

Hyponatremia: A Clinical and Practical Approach

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ABSTRACT

Hyponatremia is a frequent trouble encountered in patients manifesting with unfocused features. The etiology can be multiple, and diagnosis of each cause is demanding. Hyponatremia may be euvoletic, hypovolemic, or hypervolemic. Appropriate analysis of a variety of laboratory investigations helps distinguish the various types of hyponatremia. Management differs with the character of start, whether it is acute or chronic, severity and features.

Keywords: Critical care, Electrolytes, Hyponatremia.

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INTRODUCTION

Hyponatremia is defined as a serum sodium <135 mEq/L.¹ This condition is a chronic and constant nightmare to clinicians and pathologists due to its varied or broader etiopathogenesis. Multiple etiologies and variety of symptoms make it a puzzle which cannot be solved easily. Varying and ever-changing guidelines did not help the cause. These articles pave light to the disorder and its management. Hyponatremia is the electrolyte disorder typically present in day-to-day life of physician, with a stated occurrence of 15–30%.² It creates substantial diagnostic and management trouble for clinicians. This state has many reasons and influencing factors. The important and immediate attention should be given for the prompt and correct identification of the reason and its management. In the delicate setting, management frequently has to be started before an optimistic judgment can be made and results of helpful biochemical investigations are obtainable. Both over treatment and under treatment can create overwhelming effects on cerebral function.³

A frequent clinical problem, hyponatremia commonly increases in hospitalized patients. Although morbidity varies extensively in severity, grave problems can occur from the disorder itself as well as from mistake in management.⁴

MATERIALS AND METHODS

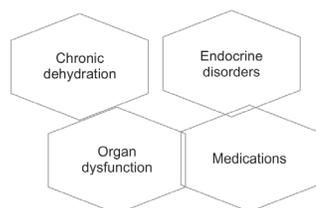
The review article was searched based on MESH terms, hyponatremia, causes, pathogenesis, and management. The data search was extensively done on PubMed, Google scholar, and Google sites.

PREVALENCE

Hyponatremia (serum sodium level <135 mEq/L) is the most frequent electrolyte defect in hospitalized patients with the stated occurrence in range 5% to almost 35% in foreign countries.^{5,6}

Increased mortality, duration of hospital stay, and emerging of complications are unknown implications of hyponatremia.^{7,8}

CAUSES OF HYPONATREMIA^{9–11}



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Medications

Diuretics, antidepressants, opioids, and drug-ecstasy.

Endocrine Disorders

Hypothyroidism and hypocortisolism, SIADH (syndrome of inappropriate ADH secretion), and Addison's disease.

Organ Dysfunction

Heart failure, kidney, and liver diseases.

Excessive Diuretic Therapy

Hyponatremia as such can be categorized based on the volume of body fluid, low, normal, and high volume. Low happens when something happens leading to loss of body fluid. Circumstances that can guide to incorrectly low sodium measurements elevated blood sugar, protein, and deranged lipid profile.^{11–13}

SYMPTOMS OF HYPONATREMIA^{11,14}

Acute hyponatremia has a typical start of symptoms in less than 48 hours. Patients build up neurological features causing from cerebral edema causing seizures, altered mentation leading to coma, and death.

CHRONIC HYPONATREMIA

Hyponatremia just beginning over >48 hours. Major chunk of patient population is suffering from this. The serum sodium concentration is usually above 120 mEq/L. There is a protective adaptive mechanism of brain to reduce the degree of cerebral edema. Hence, in chronic hyponatremia, patients may appear

symptom less. Mild hyponatremia can cause vague nausea vomiting, and rarely subclinical neurologic defect may be present when the serum sodium is between 120 mEq/L and 130 mEq/L. Hyponatremia in the elder person may be obviously visible with recurrent falls and gait instabilities.

Hyponatremia is divided as pseudohyponatremia, true and translocational hyponatremia.

