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A CASE SERIES OF HYPONATREMIA

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ABSTRACT

Hyponatremia is one of the challenging electrolyte abnormalities encountered in clinical medicine, posing significant diagnostic and therapeutic challenges. Even minor deviations from the physiological sodium baseline are associated with considerable morbidity and an exponentially increased risk of mortality. While the fundamental tenets of volume regulation and osmolality are well-established, the clinical presentation of hyponatremia is frequently confounded by overlapping systemic illnesses, neuroanatomical vulnerabilities, and iatrogenic interventions. This case series meticulously details the clinical trajectories of four unique patients presenting with hyponatremia in the context of highly complex, multifactorial etiologies. The first case examines hyponatremia and complicating acute bilateral pyelonephritis and uncontrolled diabetes mellitus. The second case elucidates a catastrophic instance of Osmotic Demyelination Syndrome (ODS) that was insidiously unmasked following an episode of hypertensive encephalopathy and the subsequent diagnosis of the Syndrome of Inappropriate Antidiuretic Hormone (SIADH). The third case details a highly volatile presentation of fluctuating hyponatremia, SIADH and multi-lobar consolidation in a patient with severe chronic alcohol use disorder and the last case demonstrates hyponatremia secondary to a CNS infection. Through an exhaustive analysis of these clinical scenarios, this report highlights the critical necessity of proper diagnosis and individualised mathematically constrained sodium correction protocols. It demonstrates that uncommon and devastating sodium-related complications, such as pontine myelinolysis and SIADH, frequently arise when acute infectious processes or mechanical vascular trauma overwhelm the cellular osmotic buffering capacity of the central nervous system.

INTRODUCTION

The tonicity of the human body is fundamentally determined by the concentration of sodium within the extracellular fluid (ECF). Because sodium is the primary extracellular cation, its concentration directly mirrors the relative concentration of water in the extracellular space. Absolute or relative changes in total body water dictate systemic sodium levels, necessitating a highly conserved physiological system to maintain homeostasis. Under normal physiological conditions, total body water is rigorously maintained within a narrow window by a complex feedback loop involving vascular baroreceptors, hypothalamic osmoreceptors, and the secretion of arginine vasopressin (AVP), also known as antidiuretic hormone (ADH).

AVP serves as the paramount hormonal regulator of this homeostatic system. It exerts its primary physiological effect by binding to highly specific vasopressin (V2) receptors located on the basolateral membrane of the principal cells within the renal collecting ducts. Following this receptor activation, an intracellular signaling cascade initiates the fusion of cytoplasmic vesicles containing aquaporin-2 water channels with the apical (luminal) membrane. This structural modification facilitates the rapid, passive movement of free water

from the hypotonic tubular lumen into the hypertonic renal medulla via aquaporin-3 and aquaporin-4 channels constitutively expressed on the basolateral membrane. AVP secretion is exquisitely sensitive to both hemodynamic alterations (such as severe volume depletion or hypotension detected by baroreceptors) and non-hemodynamic changes mediated through osmoreceptors located in the anterior hypophysis.

Hyponatremia is defined as a serum sodium level <135 mEq/L. While many patients with chronic, mild hyponatremia remain clinically asymptomatic due to gradual cerebral adaptation, acute or severe hyponatremia rapidly precipitate debilitating neurological symptoms. These manifestations range from mild nausea, lethargy, and confusion to intractable generalized seizures, profound coma, and irreversible structural brain damage. The most devastating complication associated with the clinical management of hyponatremia is Osmotic Demyelination Syndrome (ODS).Originally described in 1959 by Adams, Victor, and Mancall as Central Pontine Myelinolysis (CPM), this pathology was initially observed exclusively at autopsy in chronic alcoholics and severely malnourished patients presenting with a rapidly progressive, fatal cascade of pseudobulbar palsy and quadriplegia. Decades of subsequent research, notably the seminal animal models developed by Laureno in 1983, definitively established that ODS is not intrinsically caused by the state of hyponatremia itself, but rather by the overly rapid therapeutic correction of chronic hyponatremia. When the central nervous system is subjected to a chronic hypotonic environment (typically developing over a period exceeding 48 hours), astrocytes and glial cells adapt to the osmotic stress by actively expelling intracellular inorganic ions and systematically purging organic osmolytes, such as myo-inositol, taurine, and glutamine. This vital compensatory mechanism successfully prevents fatal cerebral edema by establishing a new osmotic equilibrium. However, if the serum sodium concentration is subsequently corrected too rapidly (exceeding established safety thresholds of 8 to 10 mmol/L per 24 hours), the adapted, osmolyte-depleted astrocytes are subjected to violent osmotic shock. The rapid influx of extracellular tonicity forcefully draws water out of the cells, causing severe intracellular dehydration, structural shrinkage, and the mechanical tearing of the blood-brain barrier (BBB).This catastrophic breach permits the massive infiltration of myelinotoxic substances and complement proteins, triggering widespread astrocyte apoptosis and the subsequent degeneration of oligodendrocytes.

CASE REPORTS

CASE 1– HYPONATREMIA AND UNCONTROLLED HYPERGLYCEMIA

A 67-year-old male with a four-year history of known Systemic Hypertension on regular medical therapy presented to the emergency department and his complaints included a ten- day history of high-grade, continuous fever associated with profound chills. This was accompanied by persistent, intractable hiccups for five days and recurrent non-blood-stained vomiting (4-5 episodes per day) for three days. The patient's family reported a distinct alteration in his sensorium over the preceding 72 hours. He denied any history of cough, breathlessness, loose stools, abdominal pain, red colored urine, dysuria, or burning micturition. He had no known history of coronary artery disease, chronic kidney disease, chronic liver disease, bronchial asthma, or thyroid disorders.

