EVALUATION OF SERUM ELECTROLYTE ABNORMALITIES IN PATIENTS WITH SEVERE HEAD INJURY AT THE KENYATTA NATIONAL HOSPITAL IN KENYA

Dissertation submitted in partial fulfilment of the requirements for the award of Master of Medicine in Neurosurgery degree at the University Of Nairobi.

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DECLARATION

I declare that this dissertation is my original work and to the best of my knowledge, it has not been presented anywhere else for consideration of publication or the award of another degree.

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LIST OF ABBREVIATIONS

KNH.....Kenyatta National Hospital

UON.....University of Nairobi

ERC.....Ethics and Research Committee

TBI.....Traumatic Brain Injury

SEA.....Serum electrolyte Abnormalities

OR.....Odds ratio

GCS.....Glasgow Coma Scale

BP.....Blood Pressure

CT.....Computed Tomography scan

ISS.....Injury Severity Score

ICP.....Intracranial Pressure

BTF.....Brain Trauma Foundation

ICU..... Intensive Care Unit

SIADH.....Syndrome of Inappropriate secretion of Antidiuretic Hormone (SIADH)

CSW..... Cerebral Salt Wasting syndrome

SAH..... Subarachnoid haemorrhage

EDH..... Epidural Hematoma

SDH..... Subdural hematoma

CI..... Confidence Interval

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SUMMARY

Background: Severe traumatic brain injury (TBI) defined as Glasgow Coma Scale ≤ 8 is a significant cause of death and disability worldwide. Studies conducted at Kenyatta National Hospital (KNH) report a mortality rate of > 50 per cent in this group of patients. These poor outcomes have been associated with secondary brain insults, such as electrolyte dysfunction. Serum electrolyte abnormalities (SEAs) may occur due to the initiation of destructive inflammatory and biochemical cascades of primary brain injury, or as a result of interventions such as hyperosmolar therapy. The SEA may explain the high mortality rate seen in our local setting. However, there is lack local data on the occurrence of SEA among severe TBI patients.

Aim: The study was conducted to determine the prevalence of serum electrolyte abnormalities in severe TBI patients seen in KNH and to determine the association between electrolyte abnormalities and specific clinical, radiological and acid-based parameters.

Methodology: This was a cross-sectional analytic study of 124 severe TBI patients seen at the KNH Accident and Emergency and Intensive Care Units between November 2019 and February 2020. The study started with the approval of the KNH / UON Ethics and Research Committee. Data collected included patient demographics, pre-hospital interventions, clinical examination findings, CT Scan head findings, serum electrolyte findings (admission and 48 hours later), arterial blood gas, and outcome (30 days). The data collected was entered into the statistical package for social sciences Package for analysis. Descriptive statistics such as mean, standard deviation and frequency were calculated. Variables were tested for normal distribution using the Kolmogorov-Smirnov test in addition to histograms. If the assumption of normality had been violated, the

Kruskal-Wallis test was performed to test for differences between groups, instead of the ANOVA (Analysis of Variance) test. Admission and 48hrs post-admission variables were compared with the paired t-test. Categorical data were analyzed by Pearson's Chi-square test. The correlation between the serum electrolytes and the study variables (clinical, radiological and acid-based) was determined using the Pearson correlation coefficient (r). The odds ratio was calculated for each electrolyte abnormality to determine the associated risk of mortality (30-day mortality). The p-value of < 0.05 was considered to be significant.

Results: Serum sodium ion abnormalities were seen in 21 (21.8 per cent) patients at admission and in 59 (67%) patients 48 hours after admission. Hypernatremia was the predominant serum sodium ion abnormality reported in 56 (63.6%) cases 48 hours after admission ($p<0.001$). It was significantly associated with the use of mannitol ($p=0.044$), lower GCS score ($p=0.047$), higher Injury Severity Score ($p=0.015$), subdural hematoma on CT Scan ($p=0.044$), midline shift > 5 mm ($p=0.048$), compressed / absent basal cisterns ($p=0.010$), higher Rotterdam CT Score ($p=0.003$), low pCO2 ($p=0.021$), low HCO3 ($p=0.018$) and low base deficit ($p=0.046$). Hypernatremia was associated with a higher mortality odds ratio of 3.55 (95% CI 1.36-9.23, p 0.0095) compared to hyponatremia OR 1.26 (95% CI 0.41-3.93, p 0.688).

Hypokalemia was the most common potassium ion abnormality reported in 25(21.4%) and 21(23.9 per cent) of admission cases and 48hrs post-admission assays, respectively. Hypokalemia was associated with epidural hematoma ($p=0,005$), higher levels of HCO3 ($p=0,026$) and base deficit ($p=0,024$). At the same time, increased pulse rate ($p=0.007$) and traumatic SAH ($p=0.045$) were observed in patients with hyperkalemia. Mortality risk associated with hypokalemia was significantly increased OR 4.12 (95% CI: 1.14-14.83, $p=0.031$) and OR 5.12 (95% CI: 1.08-24.25, $p=0.039$) at admission and 48 hours post-admission, respectively.

Hypocalcemia was the most common calcium ion abnormality reported in 84 (72.4%) patients on admission and in 34 (37.8%) patients 48 hours after admission. Patients with hypocalcemia were significantly older (p=0.044), with higher HCO_3 (p=0.039) and base deficits (p=0.048). Patient age, injury severity score, heart rate, and systolic blood pressure reported statistically significant negative correlations with calcium ion levels. Hypocalcemia noted 48hrs after admission was associated with a high risk of mortality (OR 5.70, 95 % CI 1.15-28.33, p=0.033) compared to that at admission (OR 3.2, 95 % CI: 0.52-19.84, p=0.212).

Hypomagnesemia was the most common magnesium ion abnormality reported in 36 (33.3%) and 30 (34.5%) of admission and 48 hours post-admission cases, respectively. Mortality risk associated with hypomagnesemia at admission and 48 hours post-admission was OR 2.4 (95% CI: 0.39-14.88, p=0.35) and OR 0.3 (95% CI: 0.03 to 2.69, p=0.27) respectively. Patient age and systolic BP showed a significant negative correlation with magnesium ion levels. None of the radiological or acid-based parameters showed significant correlations.

Hypophosphatemia was the predominant phosphate ion abnormality, noted in 40(42.1%) and 29(48.3%) of the cases at admission and 48hrs post-admission respectively. Low levels of phosphate were significantly correlated with pre-hospital use of IV fluids (p=0.041), mannitol use (p=0.048), lower diastolic pressure (p=0.043), tachypnoea (p=0.044), hypoxemia (p=0.011) and respiratory alkalosis (p<0.001). Hypophosphatemia was associated with a high risk of mortality; OR 4.12 (95% CI: 1.14-14.83, p=0.031) at admission and OR 7.5 (95% CI: 1.08-90.24, p=0.098) 48 hours post-admission.

Conclusion: Serum sodium, potassium, calcium, magnesium and phosphate ion abnormalities are common in severe traumatic brain injury patients in our setting. They are associated with higher

risk of mortality and can be expected to occur in patients with abnormalities in specific clinical, radiological and acid-based parameters.

CHAPTER 1. INTRODUCTION

Traumatic brain injury (TBI) is an acute insult to the brain that results from external mechanical energy applied to the head, leading to a transient or permanent impairment of cognitive, physical, and psychosocial functions (1–3). Severe Traumatic brain injury, defined as Glasgow Coma Scale ≤ 8, is a significant cause of death and incapacity worldwide and is associated with substantial direct and indirect costs to the public (1,4,5). Moreover, the World Health Organization has projected that TBI will be the leading cause of death and disability by 2020 (6). TBI is more prevalent in developing countries, especially in Kenya, due to the increasing number of road accidents(7–9).

Although the national prevalence of traumatic brain injury in Kenya is not known, most hospital-based studies have shown that severe head injury is associated with mortality of > 50 per cent and poor functional outcomes (10–12). In order to improve outcomes for patients with TBI, the Brain Trauma Foundation (BTF) has established guidelines for the prevention of secondary brain injury caused by the initiation of destructive inflammatory and biochemical cascades due to primary brain injury (13). The secondary brain insults include hypoxia, electrolyte dysfunction, ischaemia and cerebral oedema (1–3).

Serum electrolyte abnormalities (SEAs) are common in severe TBI and are associated with poor outcomes such as increased mortality, prolonged Intensive Care Unit (ICU) admission, and poor outcome scores (14–16). Commonly reported SEA includes sodium, potassium, calcium, magnesium and phosphate ions. These abnormalities may arise as a result of brain injury or interventions such as the use of hyperosmolar therapy. In addition, these abnormalities may coexist and therefore worsen the outcome (14). Electrolyte abnormalities may be one of the factors that can contribute to the high mortality reported in the local studies. However, there is a lack of local

data on electrolyte abnormalities in TBI patients. The objective of this study was to determine the prevalence of electrolyte abnormalities among severe head injury patients seen in Kenyatta National Hospital. In addition, we aimed at determining the association between the electrolyte abnormalities and specific clinical, radiological and acid base parameters. This would help clinicians predict that patients are likely to develop abnormalities and therefore initiate the necessary preventive measures.

CHAPTER 2. LITERATURE REVIEW

2.1 TRAUMATIC BRAIN INJURY (TBI)

2.1.1 EPIDEMIOLOGY OF TBI

Traumatic brain injury is an acute insult to the brain that results from external mechanical energy applied to the head, leading to temporary or permanent impairment of cognitive, physical and psychosocial functions (1–3). Traumatic injury to the brain is a major cause of disability and death (1,4,5). It is associated with enormous direct and indirect costs for the public. For example , in the United States, TBI involves 3.3–5.3 million individuals per year and has a direct annual cost of $9.2 billion (5). The indirect annual cost of lost work and productivity losses is estimated at $51.2 billion (6). In addition , the World Health Organization has projected that TBI will be the leading cause of death and disability by 2020 (6).

The incidence of TBI is higher in developing countries , particularly in Kenya, and is projected to increase due to an increasing number of road accidents (7–9,17). The national prevalence of TBI in Kenya is not known due to the lack of a national head trauma registry and population-based studies (7). Most of the traumatic brain injury studies in Kenya are hospital-based, most of them from Kenyatta National Hospital (8,10–12,18,19). It is estimated that the rate of road accident injuries in Kenya is 60 per 100,000 population (20) and that TBI accounts for > 50 per cent of road accident fatalities in Kenya (17,21). Apart from road traffic accidents, the other causes of TBI include falls and assault (10,22).

