IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 24, Issue 2 Ser. 6 (February. 2025), PP 26-31
www.iosrjournals.org

Hyponatremia In Traumatic Brain Injury: Etiology, Incidence, And Response To Sodium Supplementation – A Retrospective Analysis From MGMMC & MYH Hospital, Indore

Dr Prateek Malpani, senior resident, Department of neurosurgery, MGMMC, Indore, Dr Mahesh Kumar Agarwal, Dr Yash Madnani, Dr Rakesh Gupta, Dr Zafar sheikh , Dr Paresh sodhiya,Dr Mukesh sharma
Corresponding author – Dr Prateek Malpani
Doc.prtk@gmail.com

Abstract
Aim
This study aimed to explore the mechanisms involved in evaluating various treatment strategies for hyponatremia in traumatic brain injury patients and their effects on outcomes.
Method
130 patients more than 18 years diagnosed with traumatic brain injury with and serum sodium <135mEq/L were included in the study while patients with pre-existing electrolyte imbalances and chronic kidney disease and those who died within 24 hours of admission were excluded.
Results
Different management strategies for hyponatremia were evaluated, such as fluid restriction and monitoring, administration of hypertonic saline, and use of mineralocorticoids and vasopressin antagonists.
Conclusion
In our study, we found that differentiating cerebral salt wasting from SIADH can be challenging, but it is essential due to the distinct treatment strategies for each condition. Rapid overcorrection of sodium levels should be avoided to prevent complications. Proper diagnosis is crucial for effective management of hyponatremia.

Date of Submission: 21-02-2025 Date of Acceptance: 01-03-2025

I. Introduction

Traumatic brain injury, as a common disease entity in neurosurgery, refers to the organic damage to the brain tissue caused by mild to severe head trauma (1, 2), with particularly high morbidity rate and mortality rate. Clinical manifestations include symptoms such as disturbance of consciousness, dizziness, and headache, the delayed treatment for which may give rise to complications such as permanent dysfunction, amnesia, and epilepsy, jeopardizing patients' life safety and hindering the quality of life (3–5). Hyponatremia, defined as serum sodium < 135meq/L, is the most common electrolyte abnormality encountered in patients with traumatic brain injury (6). **After traumatic brain injury, the release of anterior pituitary gland adrenocorticotropic hormone increases due to the stress response, which has a certain impact on sodium excretion, and the application of a large amount of dehydrating drugs after traumatic injury can also lead to low sodium, which may cause impaired nerve cell function, resulting in neurological dysfunction and even disability or death in severe cases (7, 8). In addition, patients with traumatic brain injury are frequently complicated with hyponatremia, which may trigger neurological dysfunction or even death and disability in severe cases due to damages to the patients' nerve cells. It has been found clinically that the understanding of the causes of traumatic brain injury complicated by hyponatremia serves to a better prognosis of patients and drives down mortality (9–11). In addition, the clinical treatment of this disease is mainly gastrointestinal sodium supplementation, which has obvious limitations and poor efficacy (12), so it is also urgent to explore more ideal treatment methods.** The reported incidence of hyponatremia in TBI ranges from 9.6 to 51% (13–14) and it is well established that hyponatremia is an independent predictor of poor neurological outcome in patients with TBI (13–14). Despite this there are no practical management protocols, especially for use in areas where sophisticated laboratory