Normal serum osmolality is 280–295 mOsm/kg. Pseudohyponatremia is due to hypertriglyceridemia or multiple myeloma. In regular subjects, the plasma water is 93% of the plasma volume. Plasma water part falls lower than 80% in cases with noticeable hyperlipidemia (triglycerides >1500 mg/dL) or hyperproteinemia (protein >10 mg/dL).¹⁵ Rise in blood urea causes the hyponatremia in renal failure.¹⁶

True hyponatremia is having a fall in serum osmolality and is divided into hypervolemic, hypovolemic, and euvolemic based on volume status.^{17–19}

Mineralocorticoid deficit is another main reason of hypovolemic hyponatremia and may be connected with hyperkalemia.²²

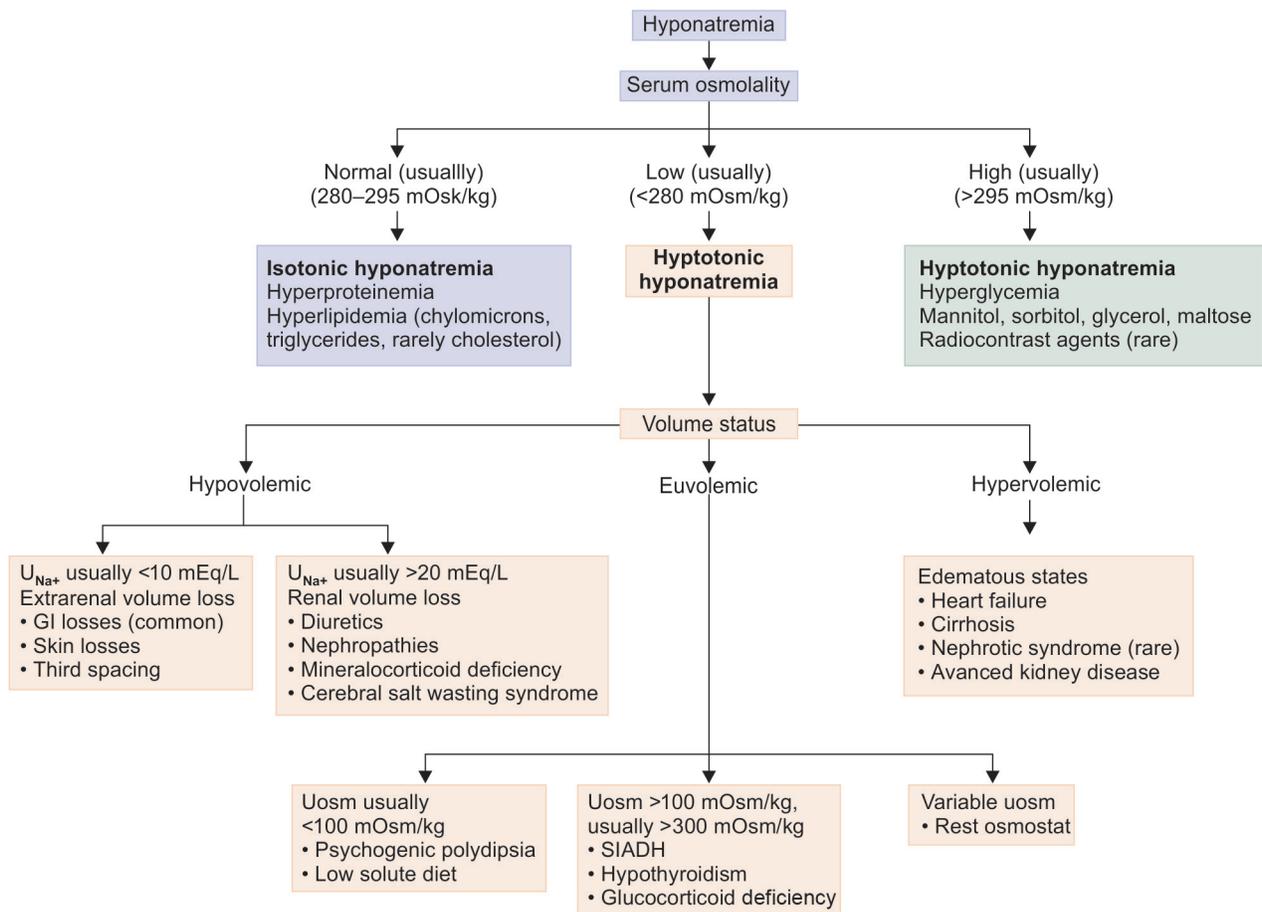
Euvolemic Hyponatremia

Sixty percent of case population has this type of hyponatremia. The usual reason of euvolemic hyponatremia is SIADH.¹⁰

Hypervolemic Hyponatremia²³

The main causes included are congestive cardiac failure, cirrhosis, and nephritic syndrome. In these cases, sodium in the body is augmented, but total body water (intracellular and extracellular fluid) is unreasonably extended leading to hyponatremia and edema.²⁴ Hyponatremia linked with CCF may also be exacerbating by diuretics management. Many studies have showed that the growth of hyponatremia in this state will have worsened prognosis.^{23,26}

TYPES OF HYPONATREMIA¹²



Hypovolemic Hyponatremia

Reduction in plasma volume may be secondary to renal cause or nonrenal cause.^{20,25} Diuretic-persuaded hyponatremia is common with thiazide diuretics, and usually it begins soon after commencement of drug, may be serious, and is frequent in elder female gender.²¹

MANAGEMENT OF HYPONATREMIA

The management of hyponatremia depended mainly on its commencement, etiology, and symptomatology. Early assessment of any patient with hyponatremia engages in recognition of the start of the state (acute or chronic), the occurrence of features, and evaluation of quantity grade. A previous analysis of disease of liver,



