Dysnatremia in Traumatic Brain Injury and its Association with Outcome

Bishokarma S,[1] Thapa U,[1] Thapa M,[2] Singh AK,[1] Gurung S,[1] Aryal B,[1] Maharjan AMS,[2] Lakshmipathy G[1]

[1]Department of Neurosurgery

[2]Department of Neurology

Upendra Devkota Memorial National Institute of Neurological and Allied Science

Bansbari, Kathmandu, Nepal.

Corresponding Author

Suresh Bishokarma

Department of Neurosurgery,

Upendra Devkota Memorial National Institute of Neurological and Allied Science,

Bansbari, Kathmandu, Nepal.

E-mail: drsureshbk@gmail.com

Citation

Bishokarma S, Thapa U, Thapa M, Singh AK, Gurung S, Aryal B, et al. Dysnatremia in Traumatic Brain Injury and its Association with Outcome. *Kathmandu Univ Med J.* 2022;78(3):155-60.

ABSTRACT

Background

Traumatic brain injury on its own results in significant mortality and morbidity but it also contributes to complications that manifest as dysnatremia in the majority of cases.

Objective

The objective of this study is to assess the association of hyponatremia and hypernatremia with the severity of traumatic brain injury and its impact on mortality.

Method

This is a retrospective, descriptive, and analytic study conducted during a 1-year period from March 2018 to March 2019. The study population was selected from the patients presenting to the emergency department with TBI in the Upendra Devkota Memorial National Institute of Neurological and Allied Sciences, Bansbari, Kathmandu, Nepal. All the patients that fulfilled the inclusion criteria of age were enrolled in the study. Patients with known renal disease due to the higher incidence of electrolyte disbalance were excluded. Association of outcome with hyponatremia and hypernatremia were sought using chi-square, fisher exact test and independent t test using SPSS ver 20.

Result

Over a period of 1 year, 367 patients with traumatic brain injuries were treated in our hospital. Hyponatremia was seen among 55 patients (14.9%) and hypernatremia was seen among 22 patients (5.99%). The age range of patients included in the study was 16 to 87 with a mean age of 37.96 ± 16.512 years. The male to female ratio was calculated as 3.2:1. Mild, moderate, and severe head injuries were 286 (77.9%), 37 (10.1%), and 44 (12%) respectively. Surgical intervention was performed among 77(21%) individuals. Our series showed an association between the severity of traumatic brain injury and hyponatremia however didn't show an association between the severity of traumatic brain injury and the development of hypernatremia.

Conclusion

We concluded that the severity of head injury is associated with severity of hyponatremia but not with severity of hypernatremia. Similarly, a strong association existed between the severity of hypernatremia and outcome of patients. However, such association was not seen with hyponatremia.

KEY WORDS

Hypernatremia, Hyponatremia, Mortality, Severity, Traumatic head injury

INTRODUCTION

A traumatic brain injury (TBI) usually results from a violent blow or jolt to the head or body. The mode of injury ranges from road traffic accidents (RTA), physical assaults as well as falls which is especially noted in the elderly. In a developing country such as Nepal, the sub-standard road conditions as well as the burning issue of driving under the influence contribute to the major burden of RTA. TBI on its own results in significant mortality and morbidity. It is further contributed to complications presenting as dysnatremia in the majority of cases.[1]

Dysnatremia refers to the presence of hyponatremia or hypernatremia. Hyponatremia was defined as a serum sodium (SNa) below 135 mmol/L, hypernatremia was defined as a SNa above 145 mmol/L, and eunatremia was defined as a SNa between 135 and 145 mmol/L.[2] The brain is central to endocrine homeostasis. Any injury to its structure can be present with neurohypophyseal dysregulation. Hypernatremia in TBI can be due to predisposing conditions such as sensory disturbances, changes in thirst, central diabetes insipidus alongside polyuria, and increased imperceptible water loss.[1] TBI patients may develop SIADH (Syndrome of Inappropriate Anti-diuretic Hormone) or CSW (Cerebral Salt Wasting), presenting clinically as hyponatremia resulting in cerebral edema.[3]

Early anticipation of these complications may help reduce or sometimes prevent mortality and morbidity. Acute hyponatremia can lead to death if brain edema is not treated promptly. Conversely, if chronic hyponatremia is rapidly corrected, osmotic demyelination occurs, which is potentially fatal.[4] Although multiple excellent studies have been conducted on hyponatremia and hypernatremia in patients with TBI, not many studies have incorporated dysnatremia as a whole and its outcome on the basis of severity, mode of injury, and clinical progress in a single study.[4-7] In this study, we have assessed the association of hyponatremia and hypernatremia with the severity of traumatic brain injury and its impact on mortality among TBI patients.

