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Review Article

Internal Medicine Section

Clinical Profile and Prevalence of Hyponatremia in Critically-ill Patients of All Age Groups

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ABSTRACT

Hyponatremia is defined as a serum sodium level of <135 mEq/L. It is the most prevalent electrolyte imbalance encountered in hospital admissions around the world. Hyponatremia has been reported to be present in between 3.4% to 39.4% of hospital admissions, and it is substantially more prevalent in an Intensive Care Unit (ICU). It has been connected to an increase in mortality, hospital stays, and morbidity. An imbalance of specific ionised salts (sodium, potassium, calcium, bicarbonate, and chloride) in the blood is known as an electrolyte problem. Volume abnormalities are the main cause of disturbances in salt homeostasis, which largely produce neurologic symptoms. Serious consequences arise when these electrolyte imbalances worsen, which are frequent clinical issues in the ICU. Hyponatremia has a multifaceted aetiology and it can be of three types: euvolemic, hypovolemic, or hypervolemic hyponatremia. Regardless of being a frequently encountered electrolyte disturbance, hyponatremia is poorly acknowledged. Its relationship with a myriad of fundamental illnesses and its many aetiologies with varying pathological and physiological pathways make diagnosis problematic. Clinicians should be skilled at recognising the symptoms, causes, and aetiologies of hyponatremia when treating sick patients. The signs, symptoms, and causes of hyponatremia should be readily apparent to clinicians treating unwell patients. The present review focuses on the symptoms and clinical findings of hyponatremia in the critically-ill patient and discusses the types, pathophysiology, and clinical profile of these patients.

Keywords: Electrolyte imbalance, Homeostasis, Intensive care unit, Pathophysiology

INTRODUCTION

In critically-ill patients of all ages, hyponatremia, described as a blood sodium content of less than 135 mmol/L, is a common electrolyte disturbance. Abnormal serum sodium concentrations are known to affect normal physiological function, and various investigations have demonstrated that hyponatremia may have negative effects. Due to the nature of the illnesses causing admissions to the ICU and iatrogenic intervention, critically-ill patients hospitalised in the ICU are especially susceptible to suffering from low sodium levels [1,2].

Aetiology

The volume status of the Extracellular Fluid (ECF) can be used to categorise the causes of hyponatremia. A patient can be categorised as hypovolemic, euvolemic, or hypervolemic depending on the volume of ECF. Hypovolemic hyponatremia is associated with low plasma volume and results from various causes such as gastrointestinal fluid loss as in diarrhoea and vomiting, cerebral salt wasting syndrome, diuretics-induced hyponatremia due to thiazides, and mineralocorticoid deficiency. On the other hand, euvolemic hyponatremia accounts for 60% of all hyponatremia cases, with the commonest cause being the Syndrome of Inappropriate Secretion of Antidiuretic Hormone (SIADH). Other causes may include glucocorticoid deficiency, hypothyroidism, and drugs like vasopressin analogs such as desmopressin and oxytocin. Hypervolemic hyponatremia is seen in congestive heart failure, cirrhosis of the liver, nephrotic syndrome, and chronic kidney disease [3].

Risk Factor and Lifestyle Conditions Lead to Hyponatremia

Hyponatremia can occur in people who use diuretics to prevent water retention, as well as in athletes who perspire a lot during exercise. To correctly diagnose and treat this electrolyte imbalance, it is essential to understand the unique risk factors for hyponatremia in each gender. Women, due to their smaller size, lower lean muscle mass, and greater water retention, are more susceptible to hyponatremia than men. The likelihood of developing hyponatremia increases with age, as alterations in kidney and/or adrenal gland function can deteriorate the body's capacity to maintain appropriate sodium levels. Several factors can elevate the risk of hyponatremia, including dehydration, excessive alcohol use, high-sodium meals, certain drugs or supplements, intense physical activity, and prolonged exposure to hot temperatures [4].

Pathogenesis

The kidneys' processing of filtered sodium and the stimulation of thirst all contribute to maintaining serum sodium and osmolality. The normal range for plasma osmolality is between 275 and 290 mOsm/kg. The amount of water consumed and excreted must balance to maintain proper osmolality. Both hyponatremia and hypernatremia result from an imbalance between water intake and excretion. The thirst mechanism, activated when body osmolality reaches 295 mOsm/kg via osmoreceptors in the hypothalamus, regulates water consumption. Antidiuretic Hormone (ADH), produced in the hypothalamus and stored in the posterior pituitary gland, closely controls water excretion. ADH secretion increases or decreases in response to tonicity changes. Increased ADH secretion triggers water reabsorption in the kidneys, while suppression has the opposite effect. Although less sensitive than osmoreceptors, baroreceptors in the carotid sinus can also trigger ADH secretion [5].

