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Hypochloraemia in patients with severe traumatic brain injury at a tertiary care hospital in India. A possible threat for mortality

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ABSTRACT

Objective: To evaluate the correlation between Individuals with severe traumatic brain injury and death from electrolyte imbalance

Methodology: In a prospective cohort study, patient records suffering from a severe brain injury caused by trauma Glasgow Coma Scale score less than 8, and electrolyte abnormalities were reviewed. To determine a correlation between the patients who passed away and the ones who lived, electrolyte levels were examined. For categorical variables, bivariate analysis was carried out using the $\chi 2$ test, which has a 95% statistical accuracy. To ascertain the correlation between electrolyte fluctuations and mortality, the $\chi 2$ test was employed in conjunction with multiple comparisons. The linkage between fatalities and electrolyte shifts was analysed using logistic regression. 95 per cent of statistical tests were reliable.

Results: In 24.5 % of patients who passed away, Elevated mortality risk was significantly correlated with hypochloremia (P 0.03). It also represents the substantial link between the Examination of Acute Physiology and Chronic Health APACHE II ($P < 0.01$) and age ($P < 0.01$).

Conclusion: Hypochloremia may be a significant prognostic factor for determining death in individuals suffering from severe TBI risk and optimising treatment.

Keywords
hypochloraemia,
severe traumatic brain injury

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INTRODUCTION

All across the world, traumatic brain injury (TBI) is a serious socioeconomic as well as public health issue. Globally, TBI is the leading death cause for young adults. [1-3]

There are 250 traumatic brain injury cases for every 100,000 people worldwide each year.4 In developed nations, falls, auto accidents, violent crimes, and motorcycle accidents are the leading causes of TBI. In Europe, the male-to-female ratio for TBI is 9:1, while in the United States it is 3:1. Traumatic brain injury happens every 7 seconds, and in young people, it happens every 5 minutes.4 TBI accounts for 45% of deaths in patients with polytrauma.1 Additionally, the majority of TBI survivors are thought to have a permanent sequel. In Colombia, there are 200 cases of head trauma for every 100,000 people annually, translating to an 18% TBI death rate. [5].

TBI also affects the blood-brain barrier, primarily through modifications to pressure gradients associated with Starling forces. Significant changes in the levels of other solutes and electrolytes also impact osmolarity. Patients with TBI may experience magnesium deficiency, hypophosphatemia, hypernatremia, hypokalemia, or hypocalcemia soon after the first injury and the recovery process. These changes are likely connected with how the lesion is developing or how medicine is being given. [7, 8]

In clinical studies, the association with in electrolyte levels and TBI fatality is not well established. The majority of trauma studies focus on hyponatremia and its clinical changes, but they don't account for electrolytes like magnesium, potassium, chlorine, or other elements.9, 10 There is only one study in Colombia that looks at patients who have both electrolyte imbalances and renal failure; no other research addresses these issues about TBI.11 Colombia's Ministry of Health and Social Protection wants to create accident prevention programs to lower death rates and secondary lesions among TBI patients. 12–14 This study's primary goal was to determine the association between altered electrolytes and higher mortality in TBI patients by using patient's cohort from Sawai Man Singh Medical College and Hospital, Jaipur.

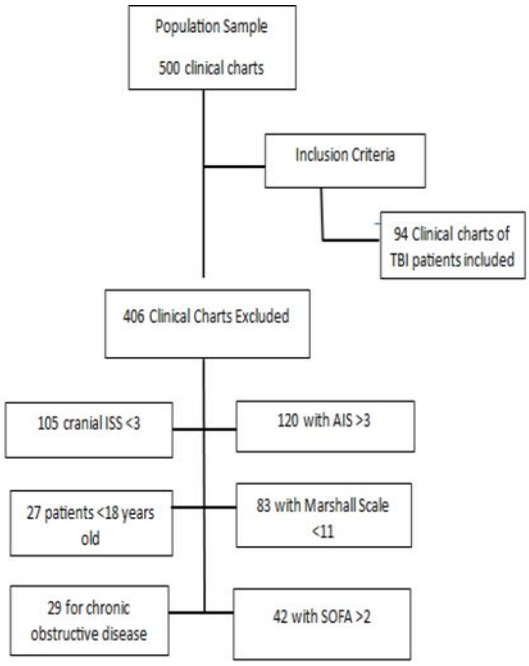

Figure 1: Flowchart of the total patients and record of exclusion. Traumatic brain injury (TBI), Abbreviated Injury Scale (AIS), Cranial Injury Severity Scale (cranial ISS), sequential organ failure score assessment (SOFA).