2.1.2 TBI AS SEEN AT THE KENYATTA NATIONAL HOSPITAL

Several studies on traumatic brain injury were conducted at Kenyatta National Hospital (8,10–12,18,19). The KNH patient record audit between January 1992 and December 1996 revealed that 670 patients had severe head injuries, with a total mortality rate of 52.6 per cent (11). According to these authors, factors associated with poor outcomes included low admission Glasgow Coma Scale (GCS), abnormal pupil reactivity, low systolic BP and other related injuries. A six-month prospective study conducted between April and September 2005 found that severe TBI accounted for 14.3 per cent of all ICU admissions and was associated with a 54% mortality rate (12). This study included 87 patients (73 male and 14 female) with an average age of 34 ± 17 years. A third of the patients had persistent vegetative status or severe disability.

A further retrospective study was conducted in patients with intracranial hematomas at the KNH between January 2000 and December 2009 (10). Of the 608 patients studied, the majority were male (89.3%) and young (26-45 years of age). The most common cause of injury was assault (48 percent), followed by road accidents (28 percent) and falls (24 percent). Most patients had either epidural hematoma (47.7 percent) or subdural hematoma (42.6 percent). Good functional recovery was associated with younger age, mild head injury, and early surgery, while poor functional outcome was seen in patients with abnormal pupil response, low GCS, advanced age, and low mean arterial blood pressure.

A study on demographic data of patients with traumatic intracranial bleeds in KNH was conducted between December 2010 and March 2011 (23). The authors studied 51 patients, 96.1 percent of whom were male, 51 percent were married, and most (56.9 percent) had primary (primary) education. The average age was 34 years. The authors reported that there was an association

between low socio-economic status and the incidence of TBI given the fact that most patients were unemployed and did not attain average or high academic levels.

Mwang'ombe and Shitsama (2013) presented a paper at a scientific conference summarizing the studies they carried out between 1979 and 2009. They divided their findings into two periods, namely the pre-CT scan era (before the computed tomography scan in KNH [1979-1985]) and the CT scan era (1999-2009) of the findings. Mortality during the CT Scan era was reported to be higher (57 per cent) compared to 16 per cent in the pre-CT scan period. This paper shows the rapid rise in TBI mortality in Kenya over the last thirty years.

A cross-sectional study of cognitive abnormalities among traumatic brain injury patients in KNH was conducted and reported as a thesis (24). The aim of this study was to evaluate both the prevalence and the extent of cognitive impairment using several neuropsychological tools. Seventy-four patients (58 males and 16 females) were interviewed. The authors reported significant cognitive impairment in visual-spatial abilities, memory, attention to language ability, and executive functions. Clinical screening of all TBI patients for cognitive dysfunction was recommended.

2.1.3 CLASSIFICATION OF TRAUMATIC BRAIN INJURY

TBI is classified into mild, moderate and severe forms based on the Glasgow Coma Scale (GCS) which describes neurologic impairment in three parameters namely eye-opening, verbal response, and motor function (5). Table 1 illustrates the components of the GCS. The score is determined by adding the scores in each of the 3 categories (GCS=V+M+E). The highest score of 15 while the least if 3. The overall score is then used to classify TBI as mild (GCS 13–15), moderate (GCS 9–12) or severe (GCS <9) (3).

Table 1. Glasgow Coma Scale scoring system

Score	Motor response (M)	Score	Verbal response (V)	Score	Eye opening (E)
6	Obeys commands	-	-	-	-
5	Localises to pain	5	Coherent	-	-
4	Withdraws to pain	4	Confused	4	Spontaneous
3	Decorticate flexion	3	Inappropriate words	3	To speech
2	Decerebrate extension	2	Incomprehensible sounds	2	To pain
1	None	1	None	1	None

2.1.4 PATHOPHYSIOLOGY OF TRAUMATIC BRAIN INJURY

The initial mechanical insult to the brain results in tissue deformation leading to damage to neurons, axons, glia, and blood vessels (1). This is called the primary injury and is usually followed by a delayed phase of injury called secondary injury that is mediated by extracellular and intracellular biologic mechanisms (1,2). The secondary injury is characterised by insults such as cerebral oedema, hypotension, hypoxia, and increased intracranial pressure (ICP). These secondary insults further aggravate TBI leading to a profound negative effect on the outcome. The primary injury to the brain results in impaired cerebral blood flow (CBF) regulation, brain tissue destruction, and alterations in brain metabolism (3). These processes lead to cytotoxicity and generalized cerebral oedema. Whereas the primary brain injury cannot be undone, the secondary injury cascade can be prevented by maintaining adequate oxygenation, adequate and stable cerebral perfusion, euglycemia, and maintenance of electrolytes (1–3). These measures should be initiated early and appropriately to prevent secondary brain injury.

2.2 ELECTROLYTE ABNORMALITIES IN TBI

Electrolyte abnormalities are common in traumatic brain injury (14,15). Electrolyte imbalance in head injury can result from the primary brain injury or as a result of an intervention, and usually has deleterious effects on the patient. Some of the reported electrolyte abnormalities involve sodium, potassium, calcium, magnesium and phosphate ions. There is however a paucity of local data regarding electrolyte abnormalities in patients with traumatic brain injury.

2.2.1 SODIUM ABNORMALITIES

a) Hypernatremia in TBI

Hypernatremia is defined as elevated serum sodium ion concentration >145mEq/L and 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 (25,26). Hypernatremia induced by hyperosmolar therapy leads to loss of cell volume resulting in a decrease in cerebral oedema (27,28). It also modulates neuroinflammatory pathways, restores membrane potentials of neurons, and reduces the viscosity of blood (25). Although this may initially appear beneficial to the brain, it is associated with a myriad of detrimental effects. It associated with increased mortality in both paediatric (29) and adult patients (25,26,30). A nation-wide study in the USA conducted by Hoffman et al. 2018, involving 90,121 patients with a head injury revealed an incidence of 5% cases with hypernatremia. These patients had increased mortality rate (odds ratio, 1.51), a longer hospitalisation (24 vs. 12 days; $P < 0.001$), and greater hospital costs ($227,110 vs. $112,500; $P < 0.001$).

b) Hyponatremia in TBI

Hyponatremia is defined as serum sodium ion concentrations less than 135mEq/L. In TBI, hyponatremia contributes to secondary brain insults by causing cerebral oedema, seizures and depression of consciousness (31). Hyponatremia in TBI is caused by Cerebral Salt Wasting Syndrome (CSW) and Syndrome of Inappropriate secretion of Antidiuretic Hormone (SIADH)(32). In Cerebral salt wasting (CSW) syndrome, there is renal loss of sodium resulting in hypovolemia and hyponatremia. The incidence of CSW varies from 0.8 - 34.6 % (33). Although the mechanisms leading to CSW unclear, it is hypothesized to result from increased production of natriuretic peptides as well as alterations in the sympathetic nervous system (33–35).

SIADH is diagnosed when the serum osmolality is <280mmol/kg, urine osmolality is inappropriately high (>100mmol/kg) and concentration of urinary sodium is >30mmol/l. Additional features include normovolemia, absence of thyroid, pituitary, adrenal, or renal insufficiency, and/or use of diuretic agents (31). The pathophysiological mechanisms of SIADH after TBI is uncertain. It may be due to injury to pituitary stalk or posterior pituitary gland resulting in hypersecretion of ADH (36,37).

2.2.2 POTASSIUM ABNORMALITIES

a) Hypokalemia in TBI

Hypokalaemia occurs when serum potassium level is <3.5mmol/L. It is classified into mild (3.0 - 3.5 mmol/L), moderate (2.5 - 3.0 mmol/L) and severe (<2.5 mmol/L) (38). Pin-on et al. 2018, revealed that hypokalemia was the most common (65% of all cases) electrolyte abnormality following traumatic brain injury. Severe hypokalaemia occurs within 24-96hrs after trauma

(38,39). Although the mechanism for hypokalemia is not clear, it is postulated that epinephrine released during stress response to trauma causes an intracellular shift of potassium ions (40–42). Hypokalemia is associated with life-threatening cardiac arrhythmias and is a major risk factor for death in TBI patients (38,39).

b) Hyperkalemia in TBI

Hyperkalaemia, defined as potassium level >5 mmol/l (43), has been reported in up to 29% of non-crush injuries (44). Post-traumatic hyperkalemia is caused by extensive tissue damage, aggressive transfusion and hemorrhagic shock (44). Intracerebral microdialysis studies on severe head injury patients have revealed elevated extracellular potassium in up to 20% of the patients and are associated with poor clinical outcomes (45–47).

2.2.3 CALCIUM ABNORMALITIES

Abnormal serum calcium is associated with a variety of clinical manifestations in TBI patients (16). Both hypercalcaemia and hypocalcaemia can occur resulting in the development of tetany or seizures (14–16,48). Hypocalcemia is associated with significant mortality in severe traumatic brain injury (49,50).

2.2.4 PHOSPHATE ABNORMALITIES

Serum phosphate is an intracellular anion that is involved in many biochemical pathways related to normal physiologic functions (51). Hypophosphatemia in TBI patients is associated with generalised muscle weakness and specifically weakness of respiratory muscles leading to difficulty weaning off the ventilator and increased incidence of respiratory infections (52–54). In addition, it is associated with ventricular muscle weakness resulting in decreased cardiac output.

Hypophosphatemia is common in head injury and early detection and prompt treatment decrease morbidity and mortality (52–54).

2.2.5 MAGNESIUM ABNORMALITIES

Magnesium plays an important role in the secondary brain injury by its effects on numerous biomechanical functions including oxidative stress, ion changes, neurotransmitter release, protein synthesis, and energy metabolism (55,56). Low serum magnesium is seen in severe head injury patients and is associated with the development of motor and cognitive deficits as well as mortality (53,57). Although the mechanism of magnesium depletion in head injury patients is largely unknown, a possible explanation could be the increased lipolysis triggered by the stress-induced catecholamine surge leading to increase in the free fatty acids which bind to Mg^{2+} and thus increase the excretion of Mg^{2+} in the urine (57).