investigations are unavailable and prolonged admission occupies precious hospital beds. The common causes of hyponatremia in TBI are CSW, SIADH, hypopituitarism and inadequate dietary intake of salt (15). Of these, inadequate salt intake can be diagnosed with reasonable certainty if the urine spot sodium is low (below 20 – 40mEq/L) and hypopituitarism can be diagnosed by biochemical evaluation of pituitary hormones. After ruling out these two entities, the clinician is left with CSW and SIADH, both of which manifest as hyponatremia with natriuresis (urine spot sodium more than 40mEq/L). The proportion of patients with hyponatremia caused by SIADH and CSW has been extensively debated in medical literature without definite consensus (16). Further review of literature takes the reader into the grey zone of differentiation between CSW and SIADH with panels of laboratory and clinical tests, none of which are conclusive (16). Measurement of ADH levels is not available at most hospitals managing head injury. Since the fluid management strategies in these two conditions are completely divergent, this results in a serious clinical dilemma. Fluid restriction is a less than ideal option when the clinical consequences of dehydrating a TBI patient are considered, especially in the setting of a tropical climate. Therefore, when serum sodium does not correct with dietary salt supplementation and hydration, though fluid restriction is possibly the appropriate treatment, the potential to cause harm must be kept in mind. Hyponatremia associated with TBI has been found to respond to salt retaining therapy in the setting of natriuresis, the reasons for which have not been clearly explained (16). This retrospective analysis was undertaken to study the incidence of hyponatremia in patients with TBI, and the results of different management strategies. We have also described a practical bedside management protocol for hyponatremia in TBI.

II. Methods

A retrospective review of 536 patients admitted with a diagnosis of traumatic brain injury (TBI) between January 2024 and October 2024 was undertaken from the hospital electronic patient records, and radiological data obtained from the institutional picture archiving and communicating system .The severity of the head injury was graded based on the GCS score as mild (GCS score 13-15), moderate (9-12) and severe (3 - 8) (22). Clinical parameters recorded were GCS score at admission, age, pupillary status, blood pressure at admission, presence of other significant injuries and need for surgical intervention. Radiological parameters recorded included the presence of hematomas, subarachnoid haemorrhage (SAH) and diffuse cerebral oedema. Hyponatremia was defined as serum sodium less than 135meq/L, and was further classified as mild (serum sodium 130-134 mEq/L), moderate (serum sodium 125-129meq/L) and severe (serum sodium < 125 mEq/L). Patients with acute kidney injury or chronic renal failure were excluded from the study. The etiology of hyponatremia was broadly dichotomized into nonnatriuretic (urine spot sodium < 40mEq/L) and natriuretic (urine spot sodium >40mEq/L).Patients with non-natriuretic hyponatremia were managed with additional dietary salt. Patients with natriuresis were managed with either hydration or fluid restriction according to the clinical suspicion of CSW or SIADH based on daily review of intake /output chart and hydration status. Hypertonic (3%) saline was used for severe or symptomatic hyponatremia. Finally patient outcome was assessed with Glasgow outcome scale.

Inclusion Criteria – Patients met the diagnostic criteria for traumatic brain injury and acute hyponatremia occurred within 7 days of onset, and the serum sodium concentration was <135 mmol/L

Exclusion Criteria – Patients with coagulation dysfunction, Pregnant and lactating women, Patients with a history of metabolic diseases and patients with hyponatremia caused by primary diseases such as chronic renal failure and nephrotic syndrome.

Diagnoses included: Skull fracture, Traumatic subarachnoid hemorrhage (SAH), Extra dural hematoma (EDH), Subdural hematoma (SDH), Cerebral contusion (CC), Diffuse axonal injury (DAI).

Treatment algorithm followed in our study included –
Hypertonic Saline
- 3%(513 mEq/L) & 1.6%(274 mEq/L)
- Strategies: Bolus / Infusion
- Bolus of (2-5ml/kg)in 15-20 mins. → Infusion at 10 ml per hour. (200-300 ml/ day.)

Tolvaptan
- Vasopressin receptor antagonist (V2 receptor antagonist).
- Used in non-acute, non-emergency settings.
- Avoided in CSW. (already plasma volume is low.)
- Starting dose → 15 mg orally once daily, which can be increased to 30 mg, and up to a maximum of 60 mg once daily if needed.

- Severe Hyponatremia→ 3% NaCl bolus 100 to 150 ml over 20-30 minutes.
- Moderate Hyponatremia→ 20 to 30 ml per hour for 10 hours.
- Vaptan→ Not for emergency→ Unpredictable→ 3% with Vaptan → Not often used → ODS.
- Fludrocortisone (promotes sodium reabsorption from kidneys)→we have not used in hyponatremia. (useful for CSW).