Upon initial evaluation in the emergency department, his vital signs demonstrated a blood pressure of 100/80 mmHg and pulse of 102 beats per minute. He was tachypneic with a respiratory rate of 34 breaths per minute and had an oral temperature of 103°F. His oxygen saturation remained stable at 98% on room air. Physical examination revealed a frail, poorly hydrated individual. While pallor, pedal edema, icterus, and cyanosis were absent, abdominal examination revealed a distended, soft abdomen with positive bowel sounds and marked bilateral renal angle tenderness. Neurologically, the patient was conscious and oriented, but his sensorium was notably fluctuating, moving all four limbs symmetrically without focal deficits. The patient was found to have severe, previously uncontrolled Type 2 Diabetes Mellitus (T2DM), with an initial random blood sugar (RBS) of 524.6 mg/dL and a profoundly elevated HbA1c of 11.2%. Urinalysis demonstrated 4+ glycosuria, negative ketonuria, 1+ albuminuria, and the presence of abundant pus cells. His initial basic metabolic panel revealed hyponatremia with a serum sodium concentration of 125 mmol/L, accompanied by an acute kidney injury (AKI) profile characterized by a blood urea of 42.0 mg/dL and a serum creatinine of 1.85 mg/dL. His serum potassium was strictly within normal limits at 4.6 mmol/L.

Table 1: Renal Function and Electrolyte Trends spanning the admission of Case 1.

Date (2026)	RBS (mg/dL)	Urea (mg/dL)	Creatinine (mg/dL)	Sodium (mmol/L)	Potass (mmol/
29/03	524.6	42.0	1.35	125	4.6
30/03	399.8	47.7	1.29	129	3.5
31/03	256.8	41.0	1.28	134	3.7
01/04	227.5	59.5	1.18	133	3.9
04/04	382.3	50.8	1.53	135	4.4
06/04	196.8	40.2	1.20	139	3.9

The initial profound hyponatremia corrected rapidly following fluid resuscitation, though secondary fluctuations occurred alongside glycemic variability.

Hematological evaluation demonstrated a normal total leukocyte count initially (9.2 x 10^3/µL) that subsequently spiked to 13.7 x 10^3/µL by hospital day three, with a persistent neutrophil predominance (87.9%). Liver function tests were largely unremarkable.

To ascertain the source of the persistent fever and right renal angle tenderness, radiological imaging was pursued. A transabdominal ultrasound revealed a 14 cm liver, a 7.6 cm spleen, a distended gallbladder, and Grade 1 prostatomegaly, with normal-sized kidneys. However, a CT of the abdomen (image 1) identified a bulky bilateral kidneys with extensive perinephric fat stranding, confirming the clinical suspicion of severe acute bilateral pyelonephritis.

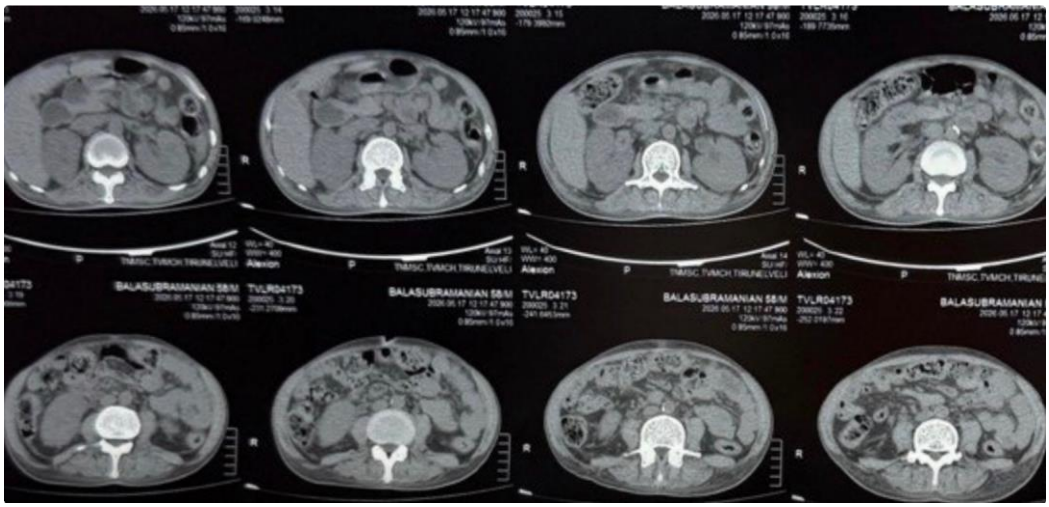


Image 1: CT Abdomen.

CONCLUSION OF CASE 1- PSEUDOHYPONATREMIA

The patient's clinical presentation was synthesized as severe metabolic encephalopathy driven by a combination of uncontrolled diabetes, hyponatremia and sepsis secondary to acute bilateral pyelonephritis. He was aggressively resuscitated with intravenous normal saline to restore intravascular volume depleted by recurrent vomiting and osmotic diuresis. A potent broad-spectrum intravenous antibiotic regimen consisting of Meropenem (500mg IV TDS), and Ciprofloxacin (200mg IV BD) was initiated. His severe hyperglycemia was actively managed and later controlled via a basal-bolus subcutaneous insulin regimen.

This was a case of pseudohyponatermia the causing being attributed to the uncontrolled hyperglycaemia which caused the apparently low sodium in the blood investigations.

SERUM OSMOLALITY – 288 (calculated)
SERUM SODIUM – 125 mEq/L

This discrepancy is the clue towards the diagnosis of pseudohyponatremia in this case. This highlights the importance of identifying the potential causes and also to suspect them in a setting that factors pseudohyponatremia which in this case was hyperglycemia which has to be treated
MANAGEMENT OF PEUDOHYPONATREMIA – THE RULE IS NOT TO TREAT THE SODIUM VALUE.

CASE 2– HYPONATREMIA AND HYPERTENSIVE ENCEPHALOPATHY

A 61-year-old male with a ten-year history of poorly compliant Type 2 Diabetes Mellitus and Systemic Hypertension presented with a highly complex neurological decline spanning late April to early May 2026.

