum sodium levels between 125 and 130 mEq/L. 27 Acute hyponatremia (less than 48 hours in duration) in a previously asymptomatic young adult can cause severe central nervous system symptoms even at serum sodium levels between 125 and 130 mEq/L. 2,48

Once the level falls below 125 mEq/L neurologic symptoms predominate. 27 Headache, muscle cramps, reversible ataxia, psychosis, lethargy, restlessness, disorientation, apathy, anorexia and agitation are symptoms seen in patients with serum sodium levels below 125 mEq/L. 27 Clinical signs include abnormal sensorium, hypothermia, depressed reflexes, pseudo bulbar palsy, and Cheyne-Stokes respiration. 5 Hypotonic hyponatremia causes entry of water into the brain, resulting in cerebral edema.

Because the surrounding cranium limits expansion of the brain intracranial hypertension develops, with a risk of brain injury. Solutes leave brain tissues within hours, thereby inducing water loss and ameliorating brain swelling. 49,50 This process of adaptation by the brain accounts for the relatively asymptomatic nature of even severe hyponatremia if it develops slowly. Nevertheless, brain adaptation is also the source of the risk of osmotic demyelination. 51-53 Although rare, osmotic demyelination is serious and can develop one to several days after aggressive treatment of hyponatremia by any method, including water restriction alone. 54-56

Shrinkage of the brain triggers demyelination of pontine and extrapontine neurons that can cause neurologic dysfunction, including quadriplegia, pseudo bulbar palsy, seizures, coma and even death. Hepatic failure, potassium depletion and malnutrition increase the risk of this complication. 50,57

2. Materials and Methods

A prospective cross-sectional study on Clinical Profile of Hyponatremia of 100 patients was undertaken after institutional clearance and with informed consent at Yenepoya Medical College Hospital to study 100 patients of hyponatremia analyzed and reported by the biochemistry laboratory from September 2011 to October 2012. Hyponatremia was defined as serum sodium of < 135 mEq/L. Information regarding age and sex distribution, clinical diagnosis were collected. The data were analyzed statistically. All patients underwent complete clinical examination of blood pressure, pulse rate and systemic examination.

Biochemical investigations included random blood sugar, blood urea, complete blood picture, serum creatinine and electrolytes, complete urine picture, urine osmolality, serum osmolality and urine sodium which was done in hospital biochemistry department. Chest –ray, TFTs, 2D echocardiography and ultrasound abdomen were done when indicated.

3. Results and Discussion

A total of 100 patients were included in the study. These patients were admitted in Yenepoya Medical College between October 2011 and September 2012.

3.1 Demographics

The study included 63% males and 37% females.

3.2 Age Distribution

There was no specific age preference. However patients below 18 yrs were excluded from the study. The patients in the study population predominantly belonged to the age groups 51 - 60 yrs and 61 - 70 yrs. The mean age was found to be 55.05 years ± 2SD.
3.3 Demographic distribution

Age-wise distribution showed that there was an equal incidence in hyponatremia in males and females in the age group 51 - 60 yrs. However there was a significant difference with male predominance in the age groups 41 - 50 yrs and 61 - 70 yrs.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Males</th>
<th>Females</th>
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<tbody>
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<td>31-40</td>
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<td>91-100</td>
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3.4 Seasonal Distribution of hyponatremia for the patients included in the study

When patients with hyponatremia were distributed on a monthly basis, admissions followed this pattern:
- December – February (Winter) : 19
- March – May (Summer) : 28
- June – September (Monsoon) : 46

3.5 Co-relation of age distribution in females included in the study to clinical profile of hyponatremia

Symptomatic age group in females was predominantly the elderly population (51 – 80) yrs with confusion being the commonest manifestation, seizures and coma also occurring in the same age group.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Confusion</th>
<th>Hemiparesis</th>
<th>Seizure</th>
<th>Psychosis</th>
<th>Tremor</th>
<th>Coma</th>
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3.6 Co-relation of age distribution in males included in the study to clinical profile of hyponatremia:

Symptomatic age group in males was predominantly the population belonging to (41 – 80) yrs with confusion being the commonest manifestation, seizures and coma also occurring in the same age group. However, confusion, seizure and coma were much more common in the 51 – 60 yrs age group.

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<th>Psychosis</th>
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Confusion

In our study of total of 100 patients, 34 patients had presentation of confusion which was highest among all variables.
Hallucination: 4 patients included in the study population had hallucinations.

Seizures: 14 patients in the study population had seizures.

