Association Between Serum Sodium Abnormalities and Clinico-radiologic Parameters in Severe Traumatic Brain Injury

Philip Mwachaka[1,2], Angela Amayo[3], Nimrod Mwang'ombe[1], Peter Kitunguu[1]

[1]Department of Surgery, Neurosurgery Unit, University of Nairobi, Nairobi, Kenya.

[2]Department of Human Anatomy, University of Nairobi, Kenya.

[3]Department of Pathology, University of Nairobi, Nairobi, Kenya.

Correspondence to: Dr. Philip Mwachaka; Email: pmaseghe@gmail.com

Received: 16 Jun 2020; Revised: 2 Feb 2021; Accepted: 19 Feb 2021; Available online: 3 Mar 2021

Abstract

Background: Secondary brain insults after traumatic brain injury such as electrolyte dysfunctions are associated with poor outcomes. This study aimed at determining the incidence of serum sodium ion abnormalities and their association with clinico-radiological parameters. **Methods:** A prospective cross-sectional study of one hundred and seventeen patients with severe head injury. Data collected included patient demographics, prehospital interventions, clinical examination findings, computed tomography (CT) scan head findings, serum sodium ion levels (at admission and 48 h later), and outcome (30 days). **Results:** At admission, 93(79.5%) patients had normal serum sodium ion levels. However, 48 h post-admission, hypernatremia was prevalent in 56(63.6%) patients ($p < 0.001$). Hypernatremia was significantly associated with the use of mannitol ($p = 0.036$), lower Glasgow Coma Score ($p = 0.047$), higher Injury Severity Score ($p = 0.015$), presence of subdural hematoma ($p = 0.044$), midline shift >5 mm ($p = 0.048$), compressed/absent basal cistern ($p = 0.010$), and higher Rotterdam CT Score ($p = 0.003$). Hypernatremia reported 48 h post-admission was associated with a high 30-day mortality rate [odds ratio (OR) 3.55, $p = 0.0095$]. Risk of mortality associated with hyponatremia and hypernatremia at admission was not statistically significant. **Conclusion:** While both hyponatremia and hypernatremia can occur in serious TBI patients, hypernatremia predominates 48 hours post-admission and is associated with statistically significant increased risk of death.

Keywords: Traumatic brain injury, hyponatremia, hypernatremia, outcomes, clinico-radiologic parameters

Ann Afr Surg. 2021; 18(3): 155-162
DOI: http://dx.doi.org/10.4314/aas.v18i3.6
Funding: None

Introduction

Serum sodium abnormalities are common in traumatic brain injury (TBI), and are usually associated with the primary brain injury or interventions such as hyperosmolar therapies used in the management of raised intracranial pressure (1, 2). Hypernatremia, defined as serum sodium ion concentration >145 mmol/L, can result from a primary brain injury resulting in central diabetes insipidus or as a result of hyperosmolar therapies such as the use of hypertonic saline (3, 4). Hypernatremia is associated with increased mortality, longer hospitalization and greater hospital costs (3–5). Hyponatremia, serum sodium ion concentrations <135 mmol/L, may also occur after TBI and contributes to secondary brain insults by causing cerebral edema, seizures, and depression of consciousness (6). Hyponatremia in TBI is usually

caused by cerebral salt wasting syndrome and syndrome of inappropriate secretion of antidiuretic hormone (7).

Severe TBI, defined as Glasgow Coma Scale (GCS) ≤8, is a major cause of death and incapacity worldwide and is associated with huge direct and indirect costs to the public (8–10). In addition, the World Health Organization projected that by 2020, TBI would be the main cause of death and disability (11). TBI is more prevalent in developing nations because of the increasing number of road traffic accidents (12, 13). In our setup, most hospital-based studies have revealed that severe head injury is associated with mortality of >50% and poor functional outcomes (14–16). These bad outcomes may be associated with secondary brain insults such as electrolyte abnormalities that arise from inflammatory and biochemical cascades initiated by the primary injury insult to the brain (9, 17, 18). This study aimed at determining the incidence of serum sodium ion abnormalities in severe TBI patients, and their association with specific clinical and radiological parameters.

Materials and methods

Study design and site

An analytic cross-sectional study carried out over 4 months (1st November 2019 to 28th February 2020). The study site was the Kenyatta National Hospital Accident and Emergency Unit and Intensive Care Unit. Kenyatta National Hospital is located in Nairobi, Kenya and is the largest hospital and the main referral center for neurotrauma cases countrywide. The hospital serves patients from different regions and socioeconomic backgrounds.