Materials and Methodology

Study Design

The clinical records of patients from Sawai Man Singh Medical College and Hospital, Jaipur who suffered from severe traumatic brain injury have been examined. Patients were divided into two groups based on the presence or absence of electrolyte abnormalities to examine the possible correlation between these abnormalities and mortality. 500 admitted TBI patients' clinical records made up the study's population sample between the November 2023 to April 2024.

The study's inclusion criteria were individuals with TBI who were over 18 and had a Marshall tomography classification of III or above. A total score of 3 was obtained from the Glasgow Coma Scale, 3 from the Trauma Severity Scale of Cranial Trauma, 3 from the Abbreviated Injury Scale data, and 8 from the Trauma Severity Scale of Body Trauma. Individuals undergoing therapy with loop diuretics, mannitol, thiazide, digitalis, or glucocorticoids were not included, nor were patients with chronic illnesses.

Patients with sepsis, septic shock, and multiorgan dysfunction with a Sequential Organ Failure Assessment greater than 2 that was unrelated to a declining Glasgow Coma Scale score were also excluded. Moreover, 406 patients were discharged from the 500 clinical charts that were analyzed; 120 Patients were not treated due to having an Abbreviated Injury Scale score of more than three; A cranial Injury Severity Scale score of less than three excluded 105 patients, and a Marshall classification of less than three excluded 83 patients. With a sequential organ failure score assessment of more than two, 42 patients suffered from severe infections. 29 patients with chronic illnesses and 27 patients under the age of 18 were assessed.

Consequently, 94 patients fulfilled the study's inclusion requirements (Figure 1). Information was taken from patient records during the initial ten days of hospital stay. Daily electrolyte readings and sociodemographic data were documented.

Analysis of Data

Levels of blood for K, Ca, Na, Mg, and Cl were monitored for 10 days after the admitting date. The Kolmogorov-Smirnov statistical analysis was used to verify the numerical variables, and the various variables were grouped based on proportions for

particular categorical variables. Nonparametric measures were employed to analyze variables that did not exhibit normality patterns. Moreover, the χ2 evaluation was carried out with 95 percent consistency for categorical variables. In the final statistical analysis, the Yates correction was applied when the frequency was less than five.

The correlation between electrolyte disturbances and mortality was ascertained through multiple comparisons by the χ2 test. Additionally, a regressional analysis was done to find out how electrolyte imbalances and mortality are related. A 95% dependability level was maintained throughout the execution of each statistical test.

Results

The medical history of 500 individuals diagnosed with severe head trauma who were admitted to Sawai Man Singh Medical College and Hospital, Jaipur between November 2023 to April 2024 comprised the population sample for this study. Out of 500 clinical charts, 406 were deemed ineligible for inclusion in the study, while 94 clinical charts satisfied the requirements and were added to the database. The clinical charts were based on whether or not there were electrolyte changes.

Table no 1. Sociodemographic and Clinical Characteristics of Patient Population (N= 94)

Characteristic	Value
Sex	
Male	78(92.6%)
Female	16(7.4%)
Age, years, average (SD)	42.1(18.6%)
Acute complications	
Renal Disease	6(4.9%)
Subarachnoid Disease	6(4.9%)
Diabetes insipidus	9(5.9%)
No complications	73(84.3%)
Marshall classification	
III	5(3.8%)
IV	24(25.1%)
V	57(64.9%)
VI	8(6.2%)
Hospital length of stay, days, average (SD) 12(12.6%)	
Patients deceased	34(24.5%)
Patients survived	60(75.5%)

The patients were 42 years old on average, with an 11:1 male-to-female ratio consisting of 78 men (92.6%) and 16 women (7.4%). Side effects, such as acute kidney disease (4.9%), subarachnoid hemorrhage (4.9%), and diabetes insipidus (5.9%), were observed in patients (Table 1).

Table no 2. Electrolyte Alteration in Patients with Severe Traumatic Brain Injury (N=94)

Electrolyte	Value
Potassium	
Hypokalemia, mean 3.1 mEq/L	41 (25.1%)
High plasma osmolarity	(42.2%)
Hyperkalemia, mean 6.0 mEq/L	9 (27.9%)
Normal values	44(46.9%)
Calcium	
Hypocalcemia, mean 6.7 mEq/L and 0.8 mmol/L 19 (16.1%)	
Hypercalcemia, average 13.9 mEq/L and 1.5 mmol/L 11(3.5%)	
Normal values	64 (79.5%)
Magnesium	
Hypomagnesemia, mean 1.3 mEq/L	38 (38.7%)
Hypermagnesemia, mean 3.2 mEq/L	11 (3.5%)
Normal values	45 (57.8%)
Sodium	
Hyponatremia, mean 128 mEq/L	42 (55.6%)
Hypernatremia, average 150 mEq/L	14 (12.7%)
Normal values	44 (31.7%)
Chlorine	
Hypochloremia, mean 94 mEq/L	12 (46.7%)
Hyperchloremia, mean 117.8 mEq/L	9 (3.6%)
Normal values	73 (56.9%)