METHODS

This is a retrospective, descriptive, and analytic study conducted during a 1 year period from March 2018 to March 2019. The study population was selected from the patients presenting to the emergency department (ED) with TBI at the Upendra Devkota Memorial National Institute of Neurological and Allied Sciences (UDM-NINAS), Bansbari, Kathmandu, Nepal. All the patients that fulfilled the inclusion criteria of age were enrolled in the study.

Ages 16 and above are taken into consideration because the driving license for motorbikes and other two wheelers is issued at the age of 16 years in Nepal, contributing to the prevalence of RTA.

• Patients with less than 16 years of age.

• Patients with known renal disease due to the higher incidence of electrolyte disbalance.

• Patients on lithium because it can lead to lithium-induced nephrogenic diabetes insipidus which may lead to hyponatremia.

Patient data were collected retrospectively from the record section dating from March 2018 to March 2019 with subsequent evaluation of daily sodium measurements during their stay in the hospital using patient files. Our study comprises a total of 367 patients presenting with mild, moderate and severe TBI.

The variables included in this study are age, sex, mode of injury, the severity of TBI, the severity of hyponatremia, the severity of hypernatremia, type of management and patient outcome. We have demonstrated categorical variables as frequency and continuous variables as mean as well as standard deviation. Independent variables are presented as age, sex, the severity of TBI and mode of injury, whereas dependent variables include hyponatremia, hypernatremia and surgical management. The Shapiro Wilk test was used to verify any departures from normality. In the case of the normal distribution, data were summarized in terms of means and standard deviation. Where data was found to be skewed, results were summarized as a median. An independent t-test was used to compare the mean of the two groups. Fisher exact test or chi-square test was utilized for categorical variables. P value of 0.05 or less was considered statistically significant. SPSS version 20 was used as a data computation tool. The study was approved by the ethics committee of Upendra Devkota Memorial National Institute of Neurological and Allied Sciences.

Severity of TBI was based on Glasgow Coma Scale (GCS) during the presentation in the ED which was classified as[8];

a) Mild: 14-15

b) Moderate: 9-13

c) Severe: ≤ 8

The severity of Hypernatremia was classified as[9]:

a) Mild: 146-149 mEq/L

b) Moderate: 150-169 mEq/L

c) Severe: ≥170 mEq/L

The severity of Hyponatremia was classified as[9]:

a) Mild: 130-134 mEq/L

b) Moderate: 125-129 mEq/L

c) Severe: < 125 mEq/Ls

The patient outcome was categorized as mortality or survived at the time of discharge from the hospital.

RESULTS

Over a duration of 1 year, 367 patients with TBI were treated in our hospital. Among 367 patients, hyponatremia was seen among 55 patients (14.9%) and hypernatremia was seen among 22 patients (5.99%).

The age range of patients included in the study was 16 to 87 years with a mean age of 37.96 years and a standard deviation of 16.5 (table 1). In patients with hyponatremia, the mean age ranged from 38.33 to 49.17 years (table 2). In contrast, the mean age in patients with hypernatremia was found in the range of 33.38 to 66 years (table 3).