STUDY JUSTIFICATION

Severe traumatic brain injury is a major cause of death and disability in the world (1,4,5). It is associated with high direct and indirect costs to the public. The TBI is more prevalent in developing countries and is expected to increase in the coming years (7). Local studies have shown that TBI is associated with a mortality rate of over 50% and poor functional outcomes (10–12). Although primary brain insult can not be undone, measures to prevent secondary brain insults should be put in place. These include maintenance of stable cerebral perfusion, electrolyte maintenance, glycemic control, and adequate oxygenation (1–3).

Several studies have reported electrolyte abnormalities in severe TBI, including sodium , potassium , calcium, magnesium and phosphate ions (14–16). These abnormalities may be due to the nature of the brain injury itself or as a result of interventions such as the use of hyperosmolar therapy. In addition, these abnormalities may coexist and therefore worsen the outcome (14). Electrolyte abnormalities may be one of the factors that can contribute to the high mortality reported in local studies. However, there is a lack of local data on electrolyte abnormalities in patients with traumatic brain injury. The aim of this study was to determine the prevalence of electrolyte abnormalities in severe head injury patients seen at Kenyatta National Hospital. In addition, we aimed at determining the association between the electrolyte abnormalities and specific clinico-radiologic parameters. This would help clinicians predict patients likely to develop abnormalities and therefore initiate the necessary preventive measures.

RESEARCH QUESTION AND OBJECTIVES

RESEARCH QUESTION

What is the prevalence of serum electrolyte abnormalities among severe traumatic brain injury patients seen at Kenyatta National Hospital and what is its association with clinical and radiological parameters?

STUDY OBJECTIVES

Broad objective

- To evaluate the serum electrolyte abnormalities (SEA) in severe head injury patients in Kenyatta National Hospital

Specific objectives

1. To determine the prevalence of SEA in severe head injury patients at KNH
2. To determine the association between SEA and specific clinical parameters
3. To determine the association between SEA and specific radiologic parameters
4. To determine the association between SEA and acid-base parameters

CHAPTER 3. MATERIALS & METHODS

3.1 STUDY DESIGN

Analytical cross-sectional study conducted over 4 months (1 November 2019 to 28 February 2020).

3.2 STUDY SITE

The Kenyatta National Hospital Accident and Emergency Unit and Intensive Care Units were the site of the study. Kenyatta National Hospital is situated in Nairobi, Kenya. It is the largest hospital in the country and the main referral center for neurotrauma. The Hospital serves patients from various regions and socio-economic backgrounds.

3.3 STUDY POPULATION

All patients with severe head injury defined as Glasgow Coma Scale ≤ 8 and whose next of kin had consented were enrolled in the study. Patients were enrolled consecutively by the lead investigator.

Inclusion Criteria

Patients with a diagnosis of severe head injury defined by Glasgow Coma Scale ≤ 8

Exclusion Criteria

1. Patients with known preexisting chronic illness eg. Diabetes mellitus, chronic renal disease, hypertension
2. Patients whose next of kin decline consenting to the study

3.4 SAMPLE SIZE DETERMINATION

The sample size was determined using Fisher's formula (58,59):

$$n = \frac{Z^2 p(1-p)}{d^2}$$

Where:

- n = minimal sample size required for the study.
- Z = 1.96 (normal deviate corresponding to 95% confidence level)
- d = 0.1 (degree of precision of 10%)
- P= 72.5% (estimated prevalence of SEA according to Taha and Ammar(60) = 72.5%)

By substituting above values in the formula, a minimum sample size of 77 patients was derived

$$n = \frac{1.96^2 x 0.725(1-0.725)}{0.1^2} = 76.59$$

3.5 DATA COLLECTION PROCEDURE

All patients presenting at the KNH Accident and Emergency Unit with severe TBI defined by Glasgow Coma Scale ≤ 8 were recruited into the study. The next of kin were duly informed of the nature and purpose of the study. For those who agreed to participate, written informed consent was obtained and were subsequently enrolled into the study. Data collected included patient demographics, mechanisms of injury, duration from injury to hospital, prehospital interventions such as IV Fluids, neurologic exam findings, other associated non-nervous system injuries, CT scan head findings, serum electrolyte findings, arterial blood gas findings and 30-day outcome (death or discharge).

The severity of injury to the patient was measured using the Injury Severity Score (ISS) (61–63). ISS is an anatomically based consensus-derived global severity scoring system that classifies each injury in every body region according to its relative severity. To calculate an ISS for an injured

person, the body is divided into nine body regions: head, face, neck, thorax, abdominal and pelvic contents, spine, upper extremity, lower extremity, and external. The severity of injury to each of these regions is documented on a six-point ordinal scale (Abbreviated Injury Scale): 1-Minor; 2-Moderate; 3-Serious (not life-threatening); 4-Severe (life-threatening, survival probable); 5-Critical (survival uncertain); 6-Maximal (possibly fatal). The ISS is defined as the sum of the squares of the Abbreviated Injury Scale scores of each of a patient's three most injured body regions. $ISS = A^2 + B^2 + C^2$ where A, B, C are the AIS scores of the three most injured body regions. The ISS scores ranges from 3 to 75 (i.e. AIS scores of 5 for each category). If any of the three scores is a 6, the score is automatically set at 73.

3.6 LABORATORY

Serum electrolyte assays were done at two time points: at admission (at the Accident and Emergency Unit) and 48hrs post-admission (at the Intensive Care Unit). To ensure quality was maintained, the tests were carried out in KNH's clinical chemistry laboratory by a study dedicated technician in conjunction with the principal investigator. The principal investigator was trained on sample labelling, collection, storage and transportation. All reagents were prepared following standard operating procedures used at KNH clinical chemistry laboratory. The tests were done using Biolis 50i Superior Chemistry Analyser manufactured by Tokyo Boeki Medisys – Japan.

3.7 QUALITY ASSURANCE AND CONTROL MEASURES

The principal investigator carried out all the interviews and physical examinations. The data collection tools were cross-checked for completeness and any missing entries corrected. For the laboratory test, daily internal quality control checks were done every morning to ensure that the results were valid. The Biolis 50i Superior Chemistry Analyser machine comes with its internal

quality control reagents which were used for this study. External quality control checks were done through the Randox International Quality Assessment Scheme (RIQAS). RIQAS is the world's largest global External Quality Assessment (EQA / Proficiency Testing (PT) schemes serving over 45,000 participating laboratories in more than 133 countries. KNH Clinical Chemistry laboratory is enrolled in the RIQAS scheme and sends monthly reports for external quality control.

3.8 REFERENCE RANGES & DEFINITION OF ABNORMALITIES

The normal reference ranges for the assayed serum electrolytes were as follows:

- Sodium 135-145mmol/L: hyponatremia <135mmol/L & hypernatremia >145mmol/L
- Potassium 3.5-5.0mmol/L: hypokalemia <3.5mmol/L & hyperkalemia >5.0mmol/L
- Calcium 2.25-2.75mmol/L: hypocalcemia <2.25mmol/L, hypercalcemia >2.75mmol/L
- Magnesium 0.67-1.04mmol/L: hypomagnesemia<0.67mmol/L, hypermagnesemia>1.04 mmol/L
- Phosphate 0.90-1.62mmol/L: hypophosphatemia <0.90mmol/L & hyperphosphatemia >1.62mmol/L

Low albumin level decreases the amount of calcium and magnesium ions bound with serum proteins, causing lower results of the serum calcium and magnesium levels. Thus for patients with hypoalbuminemia, correction for calcium and magnesium ions was done using the following formulae:

1. **Paynes' formula for Ca^{2+} correction (64):**

   "Corrected" Ca^{2+} (mmol/L) = Measured Ca^{2+} (mmol/L) + 0.020 (40 - albumin (g/L)).

2. **Kroll and Elin formula for Mg^{2+}correction (65):**

   "Corrected" Mg^{2+} (mmol/L) = Measured Mg^{2+} (mmol/L) + 0.005 (40 - albumin (g/L))

3.9 DATA MANAGEMENT

A structured questionnaire were used to collect data which was then be entered into Statistical Package for Social Sciences (SPSS) version 20.0 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 ANOVA (Analysis of Variance) tests respectively. Admission and 48hrs post admission variables were compared using the paired t-test. Categorical data was analysed by Pearson's Chi-square test. Correlation between the serum electrolytes and the study variables (clinical, radiologic and acid base) was determined using Pearson's correlation coefficient (r). Odds ratio 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.

3.10 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). Permission to carry out the study was also sought from the KNH administration. 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 (see APPENDIX).

