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+15878858911
editorial-office@sciformat.ca

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DIAGNOSTIC PITFALLS AND THERAPEUTIC CHALLENGES IN HYPONATREMIA IN ADULTS: A SYSTEMATIC REVIEW

Aleksandra Golec (Corresponding Author, Email: golec.aleksandra2@gmail.com)

Górnośląskie Centrum Medyczne im. Prof. Leszka Gieca Śląskiego Uniwersytetu Medycznego w Katowicach,
Katowice, Poland
ORCID ID: 0009-0004-9105-350X

Emilia Koziara

Samodzielny Publiczny Zakład Opieki Zdrowotnej MSWiA im. Sierżanta Grzegorza Załogi w Katowicach,
Katowice, Poland
ORCID ID: 0009-0005-4454-6085

Mateusz Gadzina

Samodzielny Publiczny Zakład Opieki Zdrowotnej MSWiA im. Sierżanta Grzegorza Załogi w Katowicach,
Katowice, Poland
ORCID ID: 0009-0001-6153-4896

Wojciech Sontag

Zagłębiowskie Centrum Onkologii Szpital Specjalistyczny im. Sz. Starkiewicza, Dąbrowa Górnicza, Poland
ORCID ID: 0009-0004-6749-0224

Julia Gawlak

Szpital Specjalistyczny im. Jędrzeja Śniadeckiego w Nowym Sączu, Nowy Sącz, Poland
ORCID ID: 0009-0002-4586-4200

Zofia Tarnawska

Samodzielny Publiczny Szpital Kliniczny im. Andrzeja Mielęckiego Śląskiego Uniwersytetu Medycznego w
Katowicach, Katowice, Poland
ORCID ID: 0009-0004-2265-8089

Karolina Figiel

Szpital Powiatowy w Chrzanowie, Chrzanów, Poland
ORCID ID: 0009-0002-2227-5198

Mateusz Gawin

Sosnowiecki Szpital Miejski sp. z o. o. w restrukturyzacji, Sosnowiec, Poland
ORCID ID: 0009-0006-7409-9586

Mateusz Zawisza

Górnośląskie Centrum Medyczne im. Prof. Leszka Gieca Śląskiego Uniwersytetu Medycznego w Katowicach,
Katowice, Poland
ORCID ID: 0009-0003-1981-6640

Maciej Krzesimir Kuświk

University Hospital in Poznań, Poznań, Poland
ORCID ID: 0009-0006-1925-204X

ABSTRACT

Hyponatremia is the most common disorder of water and electrolyte balance in adult clinical practice and remains a frequent cause of diagnostic uncertainty and treatment-related harm. Although the definition of hyponatremia is straightforward, its interpretation requires assessment of tonicity, chronicity, symptoms, volume status, renal water handling, medications, endocrine disease, and the risk of overly rapid correction. This systematic review summarizes current evidence on diagnostic pitfalls and therapeutic challenges in adult hyponatremia, with particular emphasis on hypotonic hyponatremia, syndrome of inappropriate antidiuresis, thiazide-associated hyponatremia and severe symptomatic presentations. PubMed/MEDLINE and PubMed Central were searched for English-language publications concerning adult hyponatremia, diagnostic pathways, correction strategies, and treatment complications. Clinical guidelines, reviews, systematic reviews, randomized trials, and observational studies were included. The literature indicates that common errors include failure to exclude pseudohyponatremia or hypertonic hyponatremia, overreliance on clinical volume assessment, delayed measurement of urine osmolality and urine sodium, under-recognition of drug-induced causes, and inadequate monitoring during therapy. Therapeutic challenges include balancing urgent treatment of cerebral edema against prevention of osmotic demyelination, managing unpredictable water diuresis, and individualizing therapy in SIAD, heart failure, cirrhosis and thiazide-associated disease. A structured, physiology-based approach can improve diagnostic accuracy and reduce avoidable harm.

KEYWORDS

Hyponatremia, SIAD, Diagnostic Pitfalls, Hypertonic Saline, Osmotic Demyelination, Thiazide-associated Hyponatremia

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Introduction

Hyponatremia, commonly defined as a serum sodium concentration below 135 mmol/L, is one of the most frequent electrolyte abnormalities encountered in emergency departments, hospital wards, intensive care units and outpatient practice. Its apparent simplicity can be misleading. Sodium concentration is not a direct measure of total body sodium stores, but rather a reflection of the relationship between body water and exchangeable solutes. For this reason, the same biochemical value may arise from several distinct pathophysiological states, including true hypotonic water excess, hyperglycemia-associated translocational hyponatremia, pseudohyponatremia, renal salt loss, diuretic exposure, heart failure, liver disease, adrenal insufficiency, and syndrome of inappropriate antidiuresis (SIAD). The clinician therefore has to interpret sodium concentration within a broader clinical and biochemical context rather than treating the number alone (Adrogué & Madias, 2000; Verbalis et al., 2013).