Table 1. Overall total variables in TBI patients (N=367)

Variables	Categories	Total (N=367)
Age (Years)		37.96±16.5
Sex	Male	281(76.6)
	Female	86 (23.4)
Severity of TBI	Mild	286 (77.9)
	Moderate	37 (10.1)
	Severe	44 (12)
Mode of Injury	RTA	190 (51.8)
	Fall	102 (27.8)
	Assault	75 (20.4)
Operation	Yes	77 (21)
	No	290 (79)
Outcome	Death	24 (6.5)
	Improved	343 (93.5)

Table 2. Prevalence of hyponatremia and associated variables in TBI patients

Variables	Categories	Mild Hyponatremia (n=34)	Moderate Hyponatremia (n=9)	Severe Hyponatremia (n=12)	P value
Age		42.32 ± 17.97	38.33 ± 17.03	49.17 ± 17.09	0.000058
Sex	Male	25 (73.5)	8 (88.9)	12 (100)	0.207
	Female	9 (26.5)	1 (11.1)	0	
Severity TBI	Mild	22 (64.7)	4 (44.4)	7 (58.3)	0.005
	Moderate	4 (11.8)	3 (33.3)	1 (8.3)	
	Severe	8 (23.5)	2 (22.2)	4 (33.3)	
Mode of Injury	RTA	22 (64.7)	7 (77.8)	6 (50)	0.029
	Fall	10 (29.4)	0	0	
	Assault	2 (5.9)	2 (22.2)	6 (50)	
Operation	Yes	14 (41.2)	2 (22.2)	2 (16.7)	0.025
	No	20 (58.8)	7 (77.8)	10 (83.3)	
Outcome	Death	3 (8.8)	0	2 (16.7)	0.386
	Improved	31 (91.2)	9 (100)	10 (83.3)	

There was total of 281 (76.6%) males and 86 (23.4%) females in this study. The male to female ratio was calculated as 3.2:1. Among the hyponatremic patients, 45 were found to be male, whereas 10 were female, with the ratio calculated as 4.5:1. In hypernatremic cases, there were 14 males and 8 females, with male to female ratio of 1.7:1. There was no significant correlation seen between gender and the development of hyponatremia (p-value 0.207) and hypernatremia (p-value 0.114) (table 2 and 3).

Table 3. Prevalence of hypernatremia and associated variables in TBI patients

Variables	Categories	Mild Hypernatremia (n=13)	Moderate Hypernatremia (n=8)	Severe Hypernatremia (n=1)	P value
Age		36.08 ± 19.9	33.38 ± 7.54	66 ± 13.7	0.001
Sex	Male	8 (61.5)	6 (75)	0	0.114
	Female	5 (38.5)	2 (25)	1 (100)	
Severity TBI	Mild	3 (23.1)	1 (12.5)	0	0.523
	Moderate	5 (38.5)	2 (25)	0	
	Severe	5 (38.5)	5 (62.5)	1	
Mode of Injury	RTA	9 (69.2)	5 (62.5)	1	0.00001
	Fall	3 (23.1)	3 (37.5)	0	
	Assault	1 (7.7)	0	0	
Operation	Yes	10 (76.9)	6 (75)	0	0.0001
	No	3 (23.1)	2 (25)	1 (100)	
Outcome	Death	1 (7.7)	6 (75)	1 (100)	0.0001
	Improved	12 (92.3)	2 (25)	0	

According to GCS, there were 286 (77.9%), 37 (10.1%), and 44 (12%) cases of mild, moderate and severe head injuries, respectively during their presentation to the ED. Patients presented with 3 major modes of injury namely RTA, fall and physical assault accounting for 190 (51.8%), 102 (27.8%) and 75 (20.4%) cases respectively (table 1). A strong correlation between the mode of injury and the development of hyponatremia was established. (p value 0.029). It showed a high incidence of hyponatremia in patients suffering from RTA (table 2).

Among 367 patients, 77(21%) individuals underwent surgical intervention, which included 18 patients (23.3%) who developed hyponatremia and 16 patients (20.7%) with hypernatremia. The association between dysnatremia and operative intervention was evident in our study (p-value: 0.025 for hyponatremia and p-value: 0.0001 for hypernatremia) (table 2 and 3). Mortality was observed in a total of 24 patients (6.5%), including 5 deaths in hyponatremics, 8 deaths in hypernatremics and the rest were seen in individuals without any sodium abnormalities. The association between hyponatremia and mortality was not seen in our study (table 2). However, a strong association existed in our series between hypernatremia and mortality (p value: 0.0001) (table 3).