3.11 STUDY PROTOCOL

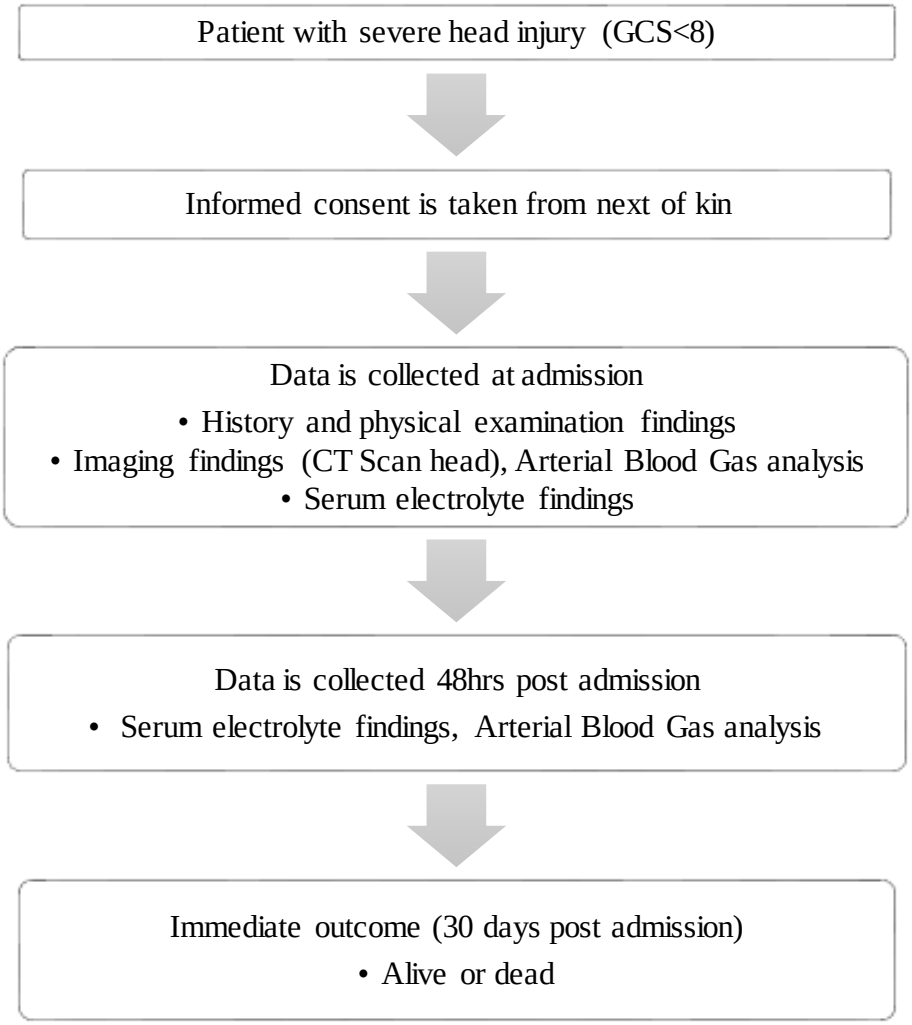


Figure 1: Study protocol

CHAPTER 4. RESULTS

4.1 GENERAL INFORMATION

4.1.1 Demographic data

One hundred and twenty-four (124) patients with severe head injury were enrolled in this study. Of these patients, 118 (95.2 per cent) were male and 6 (4.8 per cent) female. The mean age was 32.41±14.59 years (range 2 years-71 years). The average duration of time from injury to presentation at KNH was 23.31 hours (range 0.5-312 hours). The injury mechanisms were as follows: pedestrians hit by a motor vehicle 41(33.1 per cent), assault 24(19.4 per cent), motorcycle occupant 24(19.4 per cent), fall from height 14(11.3 per cent), motor vehicle occupant 4(3.2 per cent) and unknown mechanism 17(13.7 per cent).

4.1.2 Prehospital care

The majority of patients (54 per cent) were taken to KNH directly from the injury site, while the remainder were brought from other hospitals (13 per cent from private hospitals and 33 per cent from public hospitals). Before being referred to KNH, only one patient was intubated. Pre-hospital use of intravenous normal saline and mannitol solutions was reported in 67 (54 percent) and 16 (12.9 percent) of patients, respectively.

4.1.3 Physical examination findings

The mean systolic and diastolic blood pressures were 127.38±25.19mmHg and 75.90±17.92mmHg. The mean values for the other parameters were as follows: 94.76±25.49 beats/min heart rate, 36.8±0.75 °C temperature, 91.15±9.52 percent Saturation O_2, and 20.82±4.63 breaths/min respiratory rate. Most (58 percent) patients had a Glasgow Coma Scale score of either

7 or 8 (Figure 2). Up to 38.7% of patients had normal pupil-light reactions (Figure 3). Anisocoria was seen in 25 % of patients.

Figure 2: Glasgow Coma Score findings

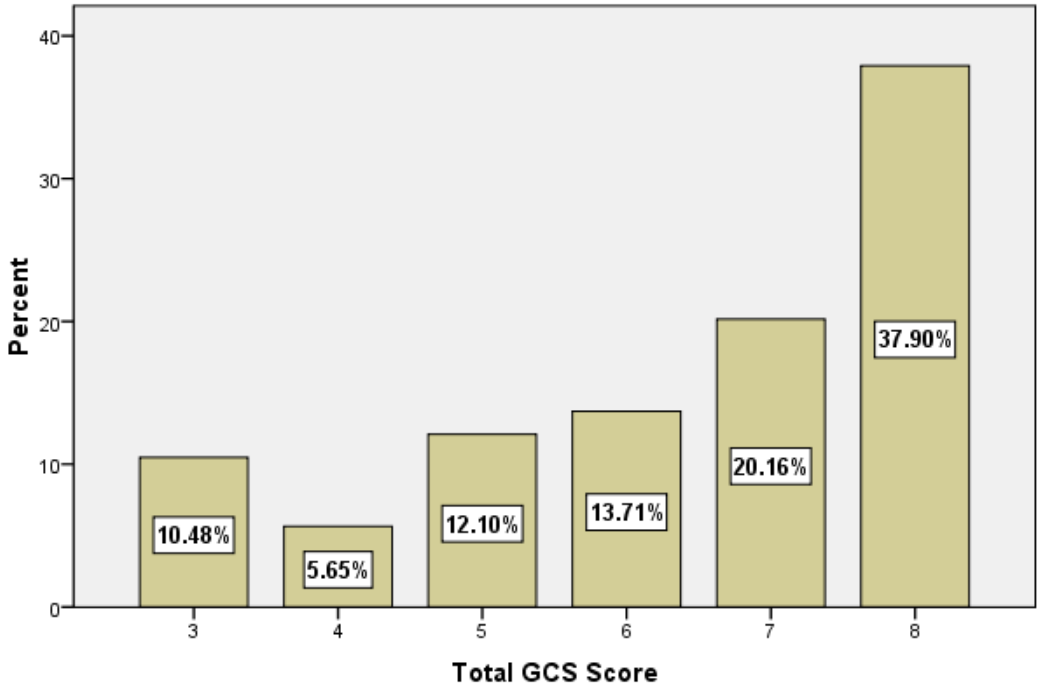
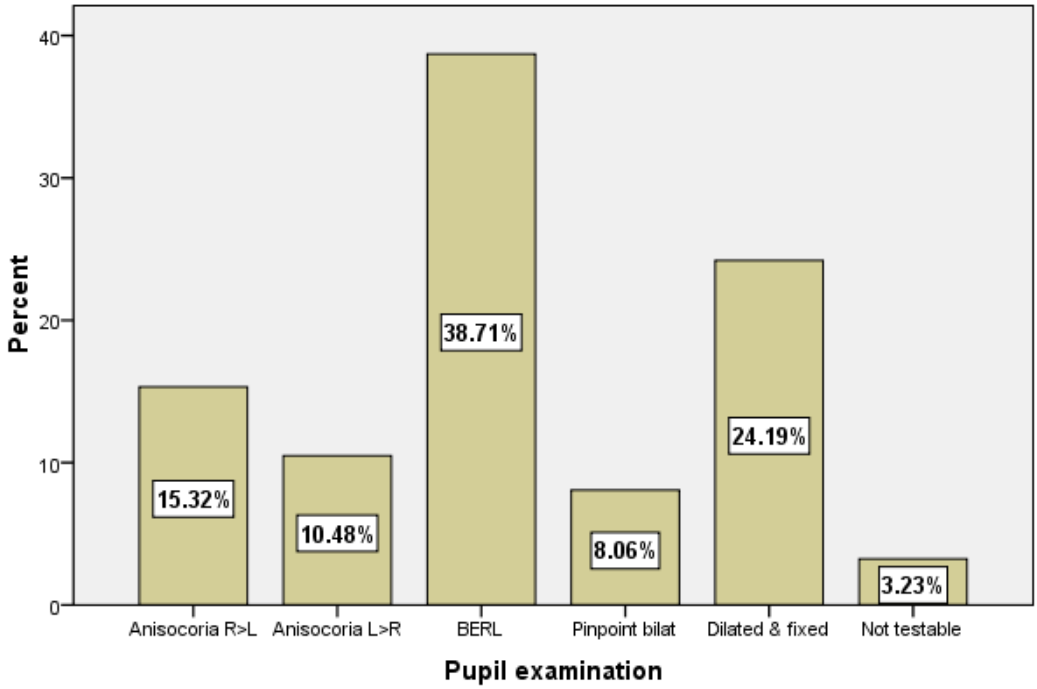


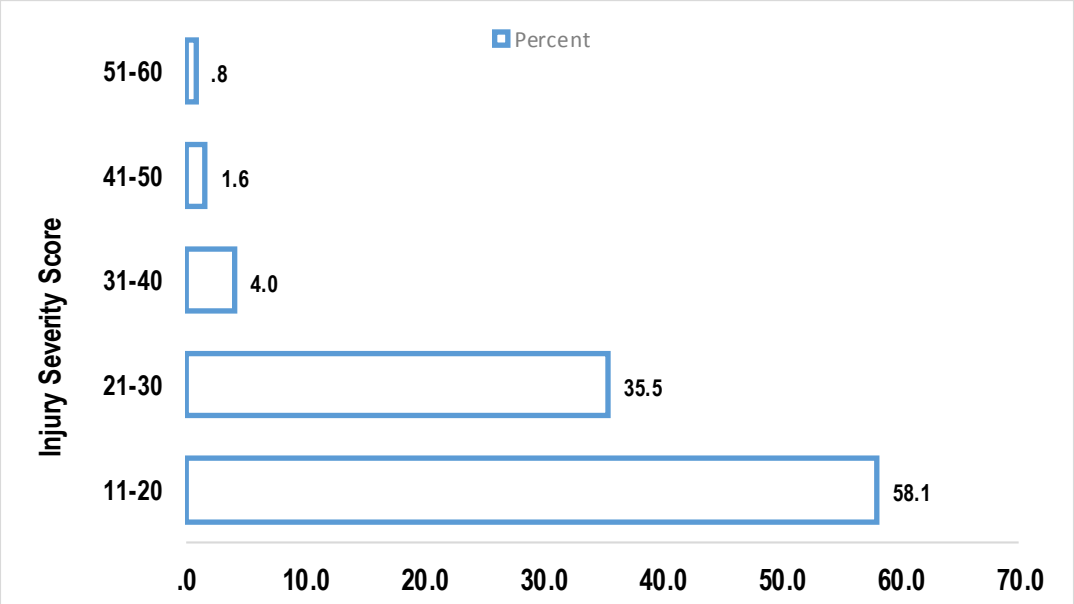
Figure 3: Pupillary light reaction findings



Injury Severity Score

The severity of the patient's injury was measured using the Injury Severity Score (ISS). The average ISS was 21.06±7.74 (range 11-57). The majority (93.6 percent) of patients had an ISS of between 11 and 30 (Figure 4). The mean Abbreviated Injury Scale for head injuries was 4.09 (range 3-5). Sixty patients suffered additional non-nervous system injuries. Associated non-nervous system injuries included: lower limb 22 (17.7 per cent), thorax 16 (12.9 per cent), upper limb 14 (11.3 per cent), abdominopelvic 10 (8.1 per cent) and neck 3 (2.4 per cent). The median Abbreviated Injury Scores (AIS) for these non-nervous system injuries was 1-3.