kidney, and heart has to be seen, as well as earlier electrolytes to differentiate acute from chronic hyponatremia. Any blood loss or extracellular fluid should be identified. An exact drug history and history of signs of headache, nausea, seizures, and confusion, which point to raised intracranial pressure should be noted. On physical examination, a precise measurement of the patient's volume status is significant.

Measurement or investigation of²⁷⁻³¹

- Serum osmolality,
- Urine osmolality,
- Urine sodium,
- Serum sodium,
- Urine to serum electrolyte ratio,
- Fractional excretion of sodium,
- Serum uric acid and urea concentrations,
- Acid-base and potassium balance,
- Saline infusion,
- Thyroid investigations, adrenal stimulation tests, CT/MRI brain, and imaging of chest.

Each investigation will be needed to differentiate the different types of hyponatremia.

The treatment of hyponatremia will be based on the volume status, length of hyponatremia (whether acute less than or equal to 48 hour or chronic more than 48 hours), presence or absence of symptoms, and cause of hyponatremia.^{32,33}

STUDIES RELATED TO HYPONATREMIA (TABLE 1)

Elderly patients in USA were included in a study on their demographic profile with regards to hyponatremia and it showed that SIADH, diuretics, and SSRIs were common causes and it had significant age-related morbidity and mortality.³⁴

In a study done in India among patients staying in hospital, confusion, headache, and tiredness were the most frequent symptoms, of them two patients had seizures, and 20% patients showed no symptoms. Nausea was significantly more frequent in patients with hyponatremia. Twenty-two patients (31.4%) had hyponatremia during their stay in the hospital. Most had multiple causative factors, reduced eating being the most common (82.9%), followed by augmented losses of blood (65.7%), and various factors (70.0%). Drugs, fluid excess, and unsuitable Ryle's tube feeds more usually precipitated hyponatremia in patients.³⁵

Shapiro et al. did a study which was done for about 5 months in the medicine wards. Eighty-six patients aged more than 65 years with serum sodium levels less than or equal to 125 mEq/L were incorporated. The occurrence of hyponatremia was 6.2%. The frequent reason of hyponatremia was the syndrome of inappropriate antidiuretic hormone secretion (SIADH) causing euvolemic hyponatremia.³⁶