The clinical importance of hyponatremia extends beyond laboratory classification. Contemporary reviews describe hyponatremia as affecting approximately 5% of adults and a much larger proportion of hospitalized patients. Even mild chronic hyponatremia has been associated with falls, gait disturbance, cognitive impairment, fractures, prolonged hospitalization and mortality, although the extent to which hyponatremia is a causal factor rather than a marker of comorbidity varies between populations (Corona et al., 2009; Rondon-Berrios & Berl, 2022; Wald et al., 2010). Severe acute hyponatremia can cause cerebral edema, seizures, respiratory arrest, and death. Conversely, overly rapid correction of chronic severe hyponatremia can lead to osmotic demyelination syndrome, a rare but potentially devastating neurological complication. This dual risk makes hyponatremia one of the most clinically delicate electrolyte disorders in adult medicine (Sterns, 2018; Bastos & Rocha, 2024).

The diagnostic process is challenging because symptoms are often nonspecific and do not correlate perfectly with the serum sodium concentration. Nausea, headache, weakness, confusion, dizziness, lethargy, gait instability, or falls may be attributed to age, neurological disease, infection, drug adverse effects, or dehydration. In older adults, the presentation may be particularly subtle, chronic hyponatremia may be

discovered only after a fall, cognitive decline, or incidental laboratory testing. At the opposite end of the spectrum, seizures, reduced consciousness or cardiorespiratory compromise require immediate treatment before a complete etiological work-up has been completed. This creates tension between diagnostic precision and urgent intervention (Rondon-Berrios & Berl, 2022; Spasovski et al., 2014).

Several evidence-based guidelines and expert recommendations have attempted to standardize evaluation and management. The European clinical practice guideline emphasized a stepwise approach based on serum osmolality, urine osmolality, urine sodium, symptoms, and risk of complications. Expert panel recommendations similarly highlighted the importance of classifying hyponatremia by tonicity, symptoms, chronicity, and underlying cause (Spasovski et al., 2014; Verbalis et al., 2013). Despite these frameworks, real-world management remains inconsistent. Observational work has shown that essential tests are frequently omitted, volume status is often misclassified, and treatment may be either insufficient for symptomatic patients or excessive for chronic cases at risk of overcorrection (Filippatos et al., 2016; Huda et al., 2006; Hoorn & Zietse, 2017).

The purpose of this systematic review is to synthesize current evidence on diagnostic pitfalls and therapeutic challenges in adult hyponatremia. The review focuses on clinically relevant problems that commonly affect patient care: distinguishing true hypotonic hyponatremia from pseudo- or hypertonic forms, interpreting urine studies, assessing volume status, recognizing drug-induced disease, diagnosing SIAD, selecting appropriate correction strategies, preventing osmotic demyelination, and managing special contexts such as heart failure, cirrhosis, thiazide-associated hyponatremia, and persistent or refractory cases. By organizing the literature around errors and decision points, this manuscript aims to provide a practical, clinically oriented framework for adult physicians.

Methodology

This manuscript was prepared as a systematic literature review following the general reporting principles of PRISMA 2020. The objective was to identify and synthesize current scientific literature concerning diagnostic errors, clinical decision-making, therapeutic risks, and management strategies in adult hyponatremia. Because the topic involves heterogeneous evidence, including guidelines, narrative reviews, observational studies, randomized clinical trials, and systematic reviews, no quantitative meta-analysis was performed (Page et al., 2021).

A literature search was conducted in PubMed/MEDLINE and PubMed Central for English-language publications involving adults. The search included studies published up to August 2026. Search terms were combined using Boolean operators and included: “hyponatremia diagnosis”, “hyponatraemia guideline”, “diagnostic pitfalls hyponatremia”, “syndrome of inappropriate antidiuretic hormone secretion”, “SIAD treatment”, “thiazide-induced hyponatremia”, “hypertonic saline hyponatremia”, “osmotic demyelination syndrome”, “overcorrection hyponatremia”, “urine osmolality hyponatremia”, “urine sodium hyponatremia”, and “severe symptomatic hyponatremia”. Reference lists of key publications were screened to identify additional relevant sources.

Eligible publications included clinical practice guidelines, expert panel recommendations, review articles, systematic reviews, randomized clinical trials, cohort studies, and clinically relevant observational studies addressing adult hyponatremia. Studies were prioritized when they directly addressed diagnostic pathways, common errors, correction strategies, SIAD, thiazide-associated hyponatremia, hypertonic saline administration, outcomes, or osmotic demyelination. Publications primarily involving pediatric patients, animal studies, isolated case reports, non-English articles, and papers not directly related to diagnostic or therapeutic decision-making were excluded from the main synthesis. Case-based evidence was considered only indirectly when summarized within systematic reviews on osmotic demyelination or related complications.

Data were extracted qualitatively, including publication type, population, diagnostic focus, therapeutic focus, and key findings relevant to clinical practice. The extracted evidence was organized into thematic categories: epidemiology and outcomes; initial diagnostic classification; pitfalls in assessment; SIAD and drug-induced hyponatremia; severe symptomatic disease; prevention of overcorrection; and management of persistent or context-specific hyponatremia. The results are presented narratively with tables summarizing diagnostic steps, common pitfalls, and therapeutic safeguards.

Table 1. Core diagnostic steps in adult hyponatremia.