Among 34 patients who had developed mild hyponatremia, 22 patients (64.7%) had sustained a mild head injury, 8 patients (23.5%) had sustained a severe head injury and 4 patients (11.8%) had developed a moderate head injury. Of the 9 patients who had developed moderate hyponatremia, 4 patients (44.4%) had a mild head injury, 3 patients (33.3%) had a moderate head injury and 2 patients (22.2%) had a severe head injury. Of 12 patients who developed severe hyponatremia, 7 patients (58.3%) had sustained a mild head injury, 4 patients (33.3%) had sustained a moderate head injury, and 1 patient (8.3%) had sustained a severe head injury. Our series showed an association between the severity of traumatic brain injury and hyponatremia (p-value < 0.005) (table 2).

Of 13 patients who had developed mild hypernatremia, 5 patients (38.5%) had severe TBI, 5 patients (38.5%) had moderate TBI and 3 patients (23.1%) had mild TBI. Of 8 patients who had developed moderate hypernatremia, 5 patients (62.5%) had severe TBI, 2 (25%) had moderate TBI and 1 patient (12.5%) had mild TBI. While one patient (100%) with severe hypernatremia had sustained a severe TBI. Our series showed no association between the severity of traumatic brain injury and the development of hypernatremia (p value 0.523). Whereas a strong association existed between the outcome of patients and hypernatremia (p value 0.0001) (table 3).

DISCUSSION

Among the 367 patients with TBI who came to our center, hyponatremia was seen among 55 patients (14.9%) and hypernatremia was seen among 22 patients (5.99%). It was found that in patients less than 45 years of age, hyponatremia was observed in 11.11% of the cases and hypernatremia was experienced in 4.1% of the patients. In contrast, hyponatremia and hypernatremia were seen in 15.59% and 6.4% of patients ≥ 45 years of age, respectively. Also, the mortality rate was 2.8% in patients younger than 45 years as compared to 7.5% observed in patients aged ≥ 45 years.

We also observed a strong correlation between the mode of injury and the development of hyponatremia which shows a higher prevalence of hyponatremia, in patients experiencing RTA. RTA was observed to be the most common cause of TBI in both age groups, while falls were the second most common cause in patients aged 45 years and older, whereas physical assault was the second most common cause in patients under 45 years of age.

The male to female ratio was calculated as 3.2:1. Among the hyponatremic patients, the male to female ratio was calculated as 4.5:1. Whereas in hypernatremic cases, a male to female ratio of 1.7:1 was observed. However, there was no significant correlation seen between gender and the onset of hyponatremia (p-value 0.207) and hypernatremia (p-value 0.114).

In our study, the prevalence of hyponatremia was 55 patients (14.9%), out of which 33 patients (60%) had a mild head injury, 8 patients (14.5 %) had a moderate head injury, and severe head injury was seen in 14 patients (25.4%). When the number of patients with a specific type of head injury was taken into account, the prevalence was 11.5%, 21.6%, and 31.8% in mild, moderate, and severe head injuries, respectively. Whereas, in studies conducted by Lohani et al. Babak et al. and Yumoto et al. hyponatremia was seen in 27.2%, 26.3% and 51% of the patients with traumatic brain injury, respectively, which is significantly higher than the observed prevalence of 14.9% in our study.[10-12]

In our study, among hyponatremic patients, decreased blood sodium levels were seen in 18 patients (23%) who underwent surgical intervention and in 37 patients (67%) who were admitted to the intensive care unit (ICU) without any intervention. Whereas, hypernatremia was seen in 16 patients (73%) undergoing surgery and 6 patients (27%) who were admitted to the ICU without any intervention. A strong association between dysnatremia and operative intervention was evident in our study (p-value: 0.025 for hyponatremia and p value: 0.0001 for hypernatremia). In contrast, many studies have found the prevalence of hyponatremia to be as high as 30-40% among ICU patients.[13-16]

Hyponatremia has been shown to have an association with the severity of brain injury.[17] Although hyponatremia has been shown to be associated with the severity of brain injuries, patients with mild to moderate TBI are considered to be at greater risk of hyponatremia than those with severe TBI.[10,17-19] However, a study conducted by Doczi et al. showed that hyponatremia was seen more in moderate head injuries than in severe ones.[18] In contrast to these studies, our results demonstrate that severe brain injury has the highest risk of development of hyponatremia (31.8%) followed by moderate and mild brain injury, with a prevalence of 21.6% and 11.5% respectively.