III. Results

A total of 536 patients were admitted with a diagnosis of traumatic brain injury at our centre during the review period of whom 130 developed hyponatremia (24.25%), with 110 males (84.60%) and a mean age was 39.2 years. 32 patients had severe, 76 moderate and 22 had mild head injuries. The incidence of mild, moderate and severe hyponatremia was 28.50%, 53.58% and 17.70% respectively. Hyponatremia was associated with natriuresis in 126/130 patients (96.92 %). Presence of subarachnoid haemorrhage on the admission CT scan of the brain was the commonest finding in these patients. The mean duration of stay for patients with hyponatremia was 12 days as opposed to 7 days for those without hyponatremia. 73 patients (56.2 %) showed good recovery out of 130 hyponatremia patients. Unfortunately three patients died, although only cause as hyponatremia could not be established. All the three patients were from severe head injury group.

SR.No.	DIAGNOSIS	No.	Hyponatremia(%)
1.	Skull fracture	102	5(4.9%)
2.	Traumatic subarachnoid hemorrhage	52	28(53.8%)
3.	Extra dural hematoma	81	9(11.1%)
4.	Subdural hematoma	160	45(28.1%)
5.	Cerebral contusion	112	29(25.8%)
6.	Diffuse axonal injury	29	14(48.27%)
	Total	536	130(24.25%)

TABLE 1 – SHOWING VARIOUS TBI DIAGNOSIS WITH HYPONATRIMIA

GENDER	
Males	110(84.6%)
Females	20(15.4%)
Total	130

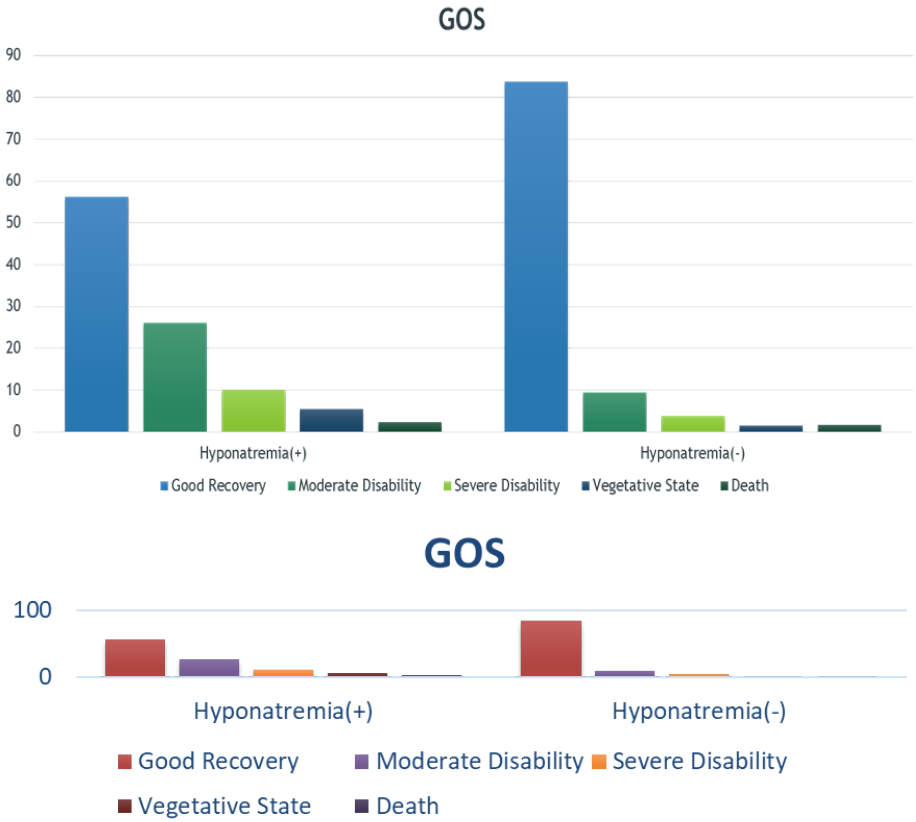
TABLE 2 – GENDER WISE DISTRIBUTION OF HYPONATRIMIA