Diagnostic step	Clinical purpose	Common error avoided
Confirm serum osmolality	Distinguishes hypotonic hyponatremia from pseudo- or hypertonic hyponatremia	Treating laboratory artifact or translocational hyponatremia as true water excess
Assess symptoms and chronicity	Determines urgency and risk of cerebral edema or osmotic demyelination	Correcting chronic disease too rapidly or delaying therapy in severe symptomatic disease
Measure urine osmolality	Identifies suppressed vs persistent antidiuretic activity	Missing low-solute intake, polydipsia, or SIAD-like states
Measure urine sodium	Supports classification by effective arterial volume and renal sodium handling	Misclassifying hypovolemia, SIAD, or diuretic-associated hyponatremia
Review drugs and endocrine causes	Identifies reversible causes	Prematurely labeling hyponatremia as idiopathic SIAD

Results

The reviewed literature consistently identifies hyponatremia as a high-frequency and high-risk clinical problem. Its prevalence varies according to setting, disease severity, and the sodium threshold used, but both guidelines and reviews emphasize that it is common among hospitalized adults and critically ill patients. The clinical consequences are not limited to severe acute cases. Mild and chronic hyponatremia may be associated with impaired attention, gait instability, falls, fractures, and worse outcomes, while severe acute reductions in sodium may produce neurological emergencies. This combination of frequency and potential harm explains why correct diagnostic classification is essential (Rondon-Berrios & Berl, 2022; Spasovski et al., 2014).

A central finding of this review is that diagnostic errors often occur at the very beginning of evaluation. The first task is not to decide whether sodium should be corrected, but to determine whether the patient has true hypotonic hyponatremia. Failure to measure or interpret serum osmolality can lead clinicians to treat pseudohyponatremia or hypertonic hyponatremia as if they were hypotonic states. Hyperglycemia, mannitol, glycine exposure, and laboratory artifacts associated with severe hyperlipidemia or hyperproteinemia may produce low measured sodium without the same pathophysiological implications as hypotonic water excess. Filippatos and colleagues specifically highlighted failure to exclude pseudo- or hypertonic hyponatremia as one of the major pitfalls in evaluation (Filippatos et al., 2016).

Once hypotonic hyponatremia has been confirmed, urine osmolality provides crucial information about whether antidiuretic hormone activity is appropriately suppressed. A very dilute urine suggests primary polydipsia or low solute intake, whereas urine osmolality above 100 mOsm/kg generally indicates impaired water excretion due to persistent antidiuretic effect, reduced effective arterial blood volume, renal impairment, endocrine disease, or drug effect. In practice, urine osmolality is often delayed or omitted, forcing clinicians to rely on symptoms, sodium concentration, and physical examination alone. This can obscure low-solute states, SIAD, adrenal insufficiency, and mixed etiologies (Hoorn & Zietse, 2017; Spasovski et al., 2014).

Urine sodium is another important test but is easily misinterpreted. Low urine sodium may support hypovolemia or reduced effective arterial blood volume, whereas higher values may occur in SIAD, renal salt wasting, adrenal insufficiency, and diuretic exposure. The interpretive challenge is greatest in patients receiving diuretics, older patients, and those with comorbid heart, kidney, or liver disease. Clinical assessment of volume status is often inaccurate, especially when hypovolemia is mild or when edema coexists with intravascular underfilling. Several reviews stress that hypovolemic and euvoletic hyponatremia are frequently confused in routine practice (Filippatos et al., 2016; Hoorn & Zietse, 2017; Rondon-Berrios & Berl, 2022).

SIAD emerged as one of the most important diagnostic categories in the reviewed literature. It is typically characterized by hypotonic hyponatremia, inappropriately concentrated urine, increased urine sodium, clinical euvoolemia, and absence of adrenal, thyroid, renal, and diuretic-related explanations. However, the concept of clinical euvoolemia is imperfect, and SIAD should not become a convenient label for every patient without obvious edema or dehydration. Medications, pulmonary disease, central nervous system pathology, malignancy, pain, nausea, and postoperative states can all contribute to inappropriate antidiuresis. Recent

reviews also emphasize that SIAD is best understood as a syndrome requiring active search for underlying triggers rather than as a final diagnosis (Warren et al., 2023; Thompson et al., 2016).

Drug-induced hyponatremia represents another major theme. Thiazide-associated hyponatremia is especially important because thiazide and thiazide-like diuretics are widely used for hypertension and can produce severe hyponatremia, particularly in older adults, patients with low baseline sodium, low solute intake, hypokalemia, and concurrent exposure to other sodium-lowering drugs. Recent reviews describe thiazide-induced hyponatremia as idiosyncratic and clinically variable, with acute or chronic presentations. Discontinuation of the diuretic may rapidly restore urinary diluting capacity, creating a risk of sudden water diuresis and overly rapid sodium correction if monitoring is inadequate (Clayton et al., 2006; Hoorn & Ellison, 2025; Ware et al., 2017).