Study population

All consecutive patients presenting with severe head injury defined by GCS ≤ 8 and whose next of kin had given informed consent were recruited into the study. Patients with known pre-existing chronic illness were excluded from the study.

Study variables

Data collected included patient demographics, mechanisms of injury, prehospital interventions, clinical examination findings, computed tomography (CT) scan head findings, serum sodium levels (at admission and 48 h later), and outcome (30 days). The Injury Severity Score (ISS) was used to quantify the severity of injury to the patient (19). The serum sodium tests were done using Biolis 50i Superior Chemistry Analyzer (Boeki Medisys, Tokyo, Japan). Daily internal quality control checks were done to ensure that the results were valid. In addition, external quality control checks were done through the Randox International Quality Assessment Scheme (RIQAS). The reference range for serum sodium from our laboratory is 135–145mmol/L.

Statistical analysis

Data gathered was entered into Statistical Package for Social Sciences (SPSS) version 20.0 (IBM Corp; New York, United States of America) for analysis. Metric data are shown as means and standard deviation, nominal data as frequency and valid percent. Variables were tested for normal distribution using the Kolmogorov–Smirnov test in addition to histograms. If the assumption of normality was violated, Mann–Whitney U and Kruskal–Wallis tests were performed to test for differences between groups, instead of Student's t-test and analysis of variance (ANOVA) tests, respectively. Admission and 48-h post-admission variables were compared using the paired t-test. Categorical data was analyzed by Pearson's chi-square test. The correlation between the serum sodium and the study variables (clinical and radiological) was determined using Pearson's correlation coefficient (r). Odds ratios were calculated for each electrolyte abnormality to determine its associated risk of mortality (30-day mortality). A p-value of < 0.05 was considered as significant.

Ethical considerations

We conducted this study in compliance with the principles of the Declaration of Helsinki. The study's protocol was reviewed and approved by the Kenyatta National Hospital – University of Nairobi Ethics and Research Committee (P723/08/2019). Written informed consent was obtained from the next of kin of the patients

as the patients could not consent in view of their low GCS.

Results

General information

The study recruited 117 patients out of which 111 (94.9%) were male. The mean age was 32.41 ± 14.59 years. Prehospital use of intravenous normal saline and mannitol solutions was reported in 65 (55.6%) and 16 (13.7%) of the patients, respectively. The mean GCS and ISS at admission were 6.41 ± 1.69 and 21.06 ± 7.74, respectively.

Prevalence of serum sodium ion abnormalities

The mean serum sodium ion levels at admission were 139.16 ± 5.93 mmol/L (n = 117) and were 149.13 ± 8.84 mmol/L (n = 88) 48 h after admission. Serum sodium ion abnormalities were seen in 24 (20.5%) patients at admission and in 59 (67%) patients 48 h post-admission. At admission, hyponatremia was the most common abnormality seen in 14 (12.0%) patients while hypernatremia was noted in 10 (8.5%) cases. Hypernatremia was the predominant abnormality in the 48-h post-admission assay, reported in 56 (63.6%) cases (Figure 1). Paired sample t-tests revealed a statistically significant difference between the admission and 48-h post-admission sodium levels ($p < 0.001$).