The First Episode: Hypertensive Encephalopathy (April 25 - May 1, 2026) The patient was last seen in his normal state of health on the night of April 25. At approximately 9:00 PM on April 26, his family noted significant behavioral changes - when he visited the restroom and exhibited a markedly abnormal gait. Shortly thereafter, he laid down on the floor and, within thirty minutes, became entirely unresponsive. He was rushed to a nearby primary care clinic where his blood pressure was recorded at a catastrophic level exceeding 200/120 mmHg. Recognizing a hypertensive emergency, he was immediately transferred to a teritiary care centre. He was diagnosed with acute hypertensive encephalopathy and adequate blood pressure control was achieved by hospital day two. It was noted that the patient initially had mild- moderate hyponatremia also, the cause of which was being evaluated. As his hemodynamics stabilized, his sensorium steadily improved from deep unresponsiveness to a drowsy but easily arousable state. By the time of his discharge, he was fully conscious, able to identify relatives, move all four limbs, and even read a newspaper. Patient was told to review with reports of TFT and cortisol as a follow up for hyponatremia.

The Second Episode - On May 2, while at home, the patient complained of severe constipation. Two hours later, while attempting to walk, he was found collapsing by the roadside in a profound state of altered sensorium. He was readmitted but was subsequently discharged at the family's request and managed in an outside hospital the details of which are not available at present. But due to worsening symptoms patient was readmitted as - by the evening of May 4, his sensorium deteriorated violently. He began making loud, uncoordinated noises and exhibited a severe inability to close his mouth. By May 6, he suffered an episode of rigors and developed profound dysphagia, characterized by the immediate regurgitation of all oral intake (food and water), for which further evaluation evaluation was done.

Table 2: Renal Function and Electrolyte parameters.

S.No.	Date (May 2026)	RBS (mg/dL)	Urea (mg/dL)	Creatinine (mg/dL)	Sodiu (mEq/L
1	11/05	116.1	19.2	0.83	128
2	13/05	-	15.0	0.74	133
3	14/05	152.3	15.0	0.63	133
4	18/05	-	17.3	0.81	129
5	20/05	-	31.2	0.81	127
6	21/05	247.0	-	-	134
7	22/05	246.4	43.9	0.87	136

Detailed neurological examination revealed a partially drowsy but arousable patient. He responded only partially to oral commands. Meningeal signs were absent, with no nuchal rigidity. Bilateral pupils were 2mm and briskly reactive to light. While cranial nerve assessment was limited by poor patient cooperation, motor system evaluation demonstrated preserved bulk and an ability to move all four limbs. However, his motor tone was elevated and he exhibited Grade 4/5 power across all extremities. The deep tendon reflexes were globally hyperactive (2+ bilaterally in upper and lower limbs), though plantar responses remained flexor. He retained the autonomic sensation of bowel and bladder fullness and passed urine without post-void residue. The patient had reviewed with the reports of thyroid function tests and serum cortisol which was normal.

The cause of hyponatremia was attributed to SIADH the cause of which could not be identified. Studies show that the percentage of SIADH with no identifiable etiology range from 15-40 percentage.
Serum sodium – 128
Urine sodium – 40
Serum osmolality – 266
Urine osmolality - 336

Given the highly suspicious biphasic clinical deterioration—from metabolic encephalopathy to apparent recovery, followed rapidly by severe bulbar dysfunction (dysphagia) and spasticity— an urgent high-resolution Magnetic Resonance Imaging (MRI) scan of the brain was obtained. The imaging revealed classic structural features highly suggestive of OSMOTIC DEMYELINATION – CPM + EPM: CENTRAL PONTINE MYELINOLYSIS + EXTRAPONTINE MYELINOLYSIS

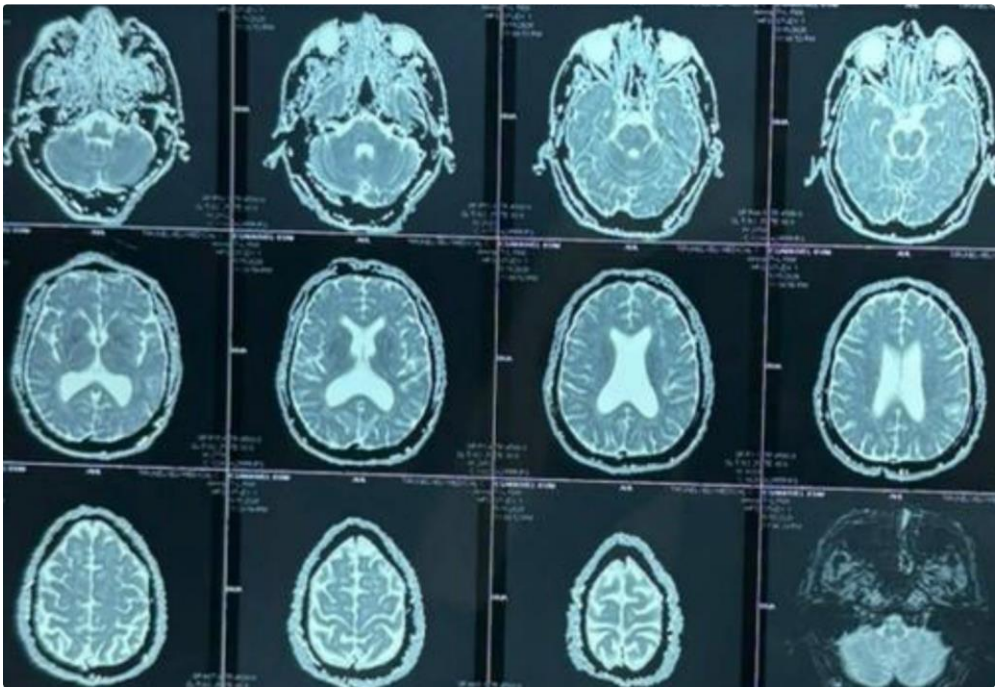


Image 2: T2 images showing pontine de myelination.