Antidepressants, antiepileptics, antipsychotics, opioids, nonsteroidal anti-inflammatory drugs, desmopressin, chemotherapy, and several other agents may also contribute to hyponatremia. Medication review is therefore not a secondary step but a central diagnostic tool. The reviewed literature suggests that failure to consider drug-related mechanisms leads to repeated investigations, delayed withdrawal of the offending agent, inappropriate classification as idiopathic SIAD, and recurrence after discharge when the medication is continued or restarted (Filippatos et al., 2016; Verbalis et al., 2013).

Table 2. Frequent diagnostic pitfalls and practical safeguards.

Pitfall	Mechanism of error	Practical safeguard
Ignoring serum osmolality	Pseudo- or hypertonic hyponatremia may be mistaken for hypotonic disease	Check measured osmolality and glucose early
Overreliance on clinical volume status	Mild hypovolemia and SIAD may look similar at bedside	Combine examination with urine studies and medication history
Late urine testing	Therapy changes urine sodium and osmolality	Collect urine before major treatment when clinically safe
Premature SIAD diagnosis	Underlying malignancy, CNS disease, pulmonary disease, adrenal disease, or medication exposure may be missed	Use SIAD as a syndrome requiring cause search
Under-recognition of thiazides	Stopping the drug can trigger brisk water diuresis and overcorrection	Monitor sodium and urine output after withdrawal

The treatment literature emphasizes that the same sodium value may require very different management depending on symptoms and chronicity. Severe symptoms such as seizures, coma, marked somnolence, or respiratory distress indicate a medical emergency. Guidelines recommend prompt administration of hypertonic saline boluses to raise serum sodium by a small but clinically meaningful amount, generally 4 to 6 mmol/L, sufficient to reduce cerebral edema without attempting immediate normalization. In contrast, chronic or minimally symptomatic hyponatremia should usually be corrected slowly while the underlying cause is addressed (Rondon-Berrios & Berl, 2022; Spasovski et al., 2014; Verbalis et al., 2013).

Evidence on hypertonic saline has evolved. The SALSA randomized clinical trial compared rapid intermittent bolus with slow continuous infusion of hypertonic saline in patients with symptomatic hyponatremia. The trial found both approaches effective and safe, with no significant difference in overcorrection risk, while bolus treatment achieved early target correction more efficiently and required less relowering therapy. This supports the guideline preference for bolus-based therapy in symptomatic severe cases, provided that serum sodium is monitored closely and that clinicians are prepared to intervene if overcorrection develops (Baek et al., 2021).

Overcorrection remains the most feared therapeutic complication in chronic severe hyponatremia. The risk is not determined only by the amount of hypertonic saline administered. It is often driven by the sudden emergence of water diuresis after reversal of the stimulus for antidiuretic hormone secretion, discontinuation of thiazides, restoration of volume, treatment of adrenal insufficiency, or improvement of nausea or pain. This means that sodium may rise rapidly even when initial therapy appears conservative. Desmopressin and

electrolyte-free water may be used to prevent or reverse excessive correction in selected patients, especially those at high risk of osmotic demyelination (Sterns, 2018; Sterns et al., 2010).

Systematic review evidence on osmotic demyelination reinforces the need for individualized correction limits. Bastos and Rocha identified published adult cases of osmotic demyelination after hyponatremia correction and found that most involved severe hyponatremia, frequently with additional risk factors such as alcoholism, gastrointestinal losses, diuretic use, or hypokalemia. Importantly, demyelination was reported even when correction was below 10 mmol/L/day in a minority of cases, supporting conservative targets in high-risk patients. More recent meta-analytic work confirms that correction rate must be interpreted alongside baseline sodium, chronicity, comorbidities, and competing mortality risks (Bastos & Rocha, 2024; MacMillan et al., 2024; Shepshelovich et al., 2025).

Persistent and refractory hyponatremia is another challenge. In SIAD, fluid restriction is usually considered first-line therapy in the absence of severe symptoms, but it is frequently ineffective or poorly tolerated, particularly when urine remains highly concentrated or when adherence is limited. Alternative or adjunctive strategies include increasing solute intake, oral urea, loop diuretics with sodium supplementation, and vasopressin receptor antagonists in selected patients. Each option has limitations: urea may have poor palatability, vaptans may cause thirst and rapid correction, and loop diuretics require careful volume and electrolyte monitoring (Warren et al., 2023; Rondon-Berrios & Berl, 2022; Thompson et al., 2016).

In hypervolemic hyponatremia associated with heart failure or cirrhosis, treatment decisions are shaped by effective arterial blood volume rather than total body water alone. Fluid restriction may be difficult and only modestly effective. Loop diuretics may be required for congestion but can complicate sodium interpretation and renal function. Vaptans can increase serum sodium but require careful selection and monitoring. The reviewed literature therefore supports an individualized strategy directed at the underlying disease, symptom burden, and risk of correction rather than an isolated focus on normalizing sodium (Rondon-Berrios & Berl, 2022; Verbalis et al., 2013).

Taken together, the results indicate that adult hyponatremia is best managed through a structured, physiology-based approach. The most consistent message across guidelines and reviews is that therapy should not begin and end with a sodium value. Safe care requires confirmation of tonicity, assessment of symptoms and chronicity, measurement of urine osmolality and urine sodium when possible, medication review, consideration of endocrine disease, frequent monitoring during treatment, and attention to overcorrection risk.