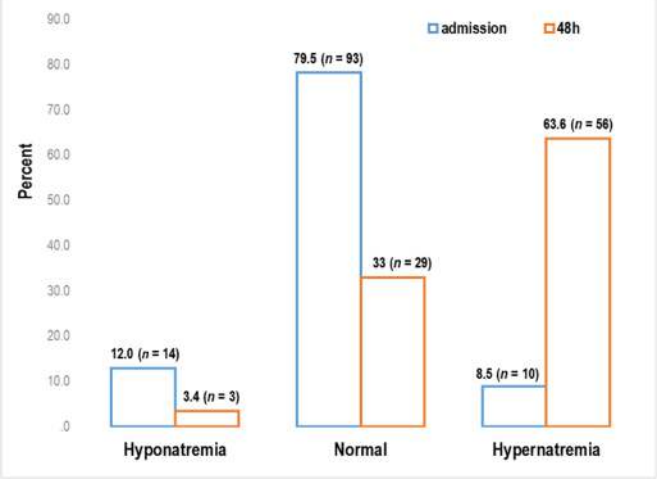

Figure 1. Serum sodium levels at admission and 48 h post-admission

Association between serum sodium and clinical parameters

Patients who presented with hyponatremia at admission took longer ($p = 0.002$) to present to the hospital compared to the other groups (Table 1). Hypernatremia at admission was significantly associated with prehospital use of mannitol ($p = 0.036$), while hypernatremia at 48 h post-admission was associated with a lower GCS ($p = 0.047$) and a higher ISS ($p = 0.015$). Statistically significant negative correlations between admission sodium ion levels and duration of time from injury to hospital presentation (r -0.226, p 0.012), pre-hospital use of mannitol (r -0.189, p 0.036), and GCS at admission (r -0.205, p 0.022) were noted (Table 2). The GCS (r -0.225, p 0.016), Abbreviated Injury Scale (AIS) for the head (r 0.314, p 0.003), and ISS (r 0.236, p 0.027) were the only clinical variables that revealed statistically significant correlations with the 48-h post-admission sodium levels.

Association between serum sodium and radiologic parameters

Hypernatremia at admission was significantly associated with the presence of subdural hematoma (SDH) ($p = 0.044$) and midline shift (MLS) >5 mm ($p = 0.048$), while compressed/absent basal cisterns ($p = 0.010$), presence of SDH ($p = 0.032$), and a higher Rotterdam CT Score ($p = 0.003$) were associated with hypernatremia developing 48 h post-admission (Table 3). These parameters also exhibited statistically significant positive correlations with the level of serum sodium ions (Table 4).

Association between serum sodium and 30-day outcome

The risk of death was higher in patients with hypernatremia compared to those with hyponatremia. Hypernatremia at admission and 48 h post-admission was associated with a higher 30-day mortality odds ratio (OR) 5.74 [95% confidence interval (CI) 0.71–46.73, p 0.103] and OR 3.55 (95% CI 1.36–9.23, p 0.0095), respectively. The risk of mortality associated with hyponatremia was OR 1.26 (95% CI 0.41–3.93, p 0.688)

and OR 2.14 (95% CI 0.17–26.33, p 0.552) at admission and 48 h post-admission, respectively.

Discussion

In the current study, most (79.5%) patients had normal serum sodium ion levels at admission. However, 48 h post-admission, hypernatremia was predominant (63.6%). Paired sample t-tests revealed statistically significant differences between the admission and 48 h post-admission sodium levels ($p < 0.001$). Previous studies have also reported similar trends of initial normonatremia followed by hypernatremia in severe TBI (5, 20).

Table 1. Association between serum sodium and clinical parameters

		Hyponatremia	Normal	Hypernatremia	*p*-value
Age (years)	Admission	32.4±13.8	31.9±14.8	36.5±14.6	0.649
	48 h post-admission	20.7±2.1	33.6±15.7	34.4±13.7	0.273
Time from injury to presentation (h)	Admission	59.7±28.7	17.1±26.1	24.1±24.9	*0.002**
	48 h post-admission	48.8±60.4	27.4±41.0	21.5±37.7	0.451
Pre-hospital use of IV fluids	Admission	42.9%	57.0%	60.0%	0.942
	48 h post-admission	33.3%	65.5%	57.1%	0.495
Pre-hospital use of mannitol	Admission	7.1%	11.8%	40.0%	*0.036**
	48 h post-admission	0%	17.2%	12.5%	0.652
Systolic BP (mmHg)	Admission	126.4±22.7	127.1±25.7	131.2±26.1	0.868
	48 h post-admission	121.3±4.5	134.6±22.2	127.8±24.2	0.364
Diastolic BP (mmHg)	Admission	74.0±19.2	76.5±18.0	73.1±16.2	0.754
	48 h post-admission	61.3±10.0	80.5±18.4	73.9±14.7	0.060
Heart rate (/min)	Admission	83.7±26.8	95.8±25.0	99.2±27.6	0.233
	48 h post-admission	69.3±5.1	89.7±23.1	95.0±26.6	0.186
Respiratory rate (/min)	Admission	19.8±5.9	20.9±4.5	21.7±4.1	0.578
	48 h post-admission	18.0±0.0	20.4±3.6	20.4±3.9	0.567
Saturation O_2 (%)	Admission	94.6±5.5	90.8±9.9	89.8±10.4	0.420
	48 h post-admission	93.5±0.7	93.2±7.7	91.8±7.6	0.746
Total GCS	Admission	7.3±1.1	6.3±1.7	5.8±1.7	0.064
	48 h post-admission	7.7±0.6	6.9±1.2	6.2±1.3	*0.047**
ISS	Admission	18.5±5.1	21.6±8.3	20.5±5.0	0.333
	48 h post-admission	18.7±1.2	18.7±8.1	22.1±7.6	*0.015**