HYPONATREMIA	
Mild	37(28.5%)
Moderate	70(53.8%)
Severe	23(17.7%)
Total	130

TABLE 3 – DISTRIBUTION OF SEVERITY OF HYPONATRIMIA

GLASGOW OUTCOME SCALE		
Hyponatremia	**Present**	**Absent**
Good Recovery	73(56.2%)	340(83.7%)
Moderate Disability	34(26.1%)	38(9.4%)
Severe Disability	13(10%)	15(3.7%)
Vegetative State	7(5.4%)	6(1.5%)
Death	3(2.3%)	7(1.7%)
Total	130	406

TABLE 4 – OUTCOME OF HYPONATRIMIA ON THE BASIS OF GLASGOW OUTCOME



IV. Discussion

Hyponatremia is **commonly seen** in patients with traumatic brain injury (TBI) and poses significant clinical risks. Hyponatremia **lowers plasma osmotic pressure**, potentially causing **vasogenic edema** and secondary brain damage in patients with central nervous system (CNS) diseases. Maintaining serum sodium levels within the normal range (targeted at 140 mEq/L) and ensuring normovolemia is crucial. Proper sodium and fluid management helps **prevent complications** like **cerebral vasospasm**. **Hyponatremia** in TBI patients is associated with **poorer clinical outcomes**, highlighting the need for effective treatment. **Differentiating** between SIADH and CSWS is critical because each requires a unique treatment approach. **Diagnosis** can be **challenging**, as clinical examination may not provide enough information to distinguish between them. **Overlapping pathophysiological features** of SIADH and CSWS add further complexity to accurate diagnosis.

Serum sodium (135-145 mEq/L) is tightly regulated in the body by many mechanisms including but not limited to the hypothalamic osmostat, renal control mechanisms, preserved thirst response and sweating. A change in the serum concentration of most ions in the body produces end organ effects due to the alteration in transmembrane potentials, such as the arrhythmias in hypokalemia or weakness in hypomagnesemia. Dysnatremias, in addition to altering transmembrane potentials, also cause alterations in cell volume due to changes in tonicity (6). A fall in the serum sodium causes osmotic shift of water from the extracellular to the intracellular compartment, causing cellular swelling and an increase in intracranial pressure.

Incidence of hyponatremia in TBI:

The incidence of hyponatremia in traumatic brain injury varies widely in literature. Sherlock et al reported an incidence of 9.6% (13), Moro et al in a retrospective analysis of 298 patients with TBI documented an incidence of 16.8% (17), Meng X et al found that one third of their patients with TBI had hyponatremia (18) and Yumoto et al have reported an incidence of 51%(19).

In our study the incidence of hyponatremia was 24.25%. More than half of our patients had moderate hyponatremia (53.58%) but 17.70% developed severe hyponatremia although serum sodium was checked either daily or on alternate days during the acute phase of the admission. Subarachnoid haemorrhage was the most common radiological abnormality observed in this cohort (53.58 %).

Differentiating between SIADH and CSW:

SIADH and CSW are the two common etiologies for hyponatremia with natriuresis in TBI. The exact incidence, pathophysiology and accurate clinical distinction between these two entities remain unclear (16, 17). SIADH is often over diagnosed because fluid restriction does raise the serum sodium even in patients with hyponatremia due to other reasons, and this is taken as proof of the diagnosis. Vingerhoets et al in their prospective study of 256 patients with TBI identified true SIADH as a cause of hyponatremia in only three out of the six suspected SIADH patients (20). Nelson et al demonstrated reduced blood volumes in 10/12 patients with clinical SIADH emphasizing the fact that the primary problem is the failure of the kidneys to conserve sodium. In a setting of TBI, the use of osmotic diuretics such as mannitol and the presence of an impaired hypothalamo-pituitary adrenal (HPA) axis, would compound the difficulty of diagnosing SIAD. Diringer et al demonstrated that patients on fluid restriction for management of a presumed SIADH are at a higher risk of developing delayed ischaemic neurological deficits (21). Wijdicks et al in their retrospective study of 134 patients with subarachnoid haemorrhage concluded that restricting fluids for correction of hyponatremia was potentially dangerous and resulted in cerebral infarction (22). There are innumerable laboratory tests suggested to establish the etiology of hyponatremia but none of them are conclusive. Since accurate differentiation between SIADH and CSW is difficult without expensive and scarce laboratory tests, we felt it was not worth attempting such a differentiation on a routine basis for all patients with hyponatremia. Salt retaining therapy - an alternative approach: Since fluid restriction is potentially hazardous and hyponatremia in TBI is commonly associated with natriuresis, salt retaining therapy using an agent with mineralocorticoid properties would be a logical option in managing such patients. Moro et al recommended the use of salt retaining therapy in managing hyponatremia associated with TBI. Mori et al in a prospective study of thirty patients with aneurysmal SAH demonstrated improved efficacy of hypervolemic therapy, when coupled with the inhibition of natriuresis using fludrocortisone. Tolvaptan was used in 38.40% (50/130) of our patients and we found that they had a significantly reduced hospital stay.