Hemiparesis: 16% of the study population had hyponatremia and associated hemiparesis.

Acute Psychosis: 3% of the study population suffered from acute psychosis.

Coma: 12% of the study population had coma.

Tremors: 4 patients in the study population had associated tremors.

The study comprised of 36% and 30% patients with past history of DM and HTN respectively.

Respective profile of hyponatremia noted during the study:
Confusion: (34%)
Tremors: (4%)
Hallucinations: (8%)
Seizures: (9%)
Psychosis: (3%)
Hemiparesis: (16%)
Coma: (12%)
Clinical profile at serum sodium level < 120 mEq / L

Confusion: (9)
Tremors: (1)
Hallucinations: (3)
Seizures: (6)
Psychosis: (0)
Hemiparesis: (3)
Coma: (7)

Figure No.13: Clinical profile at serum sodium level < 120 mEq / L

Clinical profile at serum Sodium level 120 - 125 mEq / L

Confusion: (12)
Tremors: (1)
Hallucinations: (5)
Seizures: (3)
Psychosis: (1)
Hemiparesis: (5)
Coma: (4)

Figure No.14: Clinical profile at serum Sodium level 120 - 125 mEq / L

Clinical profile at serum Sodium level 125 - 135 mEq / L

Confusion: (13)
Tremors: (2)
Hallucinations: (0)
Seizures: (0)
Psychosis: (2)
Hemiparesis: (8)
Coma: (1)

Figure No.15: Clinical profile at serum Sodium level 125 - 135 mEq / L

3.7 Systemic Involvement

In our study respiratory system was involved most which was present in 46 % of study population and CNS involvement was found in 23 % which was second most common.

Figure No.16: Systemic Involvement

3.8 Etiological classification

4 patients presented with gastroenteritis causing hyponatremia. Bronchogenic carcinoma (4%), Brain metastasis (2%) and Liver metastasis (1%) were the malignancies noted during the study. Major cause of hyponatremia was respiratory diseases, namely Pneumonia (33%) being the commonest and PTB (7%). Stroke (16%) and Meningitis (7%) were the neurological causes for hyponatremia and the second most common cause of hyponatremia during the study. CCF and renal failure causing hyponatremia were 16% and 9% respectively.
4. Conclusion

Out of 2750 patients admitted to ICU during the study period (from September 2011 to October 2012) at Yenepoya Medical College Hospital, 124 patients (4%) had various degrees of hyponatremia. This was lower in comparison to the study done by Chatterjee et al’ on descriptive study of hyponatremia (16.4%). Out of 100 patients studied, male sex was predominant (63%). which was similar to the study done by Huda et al’. However the study done by Ashraf et al’ showed a female predominance (71%). Age distribution were between 11 – 80 years of which majority were above 41 years and mean age was 55.05 ± 2D. 68% were between ages 41 – 70 years. Average lifespan of males and females in Karnataka as per 2000 Population Reference Bureau and 2001 Census of India are 62.4 and 65.5 years respectively. Considering this data, hyponatremia was common in elderly age group. Out of the 100 cases, predominant cause for hyponatremia was SIADH. In an Indian study by Lath et al, the most common causes of hyponatremia were SIADH and diuretics. The commonest cause for SIADH in our study was respiratory infections (pneumonia, PTB) and stroke. Huda et al’ in his study on hyponatremia had just 2% of patients with renal failure and no patients with hyponatremia with cardiac disease. This is in contrast to our study which comprised of 16% and 9% of CCF and renal disease respectively. Gill et al’ in his study had 5% patients with liver disease but our study showed one. Confusion was seen in 34% of patients which is much lesser than that reported by Ellis in his study where 76% of the patients had clouding of consciousness and, 11% had coma which was similar to both studies. Seizures were seen with moderate to severe hyponatremia. In the study by Chatterjee et al’ large fraction of cases (48.21%) was asymptomatic. This study comprised of 60% asymptomatic patients. Seasonal variation was noted in this study with 46.0% patients presenting during monsoon season and 28% during summer. This was probably due to variations in the ambient temperature influencing
insensible fluid losses that could possibly have altered hydration status and sodium balance. Chakrapani et al in his study of Seasonal variation of Incidence in hyponatremia concluded that hyponatremia is higher during the peak monsoon season which had a similar pattern for our study period. Mortality was seen only in the group with severe hyponatremia and majority was due to bronchogenic carcinoma accounting for 4 deaths during the study period. Study done by Gill et al also showed similar result of deaths occurring with severe hyponatremia.

References