According to Marshall Tomography classification (any surgically evacuated injuries), 25.1% of lesions were diffuse type IV lesions (shift greater than 6 mm; no high- density or mixed-density injuries greater than 26 mL). Scores 16 and 17 on the Acute Physiology and Chronic Health Evaluation (APACHE II) classification indicated that mortality would be between 156% and 22%. Changes in hydroelectrolyte levels were noted in 78 clinical charts (92.8%); the most common changes were related to sodium and potassium, with hyponatremia accounting for 55.6% and hypokalemia at 46.7 % (Table 2).

The least affected electrolytes were magnesium and calcium, with increases in each occurring in just 3.5 % of the total charts.

In 14% of the charts analyzed, hypochloremia was detected. Just 82.5% of the patients had electrolyte correction of any kind. There was a statistically significant correlation discovered among APACHE II score (P < 0.01), older age, and mortality (P < 0.01). Furthermore, hypochloremia was observed in 25.1% of individuals, which was substantially important (95% confidence interval: 1.0-15.5; P ¼ 0.03).

Despite their prevalence, hyperkalemia, hypomagnesemia, and hypermagnesemia did not significantly correlate with death. Hypochloremia and hyperkalemia, two categorical variables, displayed an odds ratio for a higher chance of dying. Furthermore, 42.2% of patients had high plasma osmolarity (292.14 SD 16.9); this result was statistically significant (P ¼ 0.03). The majority of these patients were deceased.]

Discussion

The study's findings revealed a 24.5% TBI death rate, which is significantly greater than the 10%–20% mentioned in previous research on patients with comparable traits. [17, 18] The association between hypochloremia and an elevated risk of fatality in individuals who passed away, with a statistically accurate difference (P ¼ 0. 03), was the study's most significant finding. It is possible to argue that hypochloremia is a significant threat or a mortality predictor in TBI individuals. It's also crucial to remember that hypochloremia may go undiagnosed, be an isolated finding, or be linked to hyponatremia, which is another condition that has a poor prognostic value.[19] However, hyponatremia was not a statistically important factor for death because it was found in both surviving and deceased patients with high frequency.

The investigation's findings are novel since prior studies have focused on changes in Na and K that are associated with mortality rather than Cl. [9, 20–22] Moreover, some research has demonstrated that variations in chlorine concentrations are linked to adjustments made to the microenvironment of neuronal cells because chlorine is transported out of the cell, acting in opposition to its electrical balance and favor of its chemical balance.[23]Because of this, in most mature neurons, chlorine can act as a signaling agent and a depolarizing current.[24] Potassiumchlorine, KCC1-4, SLC12A4 through SLC12A7, and sodium- dependent cotransporters of chlorine- bicarbonate, like SLC4A8 and the sodium-driven chloride/bicarbonate exchanger NDCBE, are the most significant cotransporters of chlorine. Mature g-aminobutyric acidergic postsynaptic neurons are hyperpolarized by low intracellular chlorine concentrations.[24]

On the other hand, certain immature neurons depend on g-aminobutyric acid for the expression of chlorine currents, which in turn produce postsynaptic potentials that depolarize and are essential for maintaining the stability of recently formed synapses. The partial depolarization of g-aminobutyric acid-dependent neurons, which is made worse by local ischemia that affects the sodium-potassium adenosine triphosphatase pump and reduces the hyperpolarizing effect of chlorine current, may be linked to hypochloremia and mortality.[25, 26]

Patients with TBI may experience hypochloremia due to a reduction in renal perfusion and tubular renal Claudin-2 expression, which obstructs the reabsorption of chlorine. [12, 14, 27]

The analysis of mortality showed a statistically significant correlation with age as one of the variables; the greater the patient's age, the higher their risk. The other significant variable was the APACHE II score (P less than 0.01).

This outcome is consistent with findings from previous research. Age is one risk factor included in the validated APACHE II scale for predicting death in critically ill patients.[28] The standardization of patient characteristics was made possible by the inclusion and exclusion criteria. With an approximate age of 42 and a total hospital stay of 6 months, men made up the majority of the study's patients. These attributes align with a few of the reviewed studies from Latin America. This study's male-to-female ratio of 5:1 was comparable to that reported by Guzmán et al.[5] Clinical studies conducted in the US and Europe produced findings comparable to these (e.g., Brazinova et al.[17]) There could be several reasons for the disparity in frequency of patients by gender, such as lifestyle, environment, cultural background, and occupational risks.