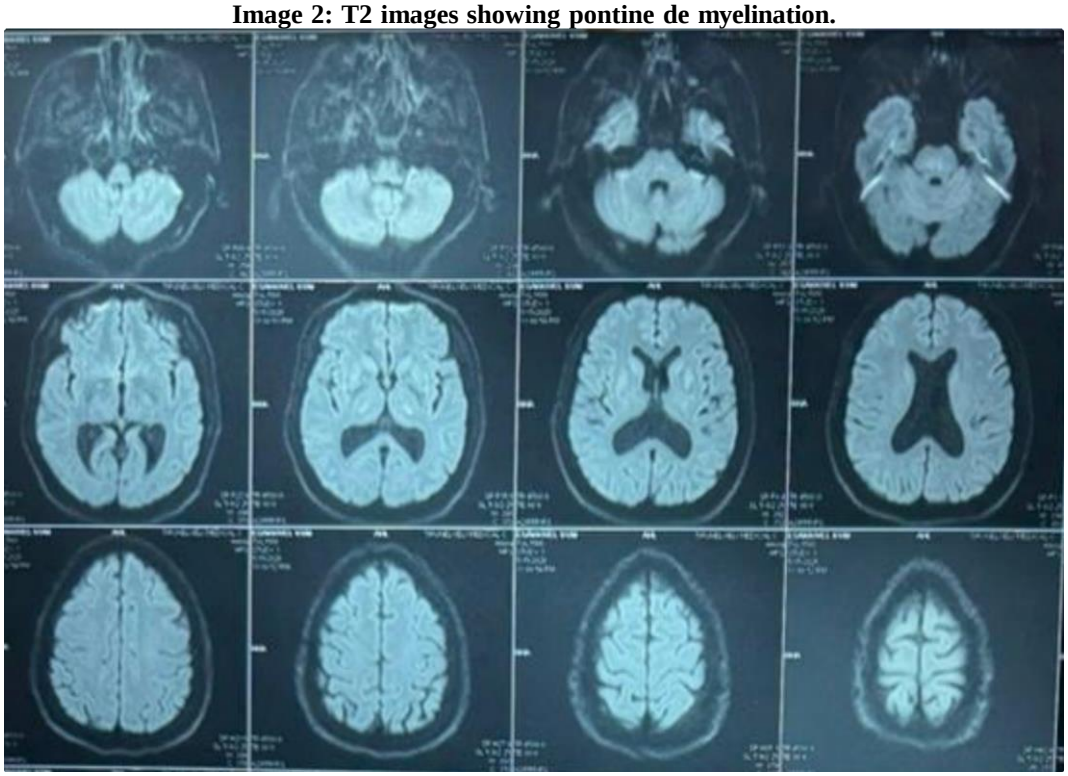


Image 3: T2 FLAIR showing osmotic demyelination.

The definitive diagnosis was established as Osmotic Demyelination Syndrome (ODS). The clinical conclusion was that the initial severe hypertensive encephalopathy had critically compromised the blood-brain barrier and the microvascular integrity of the basis pontis. This localized trauma functioned as a profound predisposing factor, rendering the pontine myelin sheaths exceptionally vulnerable to osmotic shock during the subsequent hyponatremia episode. The patient is currently managed with high-dose systemic corticosteroids and meticulous supportive care, and is demonstrating slow but significant neurological improvement.

In this case ODS developed despite adequate correction of serum sodium and when ODS develops in patients whose sodium was corrected at a rate of less than 10 mEq/L per day, it is almost exclusively seen in patients with severe underlying vulnerabilities. The brain's ability to adapt to osmotic changes is heavily compromised by certain physiological stressors.

According to clinical reviews of ODS cases that occurred within standard correction limits, the following are the primary predisposing risk factors: **Extreme Baseline Hyponatremia:** An initial serum sodium level of < 115 mEq/L, and particularly 105 mEq/L, carries a profoundly higher risk of ODS regardless of the correction speed, **Alcohol Use Disorder:** Chronic alcoholism impairs the glial cells' ability to manage osmotic shifts and regenerate organic osmolytes, **Severe Malnutrition:** Particularly thiamine (Vitamin B1) deficiency, which compromises cellular energy metabolism in the brain, **Hypokalemia:** Concurrent low potassium levels are a major independent risk factor for myelin destruction during sodium correction, **Advanced Liver Disease:** Patients with cirrhosis or those undergoing liver transplantation have a baseline inability to rapidly synthesize the osmolytes needed to protect brain cells from shrinking. Because of the rare but catastrophic risk of ODS in appropriately corrected patients, clinical targets have become increasingly conservative over the past decade. While 10 mEq/L per 24 hours was traditionally considered the "normal" upper limit, modern nephrology and critical care guidelines now recommend a much tighter limit for patients with the high-risk features listed above. For these vulnerable populations, the recommended maximum rate of serum sodium correction is **< 8 mEq/L per 24 hours**, with some experts targeting as little as 4 to 6 mEq/L per day. In this case the cause of the increased fragility of the brain can be attributed to the hypertensive insult.

CONCLUSION- CASE 2: 15 – 40 PERCENTAGE OF SIADH CASES MAYNOT HAVE AN IDENTIFIABLE ETIOLOGY AND HYPERTENSIVE ENCEPHALOPATHY CAN ALTER THE BBB PHYSIOLOGY AND MAKE THE BRAIN MORE PRONE TO OSMOTIC INSULTS.[10]

CASE 3 – HYPONATREMIA AND COMMUNITY ACQUIRED PNEUMONIA

A 49-year-old male with a profound twenty-year history of severe alcohol use disorder and concurrent tobacco use presented in a completely unresponsive and unconscious state. Initial pre-hospital assessment revealed severe, life- threatening hypoglycemia, with a capillary blood glucose dangerously low at 25 mg/dL. He had a concurrent history of fever, but no history of vomiting, abdominal pain, loose stools, or involuntary limb movements. Upon admission his vital signs demonstrated a pulse rate of 90 beats per minute and a stable blood pressure of 120/80 mmHg. However, he was visibly distressed, dyspneic, and tachypneic with a respiratory rate of 30 breaths per minute, while maintaining an oxygen saturation of 98% on room air. The patient was febrile. General physical examination revealed no pallor, icterus, cyanosis, clubbing, or pedal edema. Systemic evaluation of the cardiovascular system was normal, but respiratory examination revealed bilateral normal vesicular breath sounds interspersed with distinct crepitations localized to the axillary and infra-axillary regions.