BP, blood pressure; GCS, Glasgow Coma Score; ISS, Injury Severity Score; IV, intravenous. * *p* value < 0.05

Table 2. Correlations between serum sodium and clinical parameters

Variable	Admission (n = 117)		48 h after admission (n = 88)	
	Pearson's correlation	p-value	Pearson's correlation	p-value
Age (years)	0.054	0.574	0.123	0.278
Time from injury to presentation (h)	*-0.226*	*0.012**	-0.123	0.256
Pre-hospital use of IV fluids	-0.024	0.788	0.013	0.902
Pre-hospital use of mannitol	*-0.189**	*0.036*	0.014	0.900
Mechanism of injury	-0.053	0.558	0.075	0.486
Systolic BP	0.040	0.659	-0.078	0.471
Diastolic BP	0.000	0.996	-0.069	0.522
Heart rate	0.143	0.123	0.178	0.103
Respiratory rate	0.103	0.298	0.068	0.558
Temperature	-0.003	0.976	-0.205	0.082
Saturation O_2	-0.122	0.235	-0.090	0.454
Pupil examination	-0.046	0.611	0.195	0.068
Total GCS	*-0.205*	*0.022**	*-0.255*	*0.016**
AIS – head	0.083	0.359	*0.314*	*0.003**
ISS	0.086	0.343	*0.236*	*0.027**

AIS, abbreviated Injury Score; BP, blood pressure; ISS, Injury Severity Score; IV, intravenous. * p value < 0.05

Table 3. Association between serum sodium and radiologic parameters

		Hyponatremia	Normal	Hypernatremia	P-value
SDH thickness (mm)	Admission	10.0±5.0	11.8±4.8	9.2±2.0	0.387
	48 h post-admission	5.0±3.1	12.5±2.7	11.2±5.0	0.343
MLS > 5 mm	Admission	18.8%	36.1%	63.6%	*0.048**
	48 h post-admission	-	41.4%	46.4%	0.278
Compressed or absent basal cisterns	Admission	85.8%	85%	99%	0.555
	48hrs post admission	66.6%	82.8%	94.6%	*0.010**
Presence of epidural hematoma	Admission	7.1%	23.7%	10.0%	0.250
	48 h post-admission	.0%	31.0%	17.9%	0.245
Presence of SDH	Admission	42.9%	31.2%	70.0%	*0.044**
	48 h post-admission	33.3%	20.7%	50.0%	*0.032**
Presence of traumatic SAH	Admission	21.4%	37.6%	50.0%	0.333
	48 h post-admission	33.3%	31.0%	46.4%	0.378
Presence of contusion hemorrhages	Admission	42.9%	44.1%	40.0%	0.968
	48 h post-admission	33.3%	31.0%	48.2%	0.300
Rotterdam CT Score	Admission	3.6±1.0	3.8±1.2	4.4±1.0	0.227
	48 h post-admission	3.3±1.5	3.4±1.0	4.2±1.1	*0.003**

CT, computed tomography; MLS, midline shift; SAH, subarachnoid hemorrhage; SDH, subdural hematoma. * p value < 0.05

Table 4. Correlations between serum sodium and radiologic parameters

	Test	Admission (n = 117)	48 h after admission (n = 88)
Rotterdam CT Head Score	Pearson's correlation	0.134	*0.340*
	Sig. (two-tailed)	0.151	*0.001**
MLS (mm)	Pearson's correlation	*0.210*	0.129
	Sig. (two-tailed)	*0.019**	0.232
Basal cisterns	Pearson's correlation	0.001	*0.340*
	Sig. (two-tailed)	0.994	*0.001**
Presence of epidural Hematoma	Pearson's correlation	-0.038	0.072
	Sig. (two-tailed)	0.681	0.506
Presence of SDH	Pearson's correlation	0.096	*0.248*
	Sig. (two-tailed)	0.303	*0.020**
Presence of intracerebral hematoma	Pearson's correlation	0.025	-0.144
	Sig. (two-tailed)	0.789	0.181
Presence of traumatic SAH	Pearson's correlation	0.136	0.138
	Sig. (two-tailed)	0.143	0.199
Presence of contusion hemorrhages	Pearson's correlation	0.010	-0.154
	Sig. (two-tailed)	0.917	0.151
Epidural hematoma volume (ml)	Pearson's correlation	0.250	-0.022
	Sig. (two-tailed)	0.389	0.949
SDH thickness (mm)	Pearson's correlation	-0.070	0.073
	Sig. (two-tailed)	0.690	0.703
Intracerebral hematoma volume (ml)	Pearson's correlation	0.064	0.357
	Sig. (two-tailed)	0.880	0.432