A further recurring theme is the importance of endocrine evaluation. Adrenal insufficiency can present with hypotonic hyponatremia and may be mistaken for SIAD if cortisol deficiency is not considered. This is particularly relevant when hypotension, weight loss, hyperkalemia, unexplained fatigue, autoimmune disease, chronic glucocorticoid exposure, or pituitary disease is present. Hypothyroidism is often included in diagnostic algorithms, although clinically significant hyponatremia is usually associated with severe hypothyroidism or myxedema. The broader implication is that SIAD should be diagnosed only after excluding endocrine disorders that can produce similar biochemical patterns (Spasovski et al., 2014; Verbalis et al., 2013).

Low-solute intake represents another under-recognized mechanism. In patients with poor protein and salt intake, heavy beer consumption, frailty, eating disorders, or chronic illness, the kidney may be unable to excrete free water effectively despite preserved renal function. The resulting hyponatremia can correct rapidly once solute is reintroduced, creating a risk of unexpected overcorrection. This mechanism is clinically relevant because such patients may appear euvoletic, and the problem may be attributed incorrectly to SIAD unless diet and urine osmolality are assessed carefully (Filippatos et al., 2016; Rondon-Berrios & Berl, 2022).

The reviewed studies also indicate that hyponatremia frequently has mixed etiology. A patient with pneumonia may have nausea-related antidiuretic hormone release, reduced oral intake, hypotonic fluid administration, and exposure to antidepressants or diuretics. A patient with cancer may have SIAD, poor solute intake, pain, chemotherapy-related nausea, and renal impairment. A patient with heart failure may have both hypervolemic hyponatremia and diuretic-associated sodium loss. The assumption that only one mechanism is present can therefore lead to incomplete treatment and unstable sodium trajectories.

Monitoring emerged as a therapeutic intervention in itself. Guidelines and reviews repeatedly emphasize that serum sodium should be checked frequently during active treatment, particularly during hypertonic saline therapy, after discontinuation of thiazides, after correction of hypovolemia, and in patients at risk of osmotic demyelination. Urine output should be observed because sudden polyuria may signal loss of antidiuretic tone and impending rapid correction. In this setting, the clinician has to respond to the direction and speed of sodium change rather than only to the absolute value (Sterns, 2018; Sterns et al., 2010).

The evidence also suggests that discharge planning is part of safe hyponatremia management. Recurrent hyponatremia may occur if the cause is not addressed, if a thiazide or antidepressant is restarted, if fluid restriction is unrealistic, or if follow-up sodium measurement is not arranged. Chronic SIAD, heart failure, cirrhosis, and medication-related hyponatremia often require outpatient monitoring and clear communication with primary care physicians. Without this step, apparently successful inpatient correction may be followed by recurrence or inappropriate long-term therapy.

Finally, hospital systems can contribute to diagnostic error. Sodium values may be corrected in isolation by different teams, urine studies may not be ordered before intravenous fluids, medication reconciliation may be incomplete, and treatment plans may not specify correction targets. The literature supports a structured approach in which the intended daily correction limit, monitoring frequency, and rescue strategy for overcorrection are documented. This converts hyponatremia treatment from reactive sodium replacement into controlled risk management.

An additional finding is that laboratory timing can strongly influence interpretation. Urine sodium and urine osmolality obtained after saline, diuretics, or fluid restriction may no longer reflect the initial pathophysiology. Similarly, glucose correction, potassium replacement, and improvement in renal perfusion may change serum sodium independently of the apparent sodium prescription. For this reason, the earliest available paired serum and urine studies are often the most informative. If they were not obtained, clinicians should acknowledge the uncertainty and reassess the diagnosis dynamically rather than forcing the patient into a fixed category.

The reviewed literature also supports distinguishing correction targets from correction limits. The initial target in severe symptomatic hyponatremia is a small rise sufficient to improve neurological safety, whereas the daily limit represents a boundary intended to prevent demyelination. Confusing these concepts can lead to unnecessary normalization attempts. A patient may require immediate treatment and still require strict prevention of excessive 24-hour correction. This distinction should be included in treatment orders and handovers because it directly affects patient safety.

Discussion

The findings of this review support the view that hyponatremia is not merely a biochemical abnormality but a diagnostic and therapeutic process. The clinician must determine whether the sodium result reflects true hypotonicity, identify the mechanism of impaired water excretion, estimate acuity and neurological risk, and decide whether urgent correction is required. Each step is vulnerable to error. The most dangerous errors occur when clinicians either underestimate symptomatic acute hyponatremia or overcorrect chronic severe hyponatremia. Both errors can cause irreversible neurological injury, but they require opposite instincts: urgent action in one situation and restraint in the other (Rondon-Berrios & Berl, 2022; Sterns, 2018).

A major practical lesson is that serum sodium should be interpreted together with serum osmolality. Treating all low sodium values as hypotonic hyponatremia can lead to unnecessary or harmful therapy. Hyperglycemia-associated translocational hyponatremia requires correction of the osmotic driver rather than sodium-directed therapy. Pseudohyponatremia requires recognition of the laboratory artifact rather than fluid restriction or saline administration. This early distinction is conceptually simple but clinically important because it determines whether the patient has a disorder of water balance that requires active sodium-focused treatment (Adrogue & Madias, 2000; Filippatos et al., 2016).