Neurologically, the patient was in a profound state of altered sensorium; he was deeply drowsy, arousable only to deep painful stimuli, and entirely unable to follow oral commands. While his pupils were 3 mm and reactive to light, a detailed motor power assessment was precluded by his depressed consciousness.

Extensive laboratory and radiological investigations were immediately ordered to untangle the complex etiology of his encephalopathy.

Investigatio n Parameter	**03-May**	**06-May**	**09-May**	**11-May**	**15-May**	17-May
WBC Count (x10³/µL)	13.2	9.6	10.5	11.3	18.1	
Hemoglobin (g/dL)	12.5	12.3	12.6	12.8	12.4	
Platelets (x10³/µL)	136	170	198	318	325	
Random Glucose (mg/dL)	163.5	122.6	97.9	122.0	71.4	
Urea (mg/dL)	47.2	33.6	29.9	23.5	16.5	
Creatinine (mg/dL)	1.23	1.45	0.76	1.02	0.82	
Sodium (mEq/L)	**136**	**130**	**129**	127	**131**	
Potassium (mEq/L)	3.5	4.0	3.7	4.3	3.3	
AST (U/L)	182.9	-	39.5	-	62.3	
ALT (U/L)	57.3	-	35.8	-	39.2	

The data demonstrates volatility in serum sodium levels, transient acute kidney injury, thrombocytopenia, and transaminitis secondary to chronic alcohol use and acute sepsis.

Diagnostic imaging provided critical clarity. A high-resolution CT of the chest on May 3 revealed multiple centrilobular nodules with adjacent ground-glass opacities in the left upper lobe, alongside patchy ground-glass opacities in the bilateral superior and basal segments. These findings, in conjunction with his respiratory symptoms and altered state, definitively established the diagnosis of acute infectious aspiration pneumonitis. Furthermore, a CT of the brain on the same day, followed by a contrast-enhanced MRI on May 11, revealed a chronic lacunar infarct in the left occipital and right basifrontal lobes, accompanied by early cerebral cortical atrophic changes, painting a stark picture of chronic toxic-metabolic brain injury secondary to decades of severe alcohol abuse.

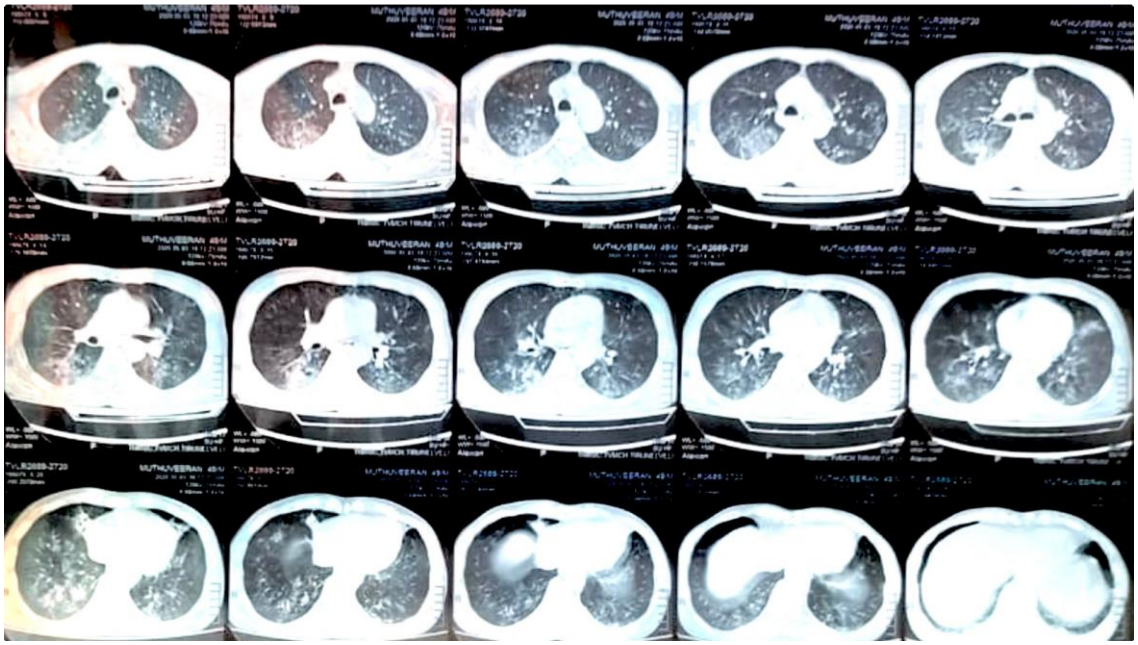
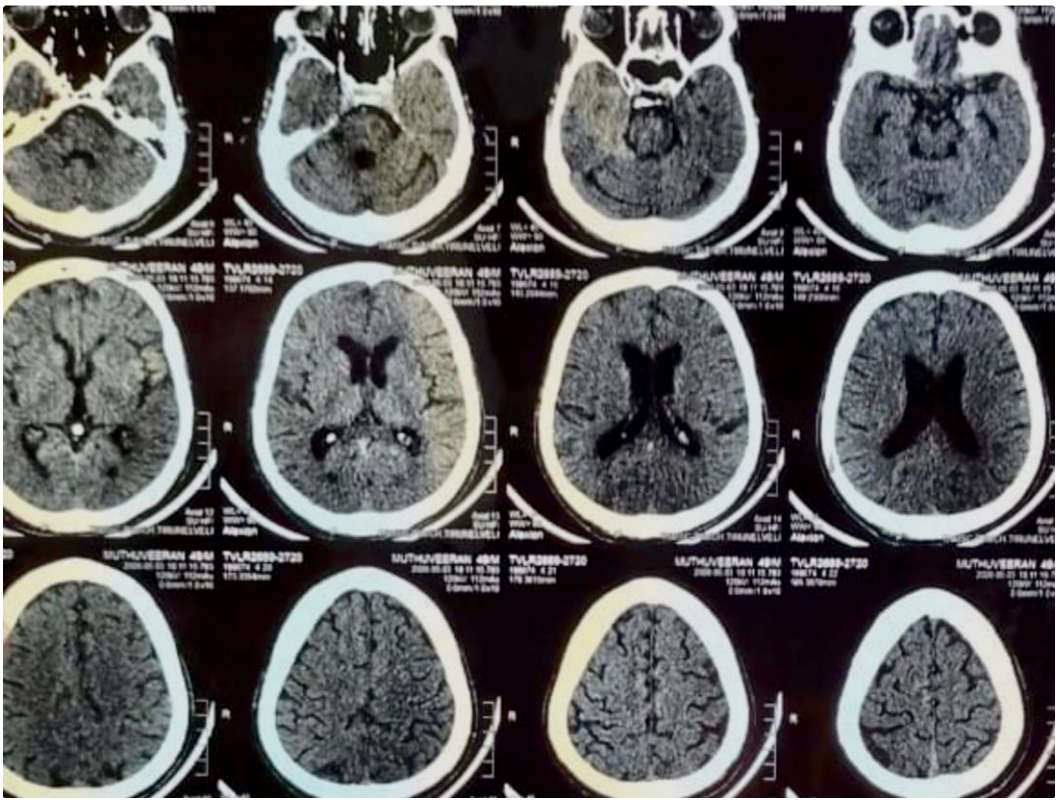