Figure 4: Injury Severity Score



4.1.4 CT Scan head findings

CT Scan head was performed on 117 (94.4%) patients, with the remaining 7 patients dying in the emergency room before the CT scan could be performed. Identifiable intracranial pathologies included: contusion haemorrhage in 51 (41.1%), traumatic subarachnoid haemorrhage in 43 (34.7%), acute subdural hematoma in 42 (33.9%) and acute epidural hematoma in 24 (19.4%) patients. Basal cisterns were compressed in 55 (47 per cent), absent in 46 (39.3 per cent) and normal in 16 (13.7 per cent) cases. These imaging findings were classified using the Rotterdam CT traumatic brain injury score. The most common scores were 4 and 5 in 36 (30.8 percent) and 30 (25.6 percent) respectively (Figure 5).

4.1.5 Acid-base findings

Compensated respiratory alkalosis was the most common finding at admission and 48 hours later (27.7% and 34.1% respectively) followed by respiratory alkalosis (18.8% and 27.3% respectively). Compensated metabolic acidosis was the third most common acid base finding (Figure 6). No statistically significant differences were observed between the acid-base findings at admission and 48hrs later ($p=0.806$). The mean pH at admission and 48 hours post-admission were 7.37±0.12 and 7.42±0.08 (p 0.001) respectively. The mean pCO2 (kPa) was 4.65±1.33 and 4.60±1.01 (p 0.756) at admission and 48 hours post-admission, respectively. Mean HCO_3 (mmol/L) was 19.6±3.5 and 21.9±4.5 ($p<0.001$) at admission and 48hours at post-admission.

4.1.6. Immediate outcome

In the 30-day follow-up period, 82 (66.1%) of patients died. Most of the patients (87.8%) died within seven days of hospitalization, of whom 53 (64.6%) died within 72 hours of hospitalization.

Figure 5: Rotterdam CT score findings

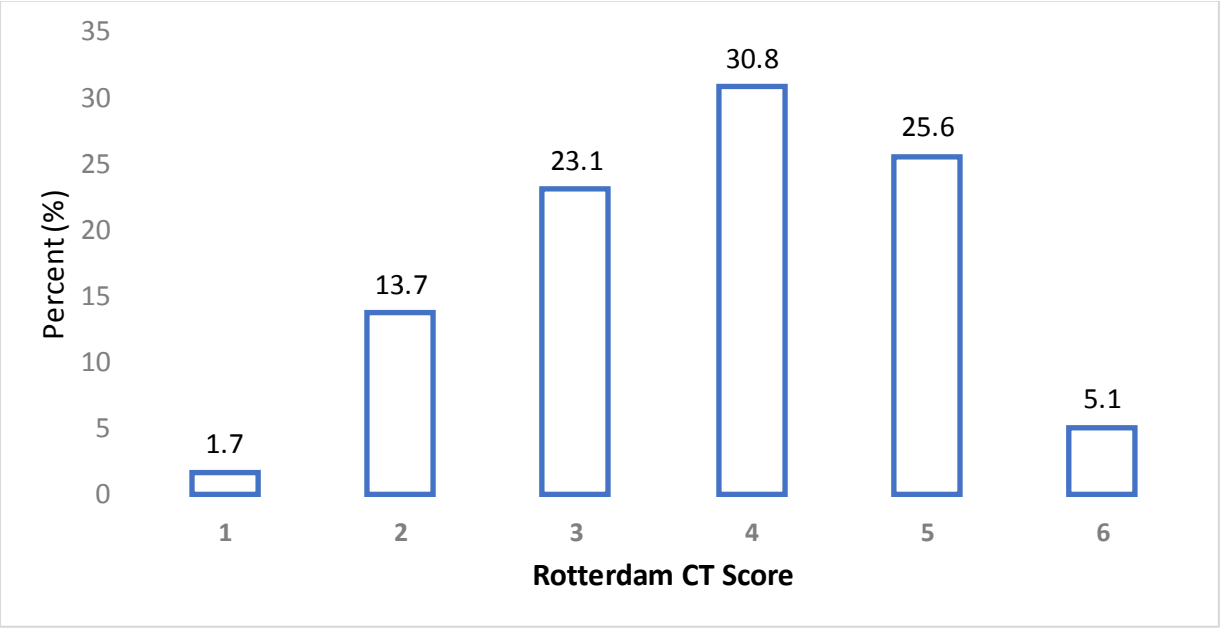
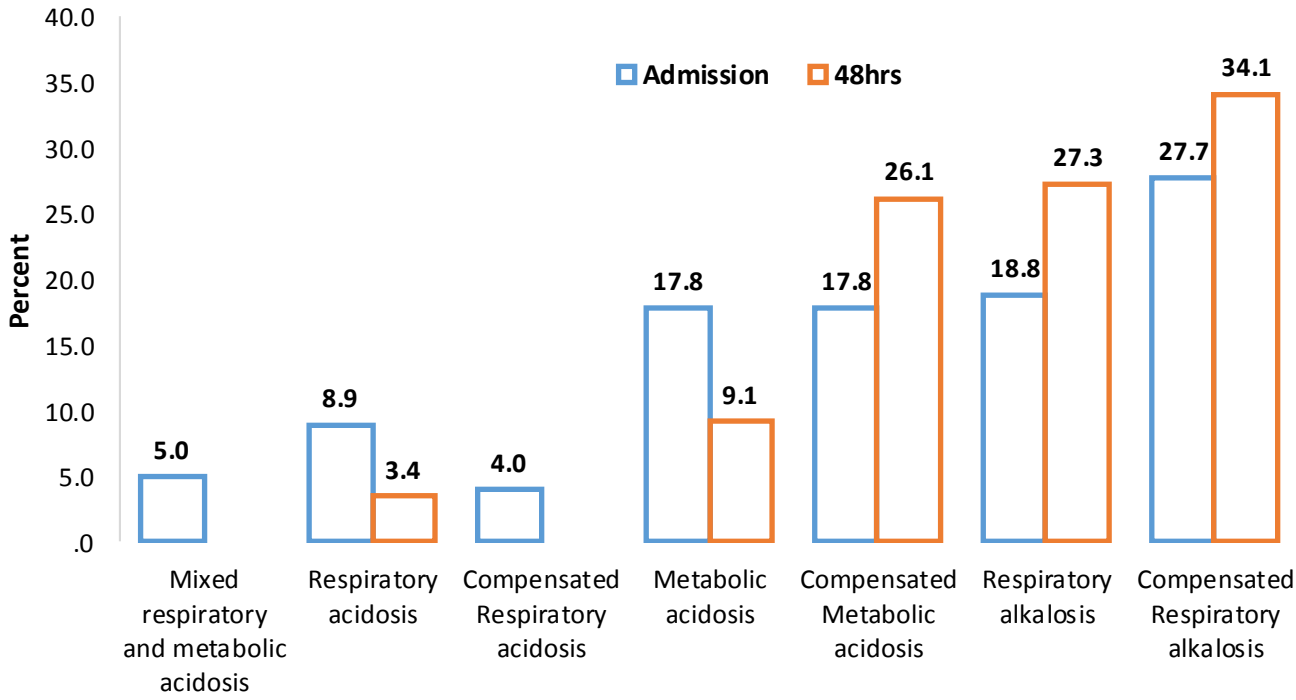


Figure 6: Acid-base findings

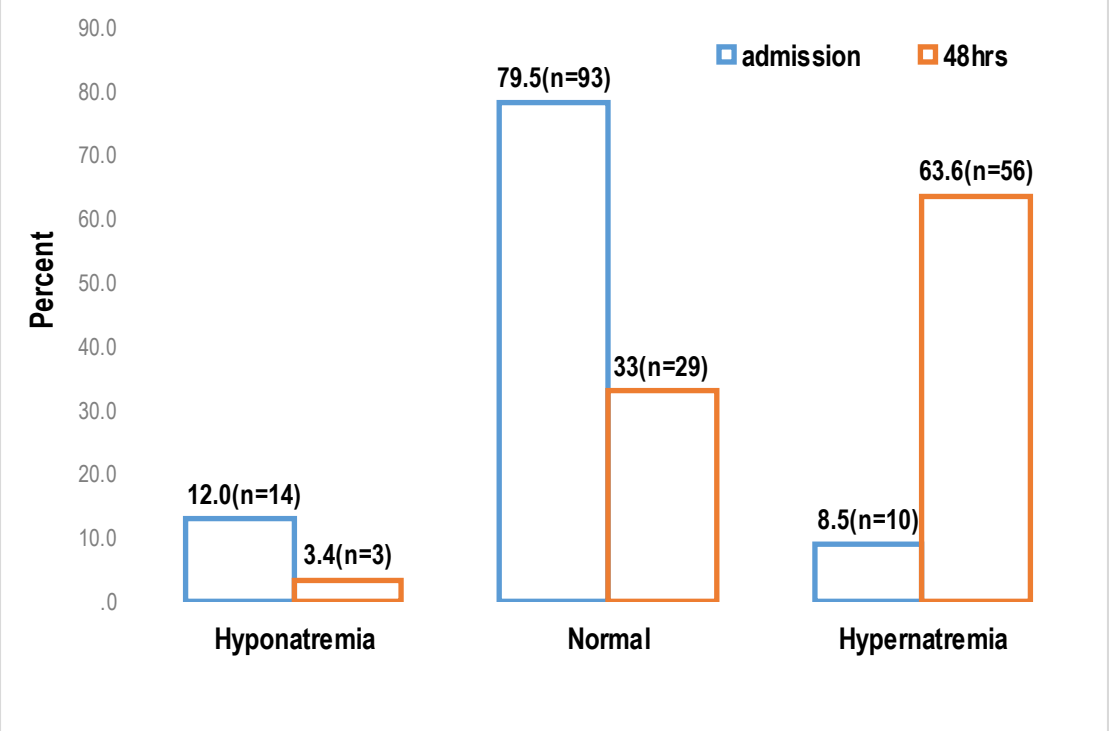


4.2 SERUM SODIUM ION ABNORMALITIES

4.2.1 PREVALENCE OF SERUM SODIUM ION ABNORMALITIES

At admission, the mean serum sodium ion levels were 139.16±5.93mmol/l (n=117), and 48hrs after admission were 149.13±8.84 mmol/l (n=88). Serum sodium ion abnormalities were observed in 24 (20.5 percent) admission patients, and 48hrs post-admission patients in 59 (67 percent). Hyponatremia was the most common abnormality seen in 14 (12.0 percent) patients at admission, while hypernatremia was found in 10 (8.5 percent) cases. The predominant abnormality in the 48hr post-admission assay was hypernatremia, recorded in 56 (63.6 per cent) cases (Figure 7). Paired t-test samples showed a statistically significant difference between sodium levels at admission and 48hrs post-admission ($p<0.001$).