Many different conditions can lead to hyponatremia [6]. These include endocrine, nutritional, metabolic, cardiovascular, renal, or hepatic disorders, in addition to common viral infections. It is important to note that admission hyponatremia and hospital-acquired hyponatremia are two types of hyponatremia linked to hospitals and may have distinct consequences. Patients with hyponatremia may present with no symptoms, especially if they are older or have mild hyponatremia. Conversely, a wide range of symptoms, including nausea, confusion, headaches, and vomiting, are present in the majority of moderate to severe, as well as acute, instances of hyponatremia. Severe cases may also lead to delirium, impaired awareness, and seizures [7,8].

Since even slight drops in plasma sodium have been found to be linked to a poor prognosis, hyponatremia should not be ignored as a benign finding in the field of neurological illnesses. In fact, hyponatremia has been demonstrated to be an independent predictor of mortality in a variety of settings, including stroke patients, adults with tuberculous meningitis, and children with pneumococcal meningitis [9-11].

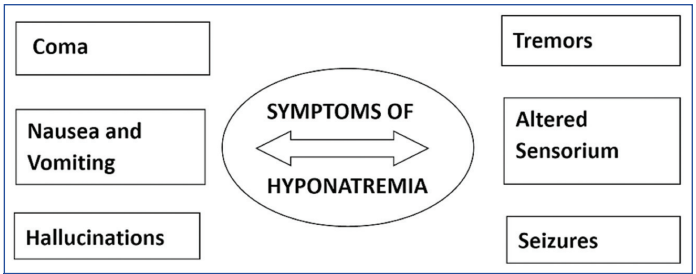
The correlation between hyponatremia and persistent inflammation is not well understood by many medical practitioners due to the non specific presentation of hyponatremia, which contributes as a risk factor for both surgical and medical patients. Therefore, early identification of symptoms, prudent fluid usage to save lives, and careful medication selection with consideration of fluid status can all be key factors in reducing patient morbidity, mortality, and duration of hospital stay [12,13].

The challenge of identifying the cause of hyponatremia in clinical practice is the motivation behind this review. In ICU settings, there is limited data on clinical presentation and aetiology, especially for patients experiencing moderate to severe hyponatremia. Clinicians must, therefore, be mindful of the widespread prevalence of hyponatremia, its early detection, and its associations with a wide range of illnesses. This review will focus on the symptoms and clinical profile of hyponatremia in paediatric and older age group patients, aiming to assist healthcare workers in better addressing this issue.

Symptoms Associated with Hyponatremia

Parajuli S et al., conducted a descriptive cross-sectional investigation over a 6-month period involving 102 patients. The trial included patients over the age of 18 with a normal serum sodium level during admission and a longer ICU stay than one day. The study recorded any changes in levels during the ICU stay as well as the serum sodium concentration during admission. Out of the included ICU patients who had hyponatremia, nine individuals were found to be symptomatic, and 12 were found to be asymptomatic. Their investigation revealed that confusion was the most prevalent symptom, affecting five patients. Among these, three were affected by Acute Gastroenteritis (AGE), one by kidney disease, and one by Subacute Haemorrhage (SAH). Patients between the ages of 40 and 60 were most affected. The research found that 57.14% of participants had no symptoms, indicating a high prevalence of 17.7% for hyponatremia [14].

Clinical hyponatremia symptoms mainly express Central Nervous System (CNS) dysfunction. The pattern of symptoms corresponds to the level of hyponatremia. An expert group has suggested a biochemical scale for measuring the seriousness of hyponatremia, serving as the foundation for the classification presented below. Symptoms of moderate hyponatremia may be limited to fatigue, mild cognitive impairment, and gait dysfunction. Patients with mild hyponatremia should be carefully examined before being considered asymptomatic, as thorough examination almost invariably reveals minor neurocognitive deficits. Conversely, the presence of severe neurological symptoms, as opposed to only slightly lower Sodium Plasma (PNa) levels, may prompt medical professionals to consider other potential reasons for neurological impairment. In mild hyponatremia, non specific symptoms like headaches, nausea, vomiting, and stomach cramps predominate the clinical picture [Table/Fig-1]. Restlessness, lethargy, disorientation, delirium, and, in severe cases, coma, seizures, and brain herniation leading to long-term brain damage and mortality are to be anticipated. Furthermore, the progression of symptoms is mainly unexpected, and despite a minor PNa reduction, the patient's clinical status could rapidly deteriorate. Therefore, seizures are regarded as the main factor causing new-onset epilepsy in the ICU and are acknowledged as the initial indicator of hyponatremia. Hypercapnic neurogenic respiratory failure, largely observed in young women in the postoperative situation, is one of the extra-neurological effects of hyponatremia [15].



[Table/Fig-1]: Showing common symptoms of hyponatremia.