Image 4: CT Chest.



CT BRAIN- showing age related atrophic changes.

The patient's diagnosis was formalized as acute encephalopathy secondary to a convergence of profound hypoglycemia, acute aspiration pneumonia. Crucially, the volatility of his serum sodium was identified as euvolemic hyponatremia driven by the Syndrome of Inappropriate Antidiuretic Hormone with the patient's thyroid functions and serum cortisol levels being within normal limits.
Serum sodium – 130 mEq/L,
Urine sodium – 53,
Serum osmolality – 269,
Urine osmolality – 335
With patient being in a euvolemic state with normal thyroid and cortisol levels.

To combat the severe aspiration pneumonia, he was administered a targeted intravenous antibiotic regimen comprising Cefotaxime 1 gm IV BD, Doxycycline (100mg BD), and Metronidazole (500mg TDS), supplemented by nebulized Salbutamol.

Following this multifaceted, aggressive care intervention, the patient demonstrated a remarkable clinical recovery. His sensorium cleared completely, the aspiration pneumonitis resolved, and his hemodynamic and neurological statuses stabilized entirely.

CONCLUSION– CASE 3: The common infectious causes of SIADH include CNS and pulmonary infections which can cause the pathology by various mechanisms.

Ectopic Production: Inflammatory cells (macrophages) within the infected lung tissue autonomously synthesize and release AVP, completely bypassing the brain's normal osmotic control loops.

- Hemodynamic Triggers: Altered lung mechanics (decreased compliance) and hypoxia reduce left atrial stretch. This unloads baroreceptors and triggers chemoreceptors, tricking the central nervous system into releasing AVP to defend perceived volume loss.[11]
- Inflammatory Drive: Systemic inflammation releases cytokines, particularly IL-6. These cytokines cross the blood-brain barrier to directly stimulate the hypothalamus, forcing AVP release and resetting the body's baseline osmostat.[12]

Case 4

A 24-year-old male presented with a history of headache and fatiguability for the past 3 weeks and one episode of GTCS. The patient had a documented past medical history of extra-pulmonary tuberculosis. He had no other known systemic comorbidities, such as diabetes mellitus, hypertension, or human immunodeficiency virus infection. He was a strict non-smoker and non- alcoholic, and he reported entirely normal bowel and bladder habits.

Upon assessment in the emergency department, the patient's vital signs were stable. The initial general physical examination (following the post-ictal phase) showed - Cardiovascular, respiratory and abdominal examination to be normal.

The initial central nervous system evaluation indicated a conscious and oriented individual. Cranial nerve assessment revealed bilateral pupils that were symmetric, measuring 3 millimeters in diameter, and briskly reacting to light. There was presence of neck stiffness, kernigs and bruzdinski sign was absent. The cerebrospinal fluid analysis demonstrated - total white blood cell count was markedly elevated at 105 cells/µL, glucose level of 19 mg/dL and a elevated protein level of 257 mg/dL. Globulin testing was positive. Furthermore, the Adenosine Deaminase level was elevated at 24 U/L.