The review also highlights the limitations of bedside volume assessment. Traditional teaching divides hypotonic hyponatremia into hypovolemic, euvolemic, and hypervolemic forms, and this remains clinically useful. However, physical examination findings such as mucous membrane dryness, edema, orthostasis, jugular venous pressure, and skin turgor may be insensitive or confounded by age, medications, heart failure, kidney disease, liver disease, and nutritional status. Mild hypovolemia may mimic SIAD, and diuretic-associated hyponatremia may present with laboratory features overlapping with euvolemic states. Therefore, volume assessment should be integrated with urine studies, medication history, and the response to cautious therapy rather than treated as a single definitive judgment (Hoorn & Zietse, 2017; Spasovski et al., 2014).

Urine osmolality and urine sodium are therefore central to diagnostic reasoning. A low urine osmolality suggests that antidiuretic hormone is suppressed and that excess intake or insufficient solute may be responsible. A high urine osmolality indicates impaired free water excretion, but the cause may be appropriate or inappropriate antidiuretic activity. Urine sodium can help distinguish low effective arterial blood volume from SIAD-like patterns, but interpretation becomes difficult in diuretic-treated patients or after intravenous fluids. A practical approach is to obtain urine studies before major therapeutic interventions whenever the patient is stable enough to allow it, because treatment itself can rapidly change urine indices (Filippatos et al., 2016; Verbalis et al., 2013).

SIAD illustrates why a diagnostic label can be both useful and misleading. It is useful because it defines a recognizable pattern of hypotonic hyponatremia with persistent antidiuresis and no obvious hypovolemia or edema. It is misleading when it ends the investigation prematurely. SIAD may be caused by drugs, pulmonary disease, central nervous system disorders, malignancy, postoperative states, pain, or nausea. Adrenal insufficiency and hypothyroidism must also be considered before the diagnosis is accepted. In practice, SIAD should trigger a structured search for causes and a medication review rather than simply fluid restriction and discharge (Warren et al., 2023; Thompson et al., 2016).

Thiazide-associated hyponatremia deserves special attention because it is common, preventable, and potentially severe. It often occurs in older adults, who may also have reduced solute intake, impaired renal water excretion, low body mass, and polypharmacy. The diagnostic trap is that thiazide-induced hyponatremia may resemble SIAD biochemically, especially if urine sodium remains high. The therapeutic trap is that stopping the thiazide and correcting volume or potassium deficits can suddenly restore free water clearance. Sodium may then rise quickly, even without aggressive hypertonic saline. Monitoring urine output and serial serum sodium after thiazide withdrawal is therefore essential (Hoorn & Ellison, 2025; Ware et al., 2017).

Therapeutic decision-making should be symptom-driven. In patients with seizures, coma, severe confusion, or respiratory compromise, delayed therapy can be fatal. Hypertonic saline boluses are intended to produce a limited early rise in sodium rather than complete normalization. The target is reversal of brain edema and stabilization of neurological status. The SALSA trial provides randomized evidence that bolus-based and continuous infusion strategies can both be safe when carefully monitored, but bolus therapy is operationally aligned with current guideline recommendations for symptomatic patients. This is important in emergency settings, where a simple bolus protocol may be easier to implement than complex infusion calculations (Baek et al., 2021; Spasovski et al., 2014).

For chronic hyponatremia, the major therapeutic challenge is avoiding excessive correction. The brain adapts to chronic hypotonicity by losing osmolytes, and rapid restoration of extracellular tonicity can injure oligodendrocytes and produce osmotic demyelination. Although modern correction limits reduce risk, they do not abolish it. Patients with very low baseline sodium, alcohol use disorder, malnutrition, liver disease, hypokalemia, or other risk factors require more conservative targets and closer monitoring. A key clinical point is that potassium repletion can contribute to a rise in serum sodium and should be considered part of the correction process (Bastos & Rocha, 2024; Sterns, 2018).

The literature also suggests that overly rigid correction rules may not capture the full clinical picture. Very slow correction of severe symptomatic hyponatremia may leave patients exposed to cerebral edema, seizures, aspiration, and prolonged hospitalization. On the other hand, rapid correction in high-risk chronic cases may lead to demyelination. Recent systematic reviews comparing correction rates and outcomes illustrate this tension. The safest approach is not to apply a single target mechanically, but to individualize treatment according to symptom severity, chronicity, baseline sodium, comorbid risk factors, and trajectory during the first hours of therapy (MacMillan et al., 2024; Shepshelovich et al., 2025).

Table 3. Therapeutic challenges and safety principles.