According to Hannon et al., current data indicates that hyponatremia in neurosurgical patients has not been implicated in excess mortality which supports our absence of statistical significance noted between hyponatremia and mortality in patients with TBI.[20]

Hypernatremia is a common finding seen in TBI patients, with some studies reporting a prevalence of 30-40% in some instances.[4,6,21] It has also been found that patients with hypernatremia tend to be associated with more severe form of TBI.[7] Our study showed that 50% of total hypernatremia cases had sustained severe TBI 11 (50) followed by moderate 7 (31.8) and mild 4 (18.2) forms of TBI, but didn't show the statistically significant association.

Our study demonstrates a strong statistically significant association between hypernatremic patients and mortality. A study by Aiyagari et al. states that only severe hypernatremia independently increased mortality in neurosurgery ICU patients.[22] Similarly, Vedantam et al. and Li et al. also state that more severe hypernatremia is associated with a lower degree of survival in patients with TBI.[6,23] Whereas various other studies have also documented a greater incidence of in-hospital mortality and longer LOS in ICU patients in comparison to cases.[7,24,25] Our study similarly showed an increased mortality rate with severe (1 patient, 100%) followed by moderate (6 patients, 75%) and mild (1 patient, 15.4%) hypernatremia, respectively. Subsequently, it can be theorized that hypernatremia is an independent predictor of mortality, which has also been mentioned in other similar studies.[23,26]

The overall mortality rate in our study was 36.36% and the studies conducted by Hoffman et al. (30.7%) and Maggiore (26%) are comparable among hypernatremic patients, which is considerably lower than the incidence reported by Li et al. (67%).[5-7]

The results of the study conducted by Babak et al. demonstrated that both hypernatremia and hyponatremia significantly increased mortality in TBI patients admitted to the ICU, but the total number of patients dying from hypernatremia was significantly higher.[11] In our study, among 24 mortality, 5 patients (20.8%) had hyponatremia and 8 patients (33.3%) had hypernatremia. There was no statistical significance between hyponatremia and mortality whereas the statistically significant association was observed between hypernatremia and mortality.

This study bears the standard limitation of being a retrospective study. The time of development of dysnatremia, could not be effectively analyzed. Any other biases that may have caused dysnatremia such as drugs like anti-hypertensive, diuretics, mannitol, and inotropes, were not assessed. Moreover, medical conditions like cardiovascular, renal and endocrinal abnormalities may impact on the sodium state of TBI patients, which we routinely failed to evaluate in all head injury patients. We would hence like to suggest future investigators proceed with consideration of these variables as they may affect the sodium state of TBI patients to avoid biases.

CONCLUSION

The severity of head injury is associated with the severity of hyponatremia but not with severity of hypernatremia. Similarly, a strong association existed between the severity of hypernatremia and outcome of patients. However, such association was not seen with hyponatremia.