Hyponatremia in Adults and Elderly Patients

Hyponatremia is the most common electrolyte disturbance observed in hospitalised patients. In a study conducted on critically-ill patients who spent 48 hours or longer in the ICU, it was demonstrated that the only modifiable factor associated with ICU-acquired hyponatremia was net volume balance. New-onset hyponatremia occurred in 16.2% of critically-ill medical patients who initially had a normal sodium concentration at the time of ICU admission. Furthermore, individuals with ICU-acquired hyponatremia were more likely to require renal replacement therapy. The study also revealed that individuals with higher potassium concentrations at ICU admission had a higher prevalence of ICU-acquired hyponatremia. These findings suggest that a single potassium concentration measurement taken at the time of ICU admission may be useful in predicting eventual hyponatremia acquired in the ICU. Additionally, the study examined several management profiles to determine if there were any modifiable causes of ICU-acquired hyponatremia. It was found that the two groups-the ICU-acquired hyponatremia group and the normonatremia group-had different net volume balances and used sodium bicarbonate and FFP [16].

Stieglmair, S et al., demonstrated that positive fluid balance accounted for the sole cause of ICU-acquired hyponatremia in 25% of patients undergoing cardiothoracic surgery. Their investigation found that both groups had similar ICU death rates, but patients with ICU-acquired hyponatremia were more likely to require renal replacement therapy [17]. The clinical profile of hyponatremia patients in the adult, old age, and paediatric age groups has been presented in [Table/Fig-2] [16,18-24].

Authors Heading adults and old age groups	Presence of hyponatremia	Clinical profile	Management
Sim JK et al., [16]	217 developed hyponatremia out of 1342 patients in ICU	Haematological malignancy	ICU patients more likely to require renal replacement therapy
Rai NK et al., [18]	100 patients of hyponatremia	Altered sensorium, vomiting, seizures	----------
Rao MY et al., [24]	100 patients of hyponatremia	Drowsiness, lethargy; SIADH and diuretics commonly involved	----------
Soiza RL and Talbot HS [20]	----------	Nausea, confusion, Immobility, falls	Isotonic saline (0.9%) infusion, loop diuretics in hyponatremia with SIADH
Paediatric age group			
Berhanu Y et al., [19]	165 out of 422 patients	Sepsis, meningitis, altered consciousness	422 patients, 69 (16.4%) underwent surgery, and 22 (31.9%) underwent laparotomy

Pintaldi S et al., [21]	142 out of 824 patients	Infection, increased C-reactive protein, high erythrocyte sedimentation rate	----------
Prasad D et al., [22]	264 out of727 patients	Respiratory illness, septicemia, acute diarrhoea	----------
Sitaraman S and Saxena M [23]	185 out of 500 patients	Meningitis most common, pneumonia, diarrhoea	----------

[Table/Fig-2]: Clinical profile in hyponatremia patients [16,18-24].

An observational research study involving 100 hyponatremia patients aged 14 years or older, with serum Na+ levels below 130 meq/L, was conducted to determine the clinical presentation of patients with hyponatremia. The study found that 43 individuals exhibited altered levels of consciousness, disorientation, or coma, and 56 patients had severe hyponatremia. Elderly individuals are more likely to have co-morbid illnesses such as hypertension, diabetes, and ischaemic heart disease, which are risk factors for hyponatremia. Additionally, they are more likely to be taking medications that can cause hyponatremia, such as diuretics. Studies have shown that males are more affected by hyponatremia than females [18].

One investigation also demonstrated that men are more likely than women to be affected. In their study, the Syndrome of Inappropriate Antidiuresis (SIAD) and renal failure were the two most frequent causes of hyponatremia. According to the Nandakumar et al., study [25], SIAD was the most common cause of hyponatremia (38.3%). In Paniker and Joseph's investigation, the primary causes of hyponatremia included stroke and respiratory infections (such as pneumonia and pulmonary tuberculosis) [26]. However, in Chatterjee, N et al.,s study, gastrointestinal fluid loss was found to be the most common underlying predisposing cause for hyponatremia, followed by cerebral accidents and pulmonary infections [27].

An observational study involving 100 ICU patients with hyponatremia and those who developed hyponatremia during hospitalisation was conducted to determine the clinical profile and its correlation with liver function tests. Alteration of the sensorium and chronic liver disease were the most frequently observed traits, and both were statistically significant. The two most prevalent co-existing diseases in patients with hyponatremia were diabetes mellitus (11%) and hypertension (24%) [28].