.

V. Conclusions

Early institution of tolvaptan for management of hyponatremia with natriuresis in TBI decreases the hospital stay significantly without any side effects. This simple approach, especially in a setting where fluid restriction might be deleterious, helps in the successful management of hyponatremia without the need to differentiate SIADH and CSW. However our study has limitation that this was a retrospective study and there was no protocol followed for the administration of tolvaptan.

References

[1] Harbert A, Northam W, Elton S, Quinsey C. Targeted Head CT Reduction For Pediatric Patients With Hydrocephalus And Traumatic Brain Injury: Academic Center Institutional Experience As An Example Of Opportunities For Further Improvement. Childs Nerv Syst. (2020) 36:583–9. Doi: 10.1007/S00381-019-04376-W

[2] Schur S, Martel P, Marcoux J. Optimal Bone Flap Size For Decompressive Craniectomy For Refractory Increased Intracranial Pressure In Traumatic Brain Injury: Taking The Patient's Head Size Into Account. World Neurosurgery. (2020). 139E430-E436. Doi: 10.1016/J.Wneu.2020.01.232

[3] Bree D, Mackenzie K, Stratton J, Levy D. Enhanced Post-Traumatic Headachelike Behaviors And Diminished Contribution Of Peripheral CGRP In Female Rats Following A Mild Closed Head Injury. Cephalalgia. (2020) 40:748–60. Doi: 10.1177/0333102420907597

[4] Guilhaume-Correa F, Cansler SM, Shalosky EM, Goodman MD, Evanson NK.Greater Neurodegeneration And Behavioral Deficits After Single Closed Head Traumatic Brain Injury In Adolescent Versus Adult Male Mice. J Neur Res. (2020) 98:557–70. Doi: 10.1002/Jnr.24535

[5] Khanuja T, Unni HN. Intracranial Pressure-Based Validation And Analysis Of Traumatic Brain Injury Using A New Three-Dimensional Finite Element Human Head Model. Proc Inst Mech Eng H. (2020) 234:3–15. Doi: 10.1177/0954411919881526

[6] Adrogué HJ, Madias NE. Hyponatremia. N Engl J Med. 2000 May 25;342(21):1581– 9.

[7] Hoffmann DB, Popescu C, Komrakova M, Welte L, Saul D, Lehmann W, Et Al. Chronic Hyponatremia In Patients With Proximal Femoral Fractures After Low Energy Trauma: A Retrospective Study In A Level-1 Trauma Center. Bone Rep. (2019) 12:100234. Doi: 10.1016/J.Bonr.2019.100234

[8] Jäckle K, Klockner F, Hoffmann DB, Roch PJ, Reinhold M, Lehmann W, Et Al. Influence Of Hyponatremia On Spinal Bone Quality And Fractures Due To Low-Energy Trauma. Medicina (Kaunas). (2021) 57:1224. Doi: 10.3390/Medicina57111224