REFERENCES

1. Langlois JA, Rutland-Brown W, Wald MM. The epidemiology and impact of traumatic brain injury: a brief overview. *J Head Trauma Rehabil.* 2006 ;21(5):375-8.
2. Agrawal V, Agarwal M, Joshi SR, Ghosh AK. Hyponatremia and hypernatremia: disorders of water balance. *J Assoc Physicians India*. 2008; 56:956-64.
3. Cui H, He G, Yang S, Lv Y, Jiang Z, Gang X, Wang G. Inappropriate Antidiuretic Hormone Secretion and Cerebral Salt-Wasting Syndromes in Neurological Patients. *Front Neurosci*. 2019; 13:1-11.
4. Ali Kiaei B, Moradi Farsani D, Ghadimi K, Shahali M. Evaluation of the Relationship Between Serum Sodium Concentration and Mortality Rate in ICU Patients with Traumatic Brain Injury. *Arch Neurosci*. 2018; 5(3):e68745.
5. Maggiore U, Picetti E, Antonucci E, Parenti E, Regolisti G, Mergoni M, et al. The relation between the incidence of hypernatremia and mortality in patients with severe traumatic brain injury. *Crit Care*. 2009;13(4):1-9.
6. Li M, Hu YH, Chen G. Hypernatremia severity and the risk of death after traumatic brain injury. *Injury*. 2013;44(9):1213-8.
7. Hoffman H, Jalal MS, Chin LS. Effect of Hypernatremia on Outcomes After severe Traumatic Brain Injury: A Nationwide Inpatient Sample analysis. *World Neurosurg*. 2018;118:e880-6.
8. Teasdale G, Maas A, Lecky F, Manley G, Stocchetti, N Murray G. The Glasgow Coma Scale at 40 years: standing the test of time. *Lancet*. 2014; 13:844-54.
9. Agrawal V, Agarwal M, Joshi SR, Ghosh AK. Hyponatremia and hypernatremia: disorders of water balance. *J Assoc Physicians India*. 2008; 56:956-64.
10. Lohani S, Devkota UP. Hyponatremia in patients with traumatic brain injury: Etiology, incidence, and severity correlation. *World Neurosurg*. 2011; 76(3-4):355-60.
11. Tamizifar B, Kheiry S, Fereidoony F. Hyponatremia and 30 days mortality of patients with acute pulmonary embolism. *J Res Med Sci*. 2015; 20(8):777-781.
12. Yumoto T, Sato K, Ugawa T, Ichiba S, Ujike Y. Prevalence, risk factors, and short-term consequences of traumatic brain injury-associated hyponatremia. *Acta Med Okayama* [Internet]. 2015; 69(4):213-8.
13. Bennani SL, Abouqal R, Zeggwagh AA, Madani N, Abidi K, Zekraoui A, et al. Incidence, causes and prognostic factors of hyponatremia in intensive care. *Rev Med Interne.* 2003; 24(4):224-9.
14. Honda O, Kato T, Ishiguro M, Uede T, Kurokawa Y, Honmou O, et al. Pathogenesis of hyponatremia following subarachnoid hemorrhage due to ruptured cerebral aneurysm. *Surg Neurol*. 1996; 46(5):500-7; discussion 507-8.
15. Zada G, Liu CY, Fishback D, Singer PA, Weiss MH. Recognition and management of delayed hyponatremia following transsphenoidal pituitary surgery. *J Neurosurg*. 2008;106(1):66-71.
16. Friedman B, Cirulli J. Hyponatremia in critical care patients: Frequency, outcome, characteristics, and treatment with the vasopressin V2-receptor antagonist tolvaptan. *J Crit Care*. 2013; 28(2):219.e1-219.e12.
17. Harrigan MR. Cerebral Salt Wasting Syndrome: A Review. *Neurosurgery*. 2004; 38(1):152-60.
18. Doczi T, Tarjanyi J, Huszka E, Kiss J. Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) after head injury. *Neurosurgery.* 1982; 10:685-8.
19. 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; 68(4):387-93.

20. Hannon MJ, Finucane FM, Sherlock M, Agha A, Thompson CJ. Disorders of water homeostasis in neurosurgical patients. *J Clin Endocrinol Metab.* 2012; 97(5):1423-33.

21. Froelich M, Ni Q, Wess C, Ougorets I, Härtl R. Continuous hypertonic saline therapy and the occurrence of complications in neurocritically ill patients. *Crit Care Med.* 2009; 37(4):1433-41.

22. Aiyagari V, Deibert E, Diringer MN. Hypernatremia in the neurologic intensive care unit: how high is too high? *J Crit Care.* 2006; 21(2):163-72.

23. Vedantam A, RobertsonCS, GopinathSP. Morbidity and mortality associated with hypernatremia in patients with severe traumatic brain injury. *Neurosurg Focus*. 2017; 43(5):E2.

24. Waite MD, Fuhrman SA, Badawi O, Zuckerman IH, Franey CS. Intensive care unit-acquired hypernatremia is an independent predictor of increased mortality and length of stay. *J Crit Care*. 2013; 28(4):405-12.

25. Shehata M, Ragab D, Khaled M, Hegazy M, Hussein A, Khaled H. Impact of hypernatremia on patients with severe traumatic brain injury. *Crit Care.* 2010; 14(Suppl 1): P355.

26. Lindner G, Funk GC, Schwarz C, Kneidinger N, Kaider A, Schneeweiss B, et al. Hypernatremia in the Critically Ill Is an Independent Risk Factor for Mortality. *Am J Kidney Dis*. 2007; 50(6):952-7.