Clinical situation	Main risk	Safety principle
Severe symptomatic hyponatremia	Cerebral edema, seizures, respiratory compromise	Use urgent hypertonic saline boluses aiming for limited early rise
Chronic severe hyponatremia	Osmotic demyelination after rapid correction	Use conservative correction limits and frequent monitoring
Thiazide-associated hyponatremia	Water diuresis after drug withdrawal	Monitor urine output and sodium closely; consider desmopressin if needed
SIAD with concentrated urine	Fluid restriction failure	Consider solute therapy, urea, loop diuretics, or selected vaptan use
High-risk ODS phenotype	Demyelination despite guideline-level correction	Aim for lower correction targets and be prepared to relower sodium

Desmopressin has become an important tool in the prevention and management of overcorrection. It can be used reactively when sodium is rising too quickly, or proactively in selected high-risk patients to create a controlled correction strategy. This is particularly relevant when the cause of hyponatremia is likely to reverse quickly, such as hypovolemia, thiazide-associated hyponatremia, adrenal insufficiency, or low-solute intake.

The desmopressin strategy requires clinical experience, frequent sodium checks, and careful fluid management, but it addresses the common problem that water diuresis, not prescribed sodium, is often the driver of overcorrection (Sterns et al., 2010; Sterns, 2018).

Chronic mild hyponatremia should not be ignored, but it should also not be treated aggressively without understanding the cause. Its associations with falls, cognition, fractures, and mortality suggest clinical significance. However, evidence that correction improves all long-term outcomes remains variable. In many cases, the best intervention may be medication adjustment, treatment of the underlying disease, improved solute intake, or careful management of fluid intake rather than pharmacological sodium correction. This is especially relevant for older adults with polypharmacy and multiple chronic diseases (Rondon-Berrios & Berl, 2022; Wald et al., 2010).

Refractory hyponatremia often reflects either an incorrect diagnosis, an unaddressed driver, or an inadequate therapeutic match. For example, fluid restriction is unlikely to work when urine osmolality is very high and electrolyte-free water clearance is low. Urea may be useful but limited by tolerability. Vaptans can be effective but may cause rapid correction and require careful monitoring. Hypertonic saline is appropriate for severe symptoms but is not a chronic outpatient strategy. A patient whose sodium fails to improve should therefore be reassessed diagnostically rather than simply subjected to progressive fluid restriction (Warren et al., 2023; Rondon-Berrios & Berl, 2022).

From a systems perspective, hyponatremia is vulnerable to errors because it crosses specialty boundaries. It is managed by emergency physicians, internists, nephrologists, endocrinologists, intensivists, geriatricians, oncologists, surgeons, and general practitioners. Different environments prioritize different risks. Emergency settings emphasize seizures and acute neurological decline; wards emphasize falls, medications, and comorbid illness; intensive care units emphasize iatrogenic fluids and organ failure. A standardized diagnostic checklist can reduce variation: confirm tonicity, assess symptoms, determine chronicity, measure urine osmolality and sodium, review medications, exclude endocrine causes, choose therapy according to severity, and monitor for overcorrection.

This review has limitations. It is based on published literature indexed in PubMed/MEDLINE and PubMed Central and includes heterogeneous evidence rather than a single intervention or diagnostic accuracy dataset. No meta-analysis was performed. Search results may have missed non-English publications or studies not indexed in the searched databases. Furthermore, many recommendations in hyponatremia management are supported by physiological reasoning, observational evidence, and expert consensus rather than large randomized trials. Nevertheless, the consistency of guideline recommendations and the recurring nature of described errors support the practical relevance of the synthesized findings.

Future research should focus on clinically meaningful outcomes rather than sodium correction alone. Important questions include how best to identify patients at highest risk of osmotic demyelination, whether early structured algorithms reduce diagnostic errors, which patients benefit from proactive desmopressin, and whether treatment of chronic mild hyponatremia improves falls, cognition, fractures, quality of life, or mortality. More pragmatic trials are needed in older adults, patients with multimorbidity, and real-world hospital settings.

The practical implications for clinical education are substantial. Many junior clinicians learn hyponatremia through classification tables but encounter patients whose physiology is mixed and whose examination is ambiguous. Teaching should therefore emphasize a small number of repeatable questions: Is the patient truly hypotonic? Are there severe neurological symptoms? Is the process acute or chronic? Is antidiuretic hormone appropriately suppressed? Is urine sodium interpretable in the presence of diuretics? What could cause sudden water diuresis after treatment? These questions map directly onto preventable errors described in the literature.

The role of electronic decision support may increase in the future. Automated alerts could prompt clinicians to check serum osmolality, urine osmolality, urine sodium, glucose, cortisol when appropriate, and medication exposure before labeling a patient as SIAD. Similarly, inpatient order sets could require specification of correction goals and monitoring intervals when hypertonic saline is prescribed. Such systems cannot replace clinical judgment, but they may reduce omissions in busy hospital environments where hyponatremia is common and often managed by non-specialists.

Another future priority is better risk stratification for osmotic demyelination. Current practice relies on clinical risk factors such as alcoholism, malnutrition, liver disease, hypokalemia, and very low initial sodium. These factors are useful but imperfect. More accurate prediction tools could help identify patients who need proactive desmopressin and stricter correction limits, while allowing faster safe correction in patients at low

risk but high risk from persistent cerebral edema. This balance is especially important because recent analyses suggest that both undercorrection and overcorrection may be harmful in different populations.