To determine the effect of the severity of hyponatremia on the in-hospital mortality of neuro-critically-ill patients, an observational study involving 903 patients was conducted in the neurosurgical ICU. In their study, 359 patients had hyponatremia, and the most frequent co-morbidities were cancer and hypertension, while the most frequent causes of ICU admission were brain tumours and intracerebral haemorrhage. In-hospital mortality did not significantly differ between the hyponatremia group and the group without hyponatremia. However, the ICU stay for the hyponatremia group was longer than that of the groups without hyponatremia. In critically-ill patients with neurological conditions, mild to moderate hyponatremia was not linked to positive clinical outcomes. However, there was a strong correlation between severe hyponatremia and in-hospital death rate. The major cause of hyponatremia in these patients, despite the multifaceted aetiology of hyponatremia in neuro-critically-ill patients, were SIAD and cerebral salt wasting syndrome [29].

A population-based retrospective analysis was conducted, and during the nine-year study period, 14,359 individuals aged 18 years and older with a primary diagnosis of low sodium level and 57,382 controls were found. They discovered that patients admitted for hyponatremia experienced a significantly elevated subsequent mortality rate that was unrelated to co-existing illness. Men experienced this increase more than twice as much as women did in the groups with cardiovascular disease, liver disease, and cancer [30].

Over 18 months, a cross-sectional observational investigation was conducted to examine the aetiology and clinical characteristics of hyponatremia and determine the proportion of patients who presented with the condition and required admission to a medical ICU. Among the ICU admissions, the various symptoms related to hyponatremia included delirium, convulsions, frequent falls, malaise, drowsiness, disorientation, and lethargy. hyponatremia in these patients was mainly due to SIADH. Lower survival was linked to lower serum sodium at admission. A worse outcome was linked to inadequate or inadequately corrected hyponatremia in the first 24 hours [31].

Hyponatremia in Children

A retrospective cross-sectional study was conducted to assess the extent of hyponatremia and its contributing factors in children, utilising records of 422 paediatric patients hospitalised in the paediatric critical care unit [19]. Among the 422 medical records, hyponatremia was present in 165 of them. Almost all patients displayed altered levels of consciousness. At the time of admission, 176 people had CNS diseases, with 146 of those instances being meningitis. Critically-ill children under the age of five were twice as likely to have hyponatremia than those between the ages of 5 and 15, possibly due to the increased risk of developing the condition due to their small bodies, resulting in their high water concentration, and elevated arginine vasopressin levels in response to their illness. Underweight children have a three times higher risk of developing hyponatremia than their peers. The analysis also indicated that hospital stays longer than two weeks were associated with a threefold increase in the incidence of hyponatremia, which is consistent with research from Saudi Arabia [32]. Additionally, individuals who spend more time in the hospital were more likely to have complications and to consume medications that could potentially result in hyponatremia [33].

To discover the cause of hyponatremia and its relationship to mortality, a retrospective analysis of 525 hyponatremia patients older than 14 years was conducted. Patients were placed into groups according to the severity of their hyponatremia: mild, moderate, and severe. In their investigation, the prevalence of hyponatremia was 5.26%. In the elderly population, which included those older than 60, it was 6.1%. In all three groups, the most common primary illnesses causing hyponatremia were malignant tumours and infectious infections. Lung cancer was the most prevalent malignant tumour among them, while pneumonia was the most prevalent infectious condition linked to hyponatremia. Patients with moderate to severe hyponatremia frequently experienced cerebral haemorrhage, with subarachnoid haemorrhage being the main primary illness linked to this range of hyponatremia; in contrast to patients with mild hyponatremia, individuals with moderate or severe hyponatremia had a higher death rate. The incidence of moderate to severe hyponatremia increased with the usage of medications like diuretics. Hospital deaths were most probable in patients with moderate to severe hyponatremia [34].

A retrospective cross-sectional study was conducted to evaluate the prevalence and severity of hyponatremia in children under the age of 14 years who were admitted to the paediatric ICU and received vasopressin for atleast 24 hours. The study involved 176 seriously ill paediatric patients. They discovered that the usage of vasopressin was linked to lower sodium levels and a higher risk of heart surgery. The severity of the hyponatremia was not significantly influenced by the vasopressin dose [35].

To ascertain the prevalence and illness correlations of hyponatremia, a cross-sectional study involving 164 children admitted to ICUs from one month to 15 years old was carried out. According to their study, children with malnutrition were more likely to have hyponatremia, which was found in 41% of children, the majority of whom had mild cases (34%) when they were admitted [36]. Similar studies showing the prevalence and clinical profile in the paediatric and adult population are presented in [Table/Fig-2] [16,18-24].

CONCLUSION(S)

Hyponatremia is a common electrolyte disorder in patients presenting to the ED, especially in elderly patients. Critically-ill patients suffer from hyponatremia due to various causes, including hypovolemia, diuretics, heart failure, cirrhosis of the liver, as well as SIADH. It presents with various symptoms and is linked to high morbidity and mortality in patients, resulting in a longer duration of hospital stay. Therefore, physicians should be aware of the signs, symptoms, and clinical profile of patients in order to reduce mortality and morbidity, and provide better care to the patients.

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