Figure 7: Serum sodium levels at admission and 48hrs later



4.2.2. ASSOCIATION BETWEEN SERUM SODIUM AND CLINICAL PARAMETERS

Patients who had hyponatremia at admission took longer (59.7±28.7hrs, p 0.002) to be in hospital compared to other groups (Table 2). Admission hypernatremia was significantly associated with the use of mannitol (p=0.044), while 48hr post-admission hypernatremia was associated with a lower GCS score (p=0.047) and a higher Injury Severity Score (p=0.015). Statistically significant negative correlations were observed between sodium ion admission and duration of hospital presentation injury (r-0.226, p 0.012), pre-hospital use of mannitol (r-0.189, p 0.036) and GCS Admission Score (r-0.205, p 0.022) (Table 3). The GCS score (r-0.225, p 0.016), head AIS (r 0.314, p 0.003) and ISS (r 0.236, p 0.027) were the only clinical variables that showed statistically significant correlations with 48hr post-admission sodium levels.

In addition, 48hr post-admission sodium levels had an impact on the immediate outcome compared to the level at admission. A majority (73.3%) of the patients with hypernatremia at 48hrs post-admission died while up to 58.4% with normal sodium levels were alive by the 30th-day post-admission (p=0.034). Hypernatremia at admission and 48hrs post-admission were associated with higher 30-day mortality OR 5.74 (95 per cent CI 0.71-46.73, p 0.103) and OR 3.55 (95 per cent CI 1.36-9.23, p 0.0095) respectively, compared with hyponatremia OR 1.26 (95 per cent CI 0.41-3.93, p 0.688) and OR 2.14 (95 per cent CI 0.17-26.33, p 0.552) respectively at admission and 48hrs post-admission.

Table 2: Association between serum sodium and clinical parameters

		Hyponatremia[1]	Normal[2]	Hypernatremia[3]	p-value
Age (yrs)	Admission	32.4±13.8	31.9±14.8	36.5±14.6	0.649
	48hrs post-admission	20.7±2.1	33.6±15.7	34.4±13.7	0.273
Time from injury to presentation (hrs)	Admission	59.7±28.7	17.1±26.1	24.1±24.9	***0.002****
	48hrs post-admission	48.8±60.4	27.4±41.0	21.5±37.7	0.451
Pre-hospital use of IV fluids	Admission	50.0%	54.6%	54.4%	0.942
	48hrs post-admission	33.3%	65.5%	57.1%	0.495
Pre-hospital use of Mannitol	Admission	6.3%	11.3%	36.4%	***0.044****
	48hrs 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
	48hrs 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
	48hrs 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
	48hrs 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
	48hrs post admission	18.0±0.0	20.4±3.6	20.4±3.9	0.567
Saturation O2 (%)	Admission	94.6±5.5	90.8±9.9	89.8±10.4	0.420
	48hrs post admission	93.5±0.7	93.2±7.7	91.8±7.6	0.746
Total GCS Score	Admission	7.3±1.1	6.3±1.7	5.8±1.7	0.064
	48hrs post admission	7.7±0.6	6.9±1.2	6.2±1.3	**0.047***
Injury Severity Score	Admission	18.5±5.1	21.6±8.3	20.5±5.0	0.333
	48hrs post admission	18.7±1.2	18.7±8.1	22.1±7.6	***0.015****

1. Hyponatremia at admission n=16, 48hrs post admission n=3.
2. Normonatremia at admission n=97, 48hrs post admission n=29
3. Hypernatremia at admission n=11, 48hrs post admission n=56

Table 3: Correlations between serum sodium and clinical parameters

Variable	Admission (n=117)		48hrs after admission (n=88)	
	Pearson Correlation	P value	Pearson Correlation	P value
Age (yrs)	0.054	0.574	0.123	0.278
Time from injury to presentation (hrs)	***-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 O2	-0.122	0.235	-0.090	0.454
Pupil examination	-0.046	0.611	0.195	0.068
Total GCS Score	***-0.205****	***0.022***	***-0.255****	***0.016***
Abbreviated Injury Score – head	0.083	0.359	***0.314****	***0.003***
Injury Severity Score	0.086	0.343	***0.236****	***0.027***

4.2.3 ASSOCIATION BETWEEN SERUM SODIUM & RADIOLOGIC PARAMETERS

Hypernatremia at admission was correlated significantly with the presence of subdural hematoma (p=0.044) and midline change > 5 mm (p=0.048), while compressed / absent basal cisterns (p=0.010), subdural hematoma (p=0.032) and a higher Rotterdam CT score (p=0.003) were correlated with hypernatremia developing 48hrs after admission (Table 4). These parameters also showed statistically significant positive correlations with serum sodium ions (Table 5).

Table 4: Association between serum sodium and radiologic parameters

		Hyponatremia[1]	Normal[2]	Hypernatremia[3]	p value
SDH Thickness (mm)	Admission	10.0±5.0	11.8±4.8	9.2±2.0	0.387
	48hrs post admission	5.0±3.1	12.5±2.7	11.2±5.0	0.343
MLS >5mm	Admission	18.8%	36.1%	63.6%	***0.048****
	48hrs 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
	48hrs post admission	.0%	31.0%	17.9%	0.245
Presence of Subdural hematoma	Admission	42.9%	31.2%	70.0%	***0.044****
	48hrs post admission	33.3%	20.7%	50.0%	***0.032****
Presence of Traumatic SAH	Admission	21.4%	37.6%	50.0%	0.333
	48hrs post admission	33.3%	31.0%	46.4%	0.378
Presence of contusion hemorrhages	Admission	42.9%	44.1%	40.0%	0.968
	48hrs 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
	48hrs post admission	3.3±1.5	3.4±1.0	4.2±1.1	***0.003****

1. Hyponatremia at admission n=16, 48hrs post admission n=3.
2. Normonatremia at admission n=97, 48hrs post admission n=29
3. Hypernatremia at admission n=11, 48hrs post admission n=56

Table 5: Correlations between serum sodium and specific radiologic parameters

		Admission (n=117)	48hrs after admission (n=88)
Rotterdam CT head Score	Pearson Correlation	0.134	***0.340*****
	Sig. (2-tailed)	0.151	***0.001***
Midline shift (mm)	Pearson Correlation	***0.210****	0.129
	Sig. (2-tailed)	***0.019***	0.232
Basal cisterns	Pearson Correlation	0.001	***0.340*****
	Sig. (2-tailed)	0.994	***0.001***
Presence of Epidural Hematoma	Pearson Correlation	-0.038	0.072
	Sig. (2-tailed)	0.681	0.506
Presence of Subdural hematoma	Pearson Correlation	0.096	***0.248****
	Sig. (2-tailed)	0.303	***0.020***
Presence of Intracerebral hematoma	Pearson Correlation	0.025	-0.144
	Sig. (2-tailed)	0.789	0.181
Presence of Traumatic Subarachnoid hemorrhage	Pearson Correlation	0.136	0.138
	Sig. (2-tailed)	0.143	0.199
Presence of Contusion hemorrhages	Pearson Correlation	0.010	-0.154
	Sig. (2-tailed)	0.917	0.151
Epidural Hematoma volume (mls)	Pearson Correlation	0.250	-0.022
	Sig. (2-tailed)	0.389	0.949
Subdural hematoma Thickness (mm)	Pearson Correlation	-0.070	0.073
	Sig. (2-tailed)	0.690	0.703
Intracerebral hematoma Volume (mls)	Pearson Correlation	0.064	0.357
	Sig. (2-tailed)	0.880	0.432

4.2.4. ASSOCIATION BETWEEN SERUM SODIUM & ACID-BASE PARAMETERS

The base deficit (Table 6) was the only parameter that displayed significant statistical difference at admission. Hypernatremia noted 48hrs post admission was associated with statistically significant lower pCO2 (p=0.021), bicarbonate (p=0.018), and base deficit (p=0.046). These parameters also showed statistically significant negative correlations with the sodium ion levels 48hr post admission (Table 7).

Table 6: Association between serum sodium and acid-base parameters

		Hyponatremia[1]	Normal[2]	Hypernatremia[3]	*P value*
pH	*Admission*	7.35±0.18	7.36±0.11	7.44±0.05	*0.158*
	48hrs post admission	7.39±0.09	7.42±0.09	7.42±0.07	0.731
pCO2	*Admission*	5.34±2.68	4.56±1.20	4.11±0.66	*0.103*
	48hrs post admission	5.18±0.87	4.95±1.18	4.35±0.85	***0.021****
HCO3	*Admission*	20.02±3.85	18.88±3.76	20.26±3.41	*0.378*
	48hrs post admission	24.13±6.37	23.55±4.10	20.77±4.41	***0.018****
Base deficit	*Admission*	-3.18±8.55	-5.73±4.55	-2.11±2.23	***0.047****
	48hrs post admission	-0.27±6.28	-0.58±4.35	-3.09±4.61	***0.046****

[1] Hyponatremia at admission n=16, 48hrs post admission n=3.
[2] Normonatremia at admission n=97, 48hrs post admission n=29
[3] Hypernatremia at admission n=11, 48hrs post admission n=56