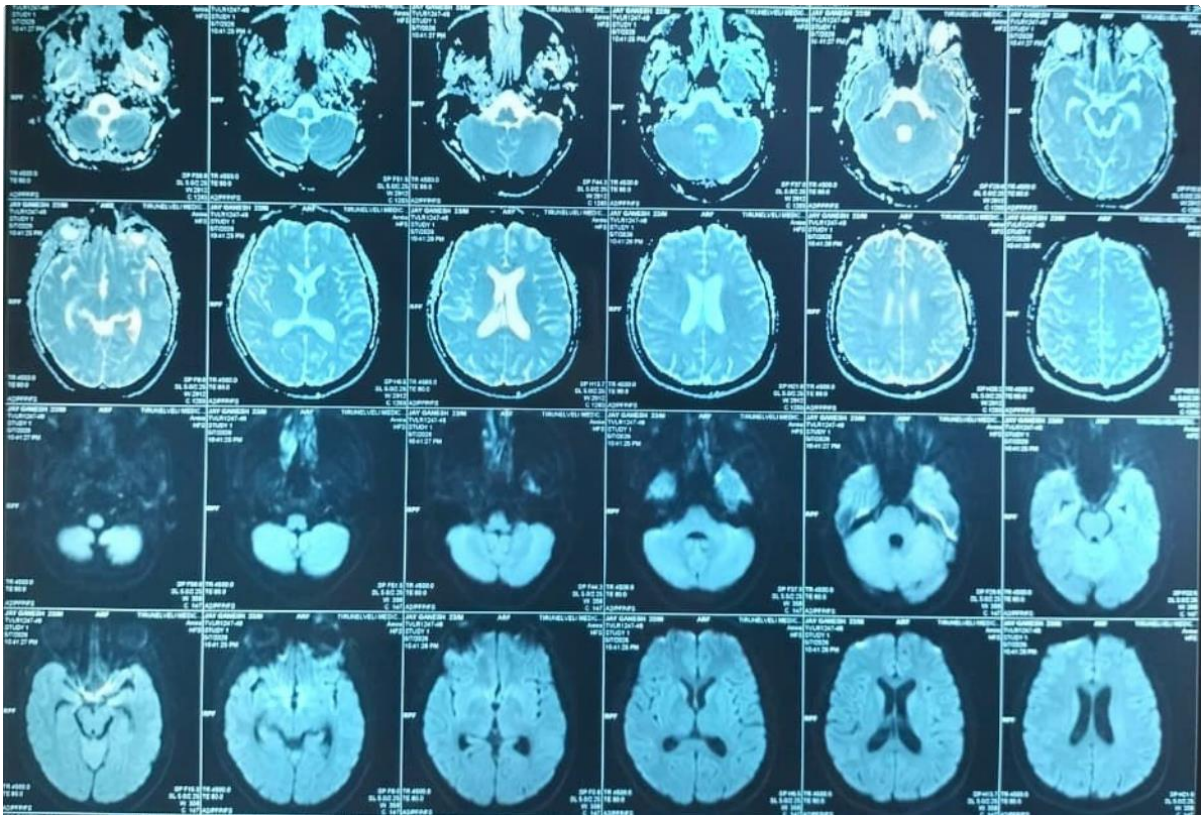


Image 6: Mri brain showing no significant abnormalities.

Patient was diagnosed as a case of TB meningitis and was started on ATT with adequate supportive care and as a part of evaluations for altered sensorium the sodium values were as follows

Serum sodium – 129

Urine sodium – 36

Serum osmolality – 129
Urine osmolality – 190

CONCLUSION - This euvolemic patient with his thyroid function tests and cortisol being within normal limits a diagnosis of SIADH was made and the cause was attributed to the CNS infection. In hyponatremia related to SIADH – if chronic and the degree is mild to moderate administering 3 percent sodium can have catastrophic results and hence the management is free water restriction and if needed – vaptans.[11,12]

DISCUSSION

The four cases detailed in this series elegantly illustrate how common electrolyte disturbances are frequently complicated by underlying organ dysfunction, leading to highly unpredictable, and potentially lethal, osmotic shifts. When systemic infectious processes, mechanical vascular damage, and toxic metabolic states converge, the standard paradigms of fluid resuscitation and sodium correction must be fundamentally recalibrated.

CASE 1- IT MAY BE NOTED THAT WHILE MANAGING HYPONATREMIA AFTER CONFIRMING TRUE HYPONATREMIA(IF PSEUDOHYPONATREMIA THE RULE IS TO CORRECT THE UNDERLYING CAUSE), RAPID BOLUS CORRECTION(WITH CALCULATED SODIUM RISE NOT MORE THAN 4-6 mmol / L)IS INDICATED ONLY FOR SEVERE AND SYMPTOMATIC-HYPONATREMIA AND CONDITIONS OTHER THAT THESE WARRANT A SLOW AND GUARDED SODIUM CORRECTION. A primary contributing factor to the hyponatremia in case 1 was translocational, or dilutional, hyponatremia driven by his profound, uncontrolled diabetes. Furthermore, the systemic inflammation, hyperpyrexia, and intense visceral pain generated by the bulky, inflamed kidney act as extraordinarily potent non-osmotic stimuli. These stimuli override the normal osmotic sensors in the hypothalamus, triggering the massive, uninhibited release of antidiuretic hormone from the posterior pituitary, culminating in secondary SIADH, the latter 2 being more predominant in the pediatric population.

CASE 2- provides a textbook demonstration of the rigid neuroanatomical vulnerabilities violently exposed by Osmotic Demyelination Syndrome. ODS, encompassing both central pontine myelinolysis (CPM) and extrapontine myelinolysis (EPM), represents an acute, non-inflammatory apoptosis of astrocytes directly triggered by severe osmotic shock.

During chronic hyponatremia the brain's glial cells engage in a highly energy-dependent survival mechanism. To prevent catastrophic cellular swelling and fatal cerebral edema, these cells actively pump out vital organic osmolytes, establishing a new, depleted osmotic equilibrium with the dilute extracellular fluid. If the serum sodium is subsequently corrected rapidly, the extracellular fluid violently transitions back to a relatively hypertonic state. Because the re-accumulation and de novo intracellular synthesis of these organic osmolytes is a biologically slow process, the depleted astrocytes are entirely defenseless. The reversed osmotic gradient forcefully pulls water out of the cells, resulting in severe intracellular dehydration and massive cellular shrinkage. This physical contraction of the perivascular astrocyte foot processes generates immense mechanical shear stress across the neural tissue, violently tearing the tight junctions that maintain the blood-brain barrier. The ensuing catastrophic breach permits the massive influx of circulating myelinotoxic complement proteins, leading to direct astrocyte apoptosis. Within 48 to 72 hours, the oligodendrocytes, completely deprived of the metabolic support normally provided by the astrocytes, undergo widespread degeneration, resulting in the classic, symmetrical demyelinating lesions observed on MRI. In certain conditions like uremia, chronic alcoholism and malnourishment the threshold for the sodium correction at which this change occurs is highly narrow and the normal range seldom holds true in these clinical scenarios which in this case might be exemplified by the presence of a hypertensive encephalopathy which rendered a strain on the BBB.