CT, computed tomography; MLS, midline shift; SAH, subarachnoid hemorrhage; SDH, subdural hematoma. * p value < 0.05

A retrospective study of 588 severe TBI patients by Vedantam et al. (5) reported a 79.3% incidence of hypernatremia diagnosed within the first week of admission, with the highest numbers being reported within 72 h. Another retrospective study of 130 severe TBI patients reported 2.3% with hypernatremia at admission, but the cases of hypernatremia increased to 51.5% in the course of intensive care unit (ICU) stay (20). Rafiq et al. also reported hypernatremia in 65.1% of all patients with severe TBI (2).

Severe TBI patients have a high risk of developing hypernatremia over the course of their ICU stay, due to the coexistence of predisposing conditions such as impaired sensorium, altered thirst, central diabetes insipidus with polyuria, increased insensible losses, and use of hyperosmolar therapies such as mannitol and hypertonic saline (3, 4, 21). Although it is possible that these mechanisms contributed to the occurrence of the delayed hypernatremia reported in the current study, either in isolation or combination, it is more likely that the sequelae of primary brain injury contributed more to this finding. In support of this, admission GCS, ISS, Rotterdam CT Head Score, degree of compression of the basal cisterns, and the presence of SDH were significantly correlated ($p < 0.001$) with the levels of serum sodium ions 48 h after admission.

Few studies have described the association between sodium abnormalities and clinic-radiologic parameters. Li et al., also reported an association between admission GCS and the severity of hypernatremia (22). These authors reported that the severe hypernatremia group had a significantly lower GCS compared to moderate, mild hypernatremia, and normal sodium groups (median GCS, 3.0 vs. 5.0, 6.0, and 8.0, respectively). In the current study, the clinical parameters that have significant correlations with sodium ion levels,

especially 48 h post-admission, were the GCS, AIS (head), and the sum ISS. In 2111, A study by Paiva et al. revealed that the presence of subdural and intracerebral hematomas was associated with the occurrence of sodium disorders in severe TBI patients (23). In the present study, the only mass lesion that was significantly associated with sodium abnormalities was the presence of an SDH. Besides, the Rotterdam CT Head Score and the state of the basal cisterns displayed statistically significant positive correlations with the sodium ion levels.

In the current study, hypernatremia was associated with a high rate of mortality of 73.3%. Hypernatremia among TBI patients has been reported as an independent risk factor for mortality in previous studies (5, 20–22). According to Maggiore et al., hypernatremia in severe TBI patients is associated with a three-fold increase in the risk of ICU death (20). Li et al. reported mortality rates for the mild, moderate, and severe hypernatremia groups as 20.6%, 42.4%, and 86.8%, respectively, while that for the normonatremia group was 2.0% (22). Vedantam et al. also reported that hypernatremia was a significant predictor of mortality in TBI patients and that the mortality rates increased with the severity of hypernatremia (hazard ratios for mild, moderate, and severe hypernatremia were 3.2, 5.1, and 7.9, respectively) (5).

Conclusion

While both hyponatremia and hypernatremia can occur in severe TBI patients, hypernatremia predominates 48 h post-admission and is associated with statistically significant increased risk of mortality.

Author Contributions

Philip Mwachaka: conceptualization, data curation, methodology, formal analysis, investigation, writing – original draft; Angela Amayo: conceptualization, methodology, resources, supervision, validation, writing – review and editing; Nimrod Mwang'ombe: conceptualization, methodology, resources, supervision, validation, writing – review and editing; Peter Kitunguu: conceptualization, methodology, resources, supervision, validation, writing – review and editing.

Conflicts of Interest: While one of the authors is a member of the editorial team, they were blinded during the review of the paper and were excluded from meetings where the manuscript was discussed

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