[9] Singh S, Das KK, Deora H, Jaiswal AK, Behari S. Traumatic Partial Posterior Cord Brachial Plexus Injury In A Patient With Aberrant Innervation Of The Long Head Of The Triceps By The Axillary Nerve: Implications In Nerve Transfer Surgery. Asian J Neurosurg. (2020) 15:391–3. Doi: 10.4103/Ajns.AJNS_160_19
[10] Gillespie CS, Mcleavy CM, Islim AI, Prescott S, Mcmahon CJ. Rationalising Neurosurgical Head Injury Referrals: Development And Validation Of The Liverpool Head Injury Tomography Score (Liverpool HITS) For Mild TBI. Br J Neurosurg. (2020) 34:127–34. Doi: 10.1080/02688697.2019.1710825
[11] Anderson TN, Hinson HE, Dewey EN, Rick EA, Schreiber MA, Rowell SE. Early Tranexamic Acid Administration After Traumatic Brain Injury Is Associated With Reduced Syndecan-1 And Angiopoietin-2 In Patients With Traumatic Intracranial Hemorrhage. J Head Trauma Rehabil. (2020) 35:317– 23. Doi: 10.1097/HTR.0000000000000619
[12] Phillips N, Dalziel SR, Borland ML, Dalton S, Lyttle MD, Bressan S, Et Al. Imaging And Admission Practices In Paediatric Head Injury Across Emergency Departments In Australia And New Zealand: A PREDICT Study. Emerg Med Australas. (2020) 32:240–9. Doi: 10.1111/1742-6723.13396
[13] Sherlock M, O'Sullivan E, Agha A, Behan LA, Owens D, Finucane F, Et Al. Incidence And Pathophysiology Of Severe Hyponatraemia In Neurosurgical Patients. Postgrad Med J. 2009 Apr;85(1002):171–5.
[14] Yumoto T, Sato K, Ugawa T, Ichiba S, Ujike Y. Prevalence, Risk Factors, And Shortterm Consequences Of Traumatic Brain Injury-Associated Hyponatremia. Acta Med Okayama. 2015;69(4):213–8.
[15] Kurokawa Y, Uede T, Ishiguro M, Honda O, Honmou O, Kato T, Et Al. Pathogenesis Of Hyponatremia Following Subarachnoid Hemorrhage Due To Ruptured Cerebral Aneurysm. Surg Neurol. 1996 Nov;46(5):500-507-508.
[16] Sterns RH, Silver SM. Cerebral Salt Wasting Versus SIADH: What Difference? J Am Soc Nephrol. 2008 Feb 1;19(2):194–6.
[17] Moro N, Katayama Y, Igarashi T, Mori T, Kawamata T, Kojima J. Hyponatremia In Patients With Traumatic Brain Injury: Incidence, Mechanism, And Response To Sodium Supplementation Or Retention Therapy With Hydrocortisone. Surg Neurol. 2007 Oct;68(4):387–93.
[18] Meng X, Shi B. Traumatic Brain Injury Patients With A Glasgow Coma Scale Score Of ≤8, Cerebral Edema, And/Or A Basal Skull Fracture Are More Susceptible To Developing Hyponatremia. J Neurosurg Anesthesiol. 2016 Jan
[19] Yumoto T, Sato K, Ugawa T, Ichiba S, Ujike Y. Prevalence, Risk Factors, And Shortterm Consequences Of Traumatic Brain Injury-Associated Hyponatremia. Acta Med Okayama. 2015;69(4):213–8.
[20] Vingerhoets F, De Tribolet N. Hyponatremia Hypo-Osmolarity In Neurosurgical Patients. "Appropriate Secretion Of ADH" And "Cerebral Salt Wasting Syndrome." Acta Neurochir (Wien). 1988;91(1–2):50–4.
[21] Diringer MN, Zazulia AR. Hyponatremia In Neurologic Patients: Consequences And Approaches To Treatment. The Neurologist. 2006 May;12(3):117–26.
[22] Wijdicks EF, Vermeulen M, Hijdra A, Van Gijn J. Hyponatremia And Cerebral Infarction In Patients With Ruptured Intracranial Aneurysms: Is Fluid Restriction Harmful? Ann Neurol. 1985