In this case the clinical progression rigidly adhered to the treacherous biphasic trajectory pathognomonic for ODS. He initially suffered from hypertensive encephalopathy and was also being evaluated for hyponatremia (the deily variation didn't cross the allowed limit of 6-8 mEq/ day) following which he entered the deceptive "Apparent Recovery Phase," regaining full consciousness and tolerating diet. However, following a standard latency period of 48-72 hours, he violently plummeted into the "Demyelination Phase". This secondary deterioration, characterized by severe dysphagia, rigidity, hyperreflexia, and hallucinations, represented the physical destruction of the descending corticobulbar and corticospinal tracts traversing the basis pontis. The extreme vulnerability of this episode was massively amplified by his preceding episode of severe hypertensive encephalopathy, where his blood pressure exceeded 200mmHg. The basis pontis possesses a uniquely rigid anatomical grid structure. Massive bundles of transverse pontocerebellar fibers tightly interdigitate at right angles with the massive descending longitudinal tracts. This structural inflexibility prevents the local tissue from safely accommodating rapid volume changes or swelling. Severe hypertensive encephalopathy generates extreme microvascular hydrostatic pressure that independently compromises endothelial integrity, frequently causing localized vasogenic edema within this rigid pontine grid. Therefore, when the subsequent osmotic stress of the SIADH correction occurred days later, his pontine microvasculature was already critically traumatized. This "two-hit" mechanism—the convergence of acute hypertensive endothelial trauma and subsequent acute osmotic dehydration—vastly lowered the physiological

threshold required to trigger myelinolysis despite the patient not being medically treated for sodium correction. The question of whether the encephalopathy triggered the alteration in sodium levels (though within limit of 8 mEq/day – with a doubtful undocumented correction in an outside hospital) to cause the demyelination needs much more clarity, though a theoretical possibility of hypertensive encephalopathy induced reduction in threshold does exist.

CASE 3- The highly volatile presentation of Case 3 exposes the profound metabolic fragility induced by decades of severe chronic alcohol use disorder. Patients suffering from chronic alcoholism exist in a persistent, precarious state of bioenergetic failure. Due to severe chronic systemic malnutrition and a lack of essential dietary precursors, their glial cell populations possess an inherently diminished reserve of the vital organic osmolytes necessary to buffer osmotic changes. Furthermore, the classic clinical phenomenon of "beer potomania" frequently contributes to massive dilutional hyponatremia .The ingestion of massive volumes of solute-poor alcoholic beverages entirely overwhelms the kidney's maximal free water excretion capacity, which is already severely blunted by poor dietary protein and solute intake, leading to water intoxication. His underlying metabolic exhaustion was immensely compounded by the acute onset of severe aspiration pneumonia. Extensive clinical literature definitively establishes that acute pulmonary infections—specifically aspiration pneumonia—are among the most potent physiological triggers for the non-osmotic, ectopic release of AVP, leading to profound SIADH. [4]In a landmark study by Miyashita et al. (2012), hyponatremia due to SIADH was proven to be strongly associated with increased in-hospital mortality and a higher risk of encephalopathy in elderly patients suffering from aspiration pneumonia. To safely manage the severe, euvolemic hyponatremia generated by the pneumonia-induced SIADH, the patient was initiated on Tolvaptan. Tolvaptan functions as a highly specific, oral vasopressin V2-receptor antagonist. By competitively blocking ADH at the renal collecting duct, Tolvaptan initiates a massive, sustained aquaresis—the targeted excretion of electrolyte-free water—without inducing concurrent sodium or potassium loss. While highly effective at raising serum sodium levels in treatment-resistant SIADH, the administration of vaptans in patients with chronic alcoholism requires extreme caution and vigilant monitoring.

CASE 4– The causes of SIADH in thee cases can be explained by Direct Hypothalamic-Pituitary Disruption: The osmoreceptors that control ADH secretion are located near the supraoptic nuclei of the hypothalamus. Inflammation, structural damage, or cerebral edema caused by a CNS infection can directly disrupt this regulatory axis, locking it into a continuous, active state that secretes excess ADH regardless of the body's serum osmolality.[12,13] Inflammatory Mediators: The localized immune response and the release of inflammatory cytokines within the cerebrospinal fluid and brain parenchyma can directly stimulate the release of ADH from the posterior pituitary. Stress and Increased Intracranial Pressure: CNS infections are often accompanied by significant physical stress and elevated intracranial pressure (ICP). The limbic system responds to these severe stressors (along with associated pain and nausea) by sending facilitatory impulses to the hypothalamus, further driving up ADH production.[13,14]

CONCLUSIONS

The clinical management of hyponatremia remains one of the most perilous and intellectually demanding aspects of internal medicine and critical care. As explicitly demonstrated by this case series, profound sodium disorders rarely occur as isolated biochemical anomalies. Rather, they are driven by complex, synergistic mechanisms that fundamentally alter the body's homeostatic landscape. Acute infectious processes, such as severe right pyelonephritis and massive aspiration pneumonia, chronic states of metabolic exhaustion—most notably severe alcohol use disorder—completely decimate the central nervous system's reserve of organic osmolytes, leaving the brain utterly defenseless against fluid shifts. Furthermore, mechanical vascular trauma resulting from extreme hypertensive encephalopathy can physically compromise the integrity of the blood-brain barrier, drastically lowering the threshold for osmotic injury. The catastrophic manifestation of Osmotic Demyelination Syndrome observed in this series serves as a stark, unforgiving reminder of the lethal consequences of overwhelming the central nervous system's adaptive capabilities. Ultimately, the successful and safe management of hyponatremia requires far more than the simple calculation of fluid deficits. It demands the mathematically constrained manipulation of systemic tonicity, the aggressive, rapid treatment of the underlying infectious or metabolic triggers, and an absolute commitment to preventing violent osmotic gradients across the fragile microvasculature of the brain, keeping in mind that in a fragile metabolic ecosystem the normal thresholds of sodium correction seldom hold true and minimal fluctuations can lead to catastrophic changes.

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