According to the results, water-electrolyte shifts were discovered in 92.8 percent of patients; as in previous clinical trials, potassium (46.9%) and sodium (55.6%) were the most affected electrolytes. Kovesdy et al.[22] discovered abnormal blood and a correlation that is statistically important between levels of potassium and sodium and mortality in

patients suffering from electrolyte imbalances, liver disease, and cardiovascular disease. However, this study did not find a correlation, and the patients who survived had more of these electrolyte abnormalities. The fact that there were methodological variations, the follow-up period was extended, and comorbidities were not utilized as an exclusion criterion must be emphasised.[22, 29]

Despite the patient population or setting, all research has concluded that there is a clear correlation between hyponatremia and a higher risk of death.[30, 31] The association between hyperosmolarity and hyperglycemia was statistically significant with a greater alteration in patients who passed away. Because hyperglycemia causes hyperosmolarity, it also raises insulin levels and causes hypokalemia, and is linked to increased levels of cortisol, glucagon, and catecholamines.[19]

Limitations

Despite the initial analysis of 500 clinical charts, the research was constrained by the ultimate sample size. Another drawback was the follow-up period, although most studies on this subject have a follow-up period of six months. The evaluation of charts from just one hospital represents the last restriction. This research's strengths include its statistical evaluation and the dearth of comparable research containing data on electrolytes more than potassium and sodium.

Conclusion

In TBI patients, hypochloremia may be a prognostic factor or a threatening factor for increased mortality. Osmolarity and electrolytes should be assessed and managed because there is a statistically accurate link between changes in these parameters and fatalities. Patients with TBI need to be treated right away if their hydro-electrolyte levels change. Changes in magnesium or chlorine electrolyte levels should also be taken into account as a potential threat to death in TBI patients.

References

1. Rubiano AM, Carney N, Chesnut R, Puyana JC. Global neurotrauma research challenges and opportunities. Nature. 2015 Nov 19; 527(7578):S193-7.
2. Puvanachandra P, Hyder AA. Traumatic brain injury in Latin America and the Caribbean: a call for research. Salud publica de Mexico. 2008;50(S1):3-5.
3. Roozenbeek B, Maas AI, Menon DK. Changing patterns in the epidemiology of traumatic brain injury. Nature Reviews Neurology. 2013 Apr;9(4):231-6.
4. Colantonio A, Hsueh J, Petgrave J, Hirdes JP, Berg K. A profile of patients with traumatic brain injury within home care, long-term care, complex continuing care, and institutional mental health settings in a publicly insured population. The Journal of Head Trauma Rehabilitation. 2015 Nov 1;30(6):E18-29.
5. Guzmán F, Moreno MC, Montoya A. Traumatic brain injury patients at Hospital Universitario del Valle: a 12 months study. Revista Colombia Médica. 2008 Jul 1;39(3s3):25-8.
6. Ballabh P, Braun A, Nedergaard M. The blood–brain barrier: an overview: structure, regulation, and clinical implications. Neurobiology of disease. 2004 Jun 1;16(1):1-3.
7. Polderman KH, Bloemers FW, Peerdeman SM, Girbes AR. Hypomagnesemia and hypophosphatemia at admission in patients with severe head injury. Critical care medicine. 2000 Jun 1;28(6):2022-5.
8. Hoffman H, Jalal MS, Chin LS. Effect of hypernatremia on outcomes after severe traumatic brain injury: a nationwide inpatient sample analysis. World neurosurgery. 2018 Oct 1; 118:e880-6.
9. Polderman KH, Schreuder WO, van Schijndel RJ, Thijs LG. Hypernatremia in the intensive care unit: an indicator of quality of care?. Critical care medicine. 1999 Jun 1;27(6):1105-8.
10. Tisdall M, Crocker M, Watkiss J, Smith M. Disturbances of sodium in critically ill adult neurologic patients: a clinical review. Journal of neurosurgical anesthesiology. 2006 Jan 1;18(1):57-63.
11. Moreno A, Insuasty MI, Londoño D, D'Achiardi R, Garcia P. Clinical characteristics of the patients of the intensive care unit of the University Hospital of San Ignacio with acute renal failure and factors associated with mortality. Acta Médica Colomb. 2011; 36:162-168.
12. Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, Bratton SL, Chesnut R, Harris OA, Kissoon N, Rubiano AM. Guidelines for the management of severe traumaticbrain injury. Neurosurgery. 2017 Jan 1;80(1):6-15.
13. Stein DM, Feather CB, Napolitano LM. Traumatic brain injury advances. Critical care clinics. 2017 Jan 1;33(1):1-3.
14. Rubiano AM, Tejada PA, Alarcón JD, et al. Colombian guide of clinical practice for the diagnosis and treatment of adult patients with severe cranioencephalic trauma. Paper presented at: XXVI International Eurocirugía Symposium. March 30 to April 1, 2017; Cali, Valle del Cauca, Colombia.
15. Maas AI, Hukkelhoven CW, Marshall LF, Steyerberg EW. Prediction of outcome in traumatic brain injury with computed tomographic characteristics: a comparison between the computed tomographic classification and combinations of computed tomographic predictors. Neurosurgery. 2005 Dec 1;57(6):1173-82.16.