Table 7: Correlation between serum sodium and acid-base parameters

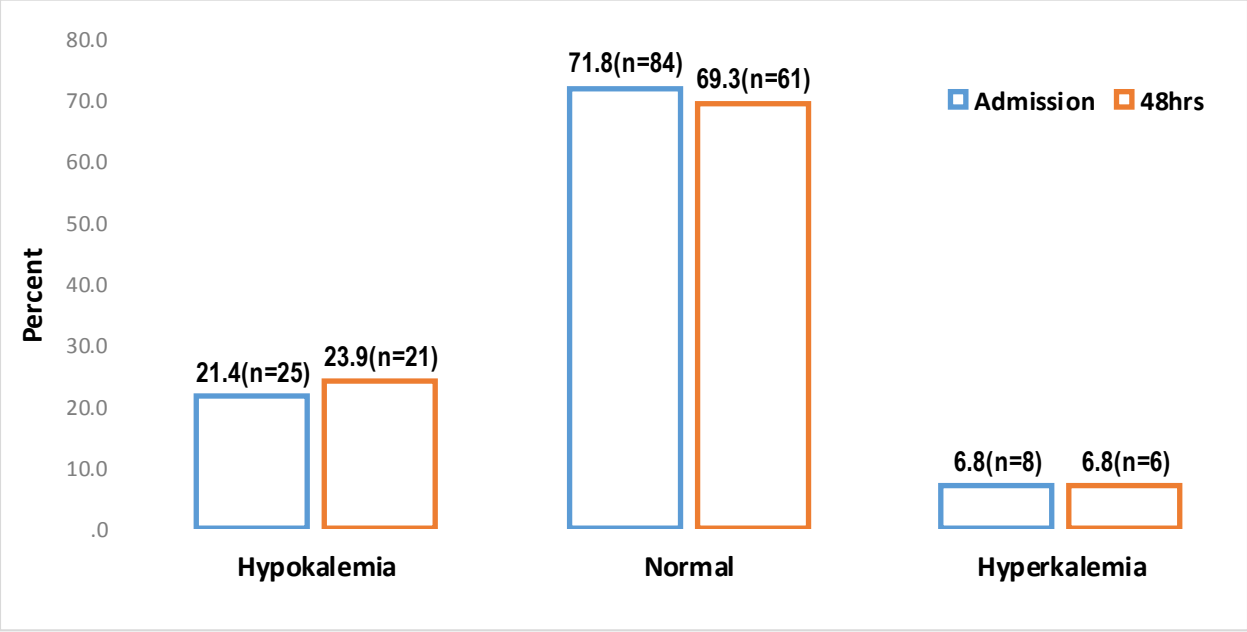
	Admission (n=117)		48hrs after admission (n=88)	
	Correlation coefficient	*P value*	*Correlation coefficient*	*P value*
pH	0.059	0.555	-0.092	0.402
pCO_2	-0.050	620	-0.306	***0.004*****
HCO_3	0.069	0.496	-0.374	***0.000*****
Base deficit	0.026	0.799	-0.367	***0.001*****

4.3 SERUM POTASSIUM ION ABNORMALITIES

4.3.1 PREVALENCE OF POTASSIUM ION ABNORMALITIES

At admission, the mean serum potassium ion level was 3,936±0,63mmol/l (n=117) and 3,99±0,81mmol/l (n=88) 48hrs after admission. No statistically significant differences between the potassium levels at admission and those at 48hrs after admission (p=0.461) were observed in the Paired T-test. The prevalent abnormality was hypokalemia observed in 25(21.4 percent) and 21(23.9 percent) of admission cases and 48hrs post-admission assays (Figure 8) respectively. Hyperkalemia was found at admission in 8(6.8 percent) cases and 48hrs post-admission in 6(6.8 percent) patients. Hypokalemia was also subclassified as mild (3-3.5 mmol / l), moderate (2.5-3 mmol / l) and extreme (< 2.5 mmol / l). Most patients had mild hypokalemia (81.3% admission, 87.5% post-admission), followed by severe hypokalemia (15.6% admission, 12.5% post-admission).

Figure 8: Serum potassium levels at admission and 48hrs later



4.3.2. ASSOCIATION BETWEEN SERUM POTASSIUM & CLINICAL PARAMETERS

The heart rate (Table 8 and Table 9) was the only parameter that showed a statistically significant difference between the three groups, as well as substantial association with serum potassium admission levels. Hypokalemia was associated with substantially increased mortality risk OR 4.12(95 percent CI: 1.14-14.83, p=0.031) and OR 5.12 (95 percent CI: 1.08-24.25, p=0.039) respectively at admission and 48 hours post admission. Although hyperkalemia was also associated with increased mortality risk, the risks at admission were not statistically significant OR 0.34(95 percent CI: 0.06-1.50, p=0.154) and OR 2.20 (95 percent CI: 0.41-11.64, p=0.36) and 48hrs post admission respectively.

Table 8: Association between serum potassium and clinical parameters

Variable		Hypokalemia[1]	Normal[2]	Hyperkalemia[3]	P value
Age	*Admission*	37.5±10.2	31.0±15.4	31.3±15.7	0.168
	48hrs post admission	35.0±16.4	33.9±13.5	24.8±14.7	0.353
Time from injury to presentation (hrs)	*Admission*	18.1±41.1	23.9±46.6	34.1±34.8	0.664
	48hrs post admission	31.2±47.1	23.4±38.3	9.3±7.1	0.469
Pre-hospital use of IV fluids	*Admission*	42.3%	60.0%	25.0%	0.066
	48hrs post admission	61.9%	57.4%	66.7%	0.871
Pre-hospital use of Mannitol	*Admission*	7.7%	15.6%		0.305
	48hrs post admission	19.0%	13.1%		0.485
Systolic BP (mmHg)	*Admission*	131.4±27.2	126.3±25.5	126.8±13.1	0.657
	48hrs post admission	135.5±26.8	129.2±22.7	116.3±7.3	0.194
Diastolic BP (mmHg)	*Admission*	78.3±19.1	75.5±18.0	72.4±14.2	0.662
	48hrs post admission	76.3±14.3	76.4±17.2	66.0±11.1	0.323
Heart rate (/min)	*Admission*	80.8±19.9	98.4±25.4	100.1±30.1	***0.007****
	48hrs post admission	91.9±30.5	93.4±24.0	83.2±23.6	0.644
Respiratory rate (/min)	*Admission*	19.5±3.9	21.3±4.9	20.5±3.7	0.257
	48hrs post admission	19.5±2.6	20.4±4.1	21.5±4.0	0.513
Saturation O2	*Admission*	92.3±7.8	90.6±10.3	93.0±6.1	0.698
	48hrs post admission	90.7±8.8	92.8±7.1	93.3±6.5	0.577
Total GCS Score	*Admission*	6.0±1.7	6.4±1.7	7.3±1.0	0.197
	48hrs post admission	5.9±1.8	6.6±1.5	6.7±2.0	0.180
ISS Score	*Admission*	21.4±7.9	21.2±7.9	18.1±5.5	0.540
	48hrs post admission	23.2±9.2	20.0±7.1	21.5±8.1	0.248

[1] Hypokalemia: admission n=25; 48hrs post admission n=21. [2] Normokalemia: admission n=84; 48hrs post admission n=61.
[3] Hyperkalemia: admission n=8; 48hrs post admission n=6.

Table 9: Correlations between serum potassium and clinical parameters

		K^+ levels at admission (n=117)	K^+ levels 48hrs post admission (n=88)
Age	Pearson Correlation	-0.144	-0.097
	Sig. (2-tailed)	0.134	0.393
Time from injury to presentation (hrs)	Pearson Correlation	0.107	-0.088
	Sig. (2-tailed)	0.243	0.420
Pre-hospital use of IV fluids	Pearson Correlation	0.024	-0.007
	Sig. (2-tailed)	0.792	0.950
Pre-hospital use of Mannitol	Pearson Correlation	-0.005	0.156
	Sig. (2-tailed)	0.960	0.147
Mechanism of injury	Pearson Correlation	0.059	-0.128
	Sig. (2-tailed)	0.516	0.234
Systolic BP	Pearson Correlation	-0.140	-0.185
	Sig. (2-tailed)	0.121	0.085
Diastolic BP	Pearson Correlation	-0.106	-0.023
	Sig. (2-tailed)	0.240	0.831
Heart rate	Pearson Correlation	***0.327****	-0.058
	Sig. (2-tailed)	***<0.001***	0.601
Respiratory rate	Pearson Correlation	0.105	0.096
	Sig. (2-tailed)	0.288	0.409
Temperature	Pearson Correlation	0.006	-0.076
	Sig. (2-tailed)	0.956	0.521
Mannitol use	Pearson Correlation	0.164	-0.025
	Sig. (2-tailed)	0.070	0.817
Pupil examination	Pearson Correlation	-0.078	-0.049
	Sig. (2-tailed)	0.388	0.648
Total GCS Score	Pearson Correlation	0.068	0.155
	Sig. (2-tailed)	0.453	0.149
Injury Severity Score [head]	Pearson Correlation	-0.078	-0.141
	Sig. (2-tailed)	0.386	0.190
ISS Score	Pearson Correlation	-0.101	-0.045
	Sig. (2-tailed)	0.264	0.678

4.3.3. ASSOCIATION BETWEEN SERUM POTASSIUM & RADIOLOGIC PARAMETERS

At admission, epidural hematoma was mainly associated with hypokalemia (p=0.005), while severe SAH was found primarily in patients with hyperkalemia (p=0.045) 48hrs after admission (Table 10). These variable showed statistically significant associations with the potassium levels 48hr post-admission (Table 11). Other radiological parameters showed no significant associations with the potassium ion levels in the serum.