The management of hyponatremia also has a patient-centered dimension. Fluid restriction, one of the most commonly recommended therapies for chronic SIAD, is often difficult to tolerate and may reduce quality of life. Urea may be effective but limited by taste and gastrointestinal symptoms. Vaptans may be effective but require monitoring and cost consideration. For long-term management, the best strategy is not always the one that raises sodium most efficiently in hospital, but the one that the patient can safely maintain after discharge.

A clinically useful way to apply these findings is to separate decision-making into emergency and non-emergency pathways. In emergency presentations, the priority is symptom control and prevention of herniation. Diagnostic precision remains important, but it should not delay the initial administration of hypertonic saline in a patient with seizures or coma likely attributable to hyponatremia. In non-emergency presentations, the priority shifts toward careful classification and prevention of treatment-induced harm. This distinction helps avoid two opposite mistakes: delaying lifesaving therapy in acute symptomatic disease and treating chronic stable hyponatremia as if rapid normalization were necessary.

Another practical issue is the interpretation of sodium changes after treatment has begun. A clinician may prescribe a small amount of hypertonic or isotonic saline and assume the correction will be proportional to the dose. In reality, sodium kinetics are dynamic because renal water excretion can change abruptly. A patient who is initially antidiuretic may become polyuric after volume repletion, relief of nausea, withdrawal of thiazide therapy, or glucocorticoid replacement. Therefore, calculations can guide therapy but cannot replace repeated sodium measurement. Trend-based monitoring is more important than confidence in a single predicted correction rate.

Hyponatremia in older adults requires special caution. Age-related reduction in glomerular filtration, higher prevalence of comorbid disease, lower dietary solute intake, and frequent use of thiazides, antidepressants, antiepileptics, and proton-pump inhibitors increase susceptibility to hyponatremia. At the same time, symptoms such as confusion, weakness, falls, and gait instability may be attributed to frailty or dementia. This may delay recognition and lead to repeated hospital admissions. A medication-centered and nutrition-centered approach is therefore especially valuable in geriatric patients.

The reviewed literature also supports a cautious attitude toward labeling chronic mild hyponatremia as benign. Although many patients are asymptomatic in the traditional neurological sense, subtle impairment in cognition and balance may matter clinically, particularly in older adults at risk of falls and fractures. However, this does not mean that every patient requires active sodium-raising therapy. Instead, mild chronic hyponatremia should prompt review of medications, fluid intake, nutrition, endocrine disease, and chronic organ failure. The goal is to reduce preventable risk without exposing patients to aggressive correction strategies.

A recurrent challenge in daily practice is communication between specialties. For example, an emergency physician may initiate hypertonic saline, an internist may continue fluid restriction, a nephrologist may recommend desmopressin, and a primary care physician may later restart a thiazide because the discharge summary does not clearly identify it as the cause. This fragmented care pathway can undermine safe management. Clear documentation of presumed mechanism, maximum correction target, monitoring plan, and contraindicated medications should be considered part of treatment rather than administrative detail.

Finally, hyponatremia management should be understood as risk management rather than numerical correction. The target is not simply to move serum sodium into the reference range, but to treat symptoms, address the mechanism, prevent recurrence, and avoid neurological injury. A patient with chronic SIAD and serum sodium of 128 mmol/L may require a very different plan from a patient with acute postoperative hyponatremia at the same value. This individualized approach is the strongest common thread across guidelines, expert recommendations, and recent reviews.

For research and publication purposes, hyponatremia remains difficult because outcome studies are affected by confounding. Low sodium often occurs in patients with serious underlying disease; therefore, its association with mortality may reflect both direct effects and severity of illness. Future studies should therefore distinguish biochemical correction from patient-centered outcomes such as neurological recovery, falls, fractures, readmission, functional status, and quality of life. Trials that only report sodium normalization may overestimate the clinical value of an intervention if tolerability, recurrence, or overcorrection risk is not considered.

Conclusions

Hyponatremia is common, clinically important, and frequently mismanaged because its diagnosis requires more than recognition of a low serum sodium value. Correct evaluation begins with confirmation of tonicity and proceeds through assessment of symptoms, chronicity, urine osmolality, urine sodium, volume status, medication exposure, and endocrine or organ-specific causes. The most important diagnostic pitfalls include failure to exclude pseudohyponatremia or hypertonic hyponatremia, overreliance on bedside volume assessment, omission of urine studies, premature diagnosis of SIAD, and under-recognition of thiazide-associated or other drug-induced hyponatremia.

Therapy must balance the urgent need to treat cerebral edema in severe symptomatic hyponatremia against the need to prevent osmotic demyelination in chronic cases. Hypertonic saline bolus therapy is appropriate for severe symptoms when carefully monitored, while chronic or minimally symptomatic hyponatremia requires correction of the underlying cause and avoidance of overly rapid sodium rise. Patients at high risk of overcorrection need conservative targets, frequent monitoring, and consideration of desmopressin or relowering therapy when sodium rises too quickly. A structured, physiology-based approach can improve diagnostic accuracy, reduce iatrogenic harm, and support safer care for adults with hyponatremia.

In practical terms, every adult with clinically relevant hyponatremia should have a documented working mechanism, monitoring plan, correction limit, and strategy for recurrence prevention before discharge or transfer of care.

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