A study was conducted among patients in hospital and found the result of severe hyponatremia with regards to mortality and duration of hospital stay, on the whole death, was 27% in hyponatremic patients in comparison to 9% in nonhyponatremic patients, and length of admission was longer in hyponatremic patients.³⁷

In a study, patients who had severe hyponatremia were evaluated in comparison with patients who gained severe hyponatremia in a 3-month hospital stay. In hospital-gained hyponatremia, treatment started significantly later and the

Table 1: Studies showing hyponatremia, causes, and treatment

Study	Year	Findings
Kutz A et al.	2020	Occurrence of hyponatremia was highest during summer season and as directly correlating with outdoor temperature, and in their population, it showed a higher female preponderance.
Alessandro Peri	2019	Vaptans are very useful in maintaining the serum sodium levels even after early correction and discharge of the patient from the hospital.
Ganguli et al.	2015	Initial hyponatremia was seen in 8.71% (n = 53) and 4.1% (n = 25) had chronic hyponatremia in the study population. The major causes of hyponatremia included SIADH and thiazide diuretics, and SSRIs.
Agarwal et al.	2011	Nausea was significantly more frequent in patients with hyponatremia. 31.4% had hyponatremia during their stay in the hospital. Drugs, fluid excess, and unsuitable Ryle's tube feeds more usually precipitated hyponatremia in in patients.
Shapiro et al.	2010	The prevalence of hyponatremia was 6.2% (8.1% female and 4.0% male). The frequent reason of hyponatremia was the syndrome of inappropriate antidiuretic hormone secretion (SIADH), whose cause could be found in only 46% of cases.
Gill et al.	2006	Mortality and duration of hospital stay were more in hyponatremic patients when compared to normonatremic patients.
Hoorn et al.	2006	At admission, hyponatremia had better detection and early correction when compared to hospital stay-gained hyponatremia, and it was directly proportional to duration of hospital stay.
Annane et al.	2009	Oral conivaptan was safe and effective in hyponatremia (euvolemic and hypervolemic).
Gerbes et al.	2003	An orally active vasopressin receptor antagonist can correct hyponatremia in patients with cirrhosis and ascites.

duration of hospitalization was longer. Factors that added to hospital-gained hyponatremia incorporated: thiazide diuretics, drugs stimulating antidiuretic hormone, surgery, and hypotonic intravenous fluids.³⁸

In a study done on occurrence of hyponatremia with seasonal variations as a primary outcome, it showed raised occurrence of hyponatremia during summer when the outdoor temperatures were highest and especially prevalent in elderly female patients.³⁹

STUDIES RELATED TO MANAGEMENT OF HYPONATREMIA

In a study with oral conivaptan, a V1A/V2-receptor antagonist, 83 patients with serum [Na] less than 130 mEq/L were randomly assigned to placebo or conivaptan 40 or 80 mg/day for 5 days. Oral conivaptan was efficient in rising serum sodium and it had greatest effect on euvolemic hyponatremia.⁴⁰

In a study, the effects of VPA-985, an orally active vasopressin V2 receptor antagonist, in patients with cirrhosis and dilutional

hyponatremia were investigated. Normalization of serum sodium concentration was attained in 27% and 50% of patients in the VPA-985 100 mg/day and 200 mg/day groups, respectively, but in none of the patients in the placebo group.⁴¹

In an analysis done by Alessandro Peri, he has stated that concurring with previous trails, vaptans had an ability to maintain serum sodium level post discharge from hospital, which have been diagnosed and corrected as euvolemic and hypervolemic hyponatremia.⁴²

SUMMARY

The correct diagnosis and cause of hyponatremia are essential in management of patients particularly hospitalized patients. The electrolyte imbalance if correctly diagnosed and treated can avoid mortality and reduce morbidity. Normal saline outlines the root of management for hypovolemic hyponatremia, while 3% NaCl and fluid limit are important for euvolemic hyponatremia. Hypervolemic hyponatremia responds well to fluid constraint and diuretic drugs.

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