16. Palmer CS, Gabbe BJ, Cameron PA. Defining major trauma using the 2008 Abbreviated Injury Scale. Injury. 2016 Jan 1;47(1):109-15.
17. Brazinova A, Rehorcikova V, Taylor MS, Buckova V, Majdan M, Psota M, Peeters W, Feigin V, Theadom A, Holkovic L, Synnot A. Epidemiology of traumatic brain injury in Europe: a living systematic review. Journal of neurotrauma. 2021 May15;38(10):1411-40.
18. McHugh GS, Engel DC, Butcher I, Steyerberg EW, Lu J, Mushkudiani N, Hernández AV, Marmarou A, Maas AI, Murray GD. Prognostic value of secondary insults in traumatic brain injury: results from the IMPACT study. Journal of neurotrauma. 2007 Feb 1;24(2):28793.
19. Audibert G, Hoche J, Baumann A, Mertes PM. Water and electrolytes disorders after brain injury: mechanism and treatment. InAnnales francaises d'anesthesie et de reanimation 2012 Jun 7 (Vol. 31, No. 6, pp. e109-15).
20. Li M, Hu YH, Chen G. Hypernatremia severity and the risk of death after traumatic brain injury. Injury. 2013 Sep 1;44(9):1213-8.
21. Beal AL, Scheltema KE, Beilman GJ, Deuser WE. Hypokalemia following trauma. Shock. 2002 Aug 1;18(2):107-10.
22. Kovesdy CP, Lott EH, Lu JL, Malakauskas SM, Ma JZ, Molnar MZ, Kalantar-Zadeh K. Hyponatremia, hypernatremia, and mortality in patients with chronic kidney disease with and without congestive heart failure. Circulation. 2012 Feb 7;125(5):677-84.
23. Duran C, Thompson CH, Xiao Q, Hartzell HC. Chloride channels: often enigmatic, rarely predictable. Annual review of physiology. 2010 Mar 17; 72:95-121.
24. Isomura Y, Sugimoto M, FujiwaraTsukamoto Y, Yamamoto- Muraki S, Yamada J, Fukuda A. Synaptically activated Cl– accumulation responsible for depolarizing GABAergic responses in mature hippocampal neurons. Journal of neurophysiology. 2003 Oct; 90(4):2752-6.
25. Elmore S. Apoptosis: a review of programmed cell death. Toxicologic pathology. 2007 Jun;35(4):495-516.
26. Liu Y, Shoji-Kawata S, Sumpter Jr RM, Wei Y, Ginet V, Zhang L, Posner B, Tran KA, Green DR, Xavier RJ, Shaw SY. Autosis is a Na+, K+-ATPase–regulated form of cell death triggered by autophagyinducing peptides, starvation, and hypoxia–ischemia. Proceedings of the National Academy of Sciences. 2013 Dec 17;110(51):20364-71.
27. Gong Y, Hou J. Claudins in barrier and transport function—the kidney. Pflügers Archiv-European Journal of Physiology. 2017 Jan; 469:105-13.
28. Berger Mm, MarazziA, Freeman J, Chioléro R. Evaluation of the consistency of Acute Physiology and Chronic Health Evaluation (APACHE II) scoring in a surgical intensive care unit. Critical care medicine. 1992 Dec 1;20(12):1681-7.
29. Upadhyay A, Jaber BL. Madias Ne. epidemiology of hyponatremia. Semin Nephrol. 2009 May;29:227-
30. Paiva WS, Bezerra DA, Amorim RL, Figueiredo EG, Tavares WM, De Andrade AF, Teixeira MJ. Serum sodium disorders in patients with traumatic brain injury. Therapeutics and clinical risk management. 2011 Aug 11:345-9.
31. Yumoto T. Prevalence, risk factors, and short-term consequences of traumatic brain injury-associated hyponatremia.