Table 10: Association between serum potassium and radiologic parameters

		Hypokalemia[1]	Normal[2]	Hyperkalemia[3]	P value
Midline shift (mm)	Admission	11.4±5.7	8.3±6.2	7.5±7.6	0.223
	48hrs post admission	12.5±6.3	9.5±5.8	5.0±5.0	0.126
Compressed/absent basal cisterns	Admission	92%	71%	77.5%	0.552
	48hrs post admission	90.5%	91.8%	66.6%	0.149
Presence of epidural hematoma	Admission	44%	14.3%	12.5%	***0.005****
	48hrs post admission	23.8%	23.0%		0.411
Presence of subdural hematoma	Admission	40%	34.5%	37.5%	0.878
	48hrs post admission	38.1%	41.0%	33.3%	0.920
Presence of traumatic SAH	Admission	40%	38.1%	12.5%	0.332
	48hrs post admission	19.0%	37.5%	50.0%	***0.045****
Presence of contusion hemorrhages	Admission	56%	39.3%	50%	0.312
	48hrs post admission	38.1%	42.6%	50%	0.861
SDH Thickness (mm)	Admission	9.4±4.2	12.2±4.4	6.7±2.9	0.059
	48hrs post admission	11.1±3.5	11.7±5.1	7.5±3.5	0.500
Rotterdam CT Score	Admission	3.9±1.3	3.8±1.1	3.5±1.2	0.726
	48hrs post admission	3.9±1.0	3.9±1.1	3.7±1.4	0.842

1. Hypokalemia: admission n=25; 48hrs post admission n=21. 2. Normokalemia: admission n=84; 48hrs post admission n=61.
3. Hyperkalemia: admission n=8; 48hrs post admission n=6

Table 11: Correlations between serum potassium and radiologic parameters

		K^+ levels at admission (n=117)	K^+ levels 48hrs post admission (n=88)
Rotterdam CT head Score	Pearson Correlation	-0.024	-0.005
	Sig. (2-tailed)	0.797	0.967
Midline shift (mm)	Pearson Correlation	-0.009	-0.093
	Sig. (2-tailed)	0.922	0.389
Basal cisterns	Pearson Correlation	-0.065	-0.115
	Sig. (2-tailed)	0.486	0.284
Presence of Epidural Hematoma	Pearson Correlation	***0.270***	0.024
	Sig. (2-tailed)	***0.003****	0.826
Presence of Subdural hematoma	Pearson Correlation	0.005	0.002
	Sig. (2-tailed)	0.956	0.989
Presence of Intracerebral hematoma	Pearson Correlation	-0.020	-0.054
	Sig. (2-tailed)	0.831	0.614
Presence of Traumatic Subarachnoid hemorrhage	Pearson Correlation	-0.117	***0.213****
	Sig. (2-tailed)	0.208	***0.047***
Presence of Contusion hemorrhages	Pearson Correlation	0.081	-0.103
	Sig. (2-tailed)	0.387	0.338
Epidural Hematoma volume (ml)	Pearson Correlation	0.104	-0.265
	Sig. (2-tailed)	0.723	0.431
Subdural hematoma Thickness (mm)	Pearson Correlation	-0.036	-0.213
	Sig. (2-tailed)	0.835	0.258
Intracerebral hematoma Volume (ml)	Pearson Correlation	0.225	-0.393
	Sig. (2-tailed)	0.593	0.383

6.3.4. ASSOCIATION BETWEEN SERUM POTASSIUM & ACID-BASE PARAMETERS

Post-admission hyperkalemia was associated with lower levels of bicarbonate (p=0.026) and base deficit (p=0.024). The other parameters did not show any statistically significant differences (Table 12). None of the variables demonstrated statistically meaningful correlations to the serum potassium ion levels (Table 13).

Table 12: Association between serum potassium and acid-base parameters

		Hypokalemia[1]	Normal[2]	Hyperkalemia[3]	P value
pH	Admission	7.36±0.14	7.37±0.11	7.39±0.07	0.856
	48hrs post admission	7.41±0.09	7.43±0.07	7.38±0.09	0.188
pCO2	Admission	4.9±1.8	4.6±1.4	4.4±0.4	0.660
	48hrs post admission	4.3±1.2	4.7±0.9	4.4±1.3	0.247
HCO3	Admission	19.6±4.7	19.0±3.5	19.5±2.6	0.804
	48hrs post admission	20.0±5.8	22.7±3.8	19.4±4.6	***0.026****
Base deficit	Admission	-5.3±5.9	-5.4±4.2	-0.8±10.5	0.109
	48hrs post admission	-4.0±6.3	-1.3±3.8	-4.9±4.3	***0.024****

[1] Hypokalemia: admission n=25; 48hrs post admission n=21. [2] Normokalemia: admission n=84; 48hrs post admission n=61.
[3] Hyperkalemia: admission n=8; 48hrs post admission n=6.

Table 13: Correlation between serum potassium and acid-base parameters

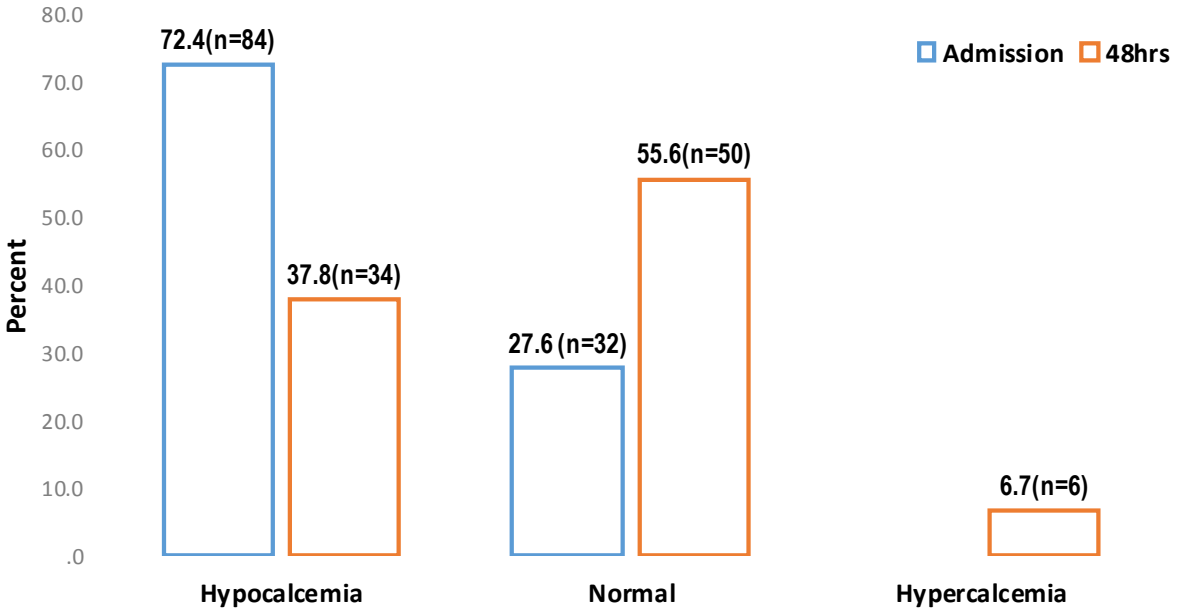
		K^+ levels at admission (n=117)	K^+ levels 48hrs post admission (n=88)
pH	*Correlation Coefficient*	0.039	0.013
	Sig. (2-tailed)	0.699	0.904
pCO2	*Correlation Coefficient*	-0.009	0.179
	Sig. (2-tailed)	0.930	0.099
HCO3	*Correlation Coefficient*	-0.046	0.074
	Sig. (2-tailed)	0.651	0.499
Base deficit	*Correlation Coefficient*	0.025	0.059
	Sig. (2-tailed)	0.803	0.590

4.4 SERUM CALCIUM ION ABNORMALITIES

4.4.1 PREVALENCE OF CALCIUM ION ABNORMALITIES

The mean corrected serum calcium levels were 2.08±0.25mmol / l (n=116) and 2.32±0.25mmol / l (n=90) at admission and 48hrs after admission respectively. Hypocalcemia was the most common calcium ion abnormality reported in 84 (72.4 per cent) patients on admission and in 34 (37.8 per cent) patients 48 hours after admission (Figure 9). Hypercalcemia was reported only in 6 (6.7%) patients 48 hours after admission. The differences were statistically significant (p=0.016).

Figure 9: Serum calcium levels at admission and 48hrs later



4.4.2 ASSOCIATION BETWEEN SERUM CALCIUM AND CLINICAL PARAMETERS

Hypocalcemia observed 48hrs after admission was associated with a high risk of death (odds ratio 5.70, 95 % CI 1.15-28.33, p=0.033) compared to admission (OR 3.2, 95 % CI: 0.52-19.84, p=0.212). Patients with hypocalcemia at admission were significantly older (p=0.044) than

patients with normocalcemia (Table 14). Statistically significant lower heart rate was observed in patients with hypercalcemia 48hrs post-admission (p=0.034). Patient age, injury severity score and systolic blood pressure showed statistically significant negative correlations with calcium ion levels at admission, while the heart rate was the only significant variable associated with the calcium ion levels 48 hours after admission (Table 15).

Table 14: Association between serum calcium and clinical parameters

		Hypocalcemia[1]	Normal[2]	Hypercalcemia[3]	p value
Age (yrs)	*Admission*	34.7±6.6	19.4±8.5	-	***0.044****
	48hrs post admission	32.9±9.6	33.6±13.6	24.5±3.5	0.592
Time from injury to presentation (hrs)	*Admission*	30.0±12.2	34.1±15.5	-	0.067
	48hrs post admission	13.7±16.0	28.2±54.1	35.5±28.9	0.490
Systolic BP (mmHg)	*Admission*	143.1±20.8	113.4±27.7	-	0.292
	48hrs post admission	131.4±16.2	126.6±23.7	146.3±29.0	0.306
Diastolic BP (mmHg)	*Admission*	76.4±17.2	68.6±19.2	-	0.894
	48hrs post admission	74.9±12.7	76.8±19.0	93.3±20.1	0.232
Heart rate (/min)	*Admission*	81.1±19.1	91.8±15.4	-	0.330
	48hrs post admission	96.4±9.7	84.5±7.9	69.7±5.5	***0.034****
Respiratory rate (/min)	*Admission*	20.4±3.1	22.6±4.3	-	0.279
	48hrs post admission	20.6±3.5	21.0±4.3	20.0±2.8	0.907
Saturation O2 (%)	*Admission*	91.4±8.1	92.6±5.0	-	0.264
	48hrs post admission	94.1±5.4	92.6±7.0	94.3±4.2	0.752
Total GCS Score	*Admission*	7.0±1.0	6.5±1.4	-	0.251
	48hrs post admission	6.3±1.7	6.8±1.6	6.3±1.5	0.643
Injury Severity Score	*Admission*	20.5±6.4	19.0±3.7	-	0.151
	48hrs post admission	20.8±10.4	19.7±4.9	24.7±9.1	0.555
Pre-hospital use of IV fluids	*Admission*	52.4%	25.0%	-	0.238
	48hrs post admission	64.7%	44.0%	66.7%	0.373
Pre-hospital use of Mannitol	*Admission*	19.0%	25.0%	-	0.724
	48hrs post admission	17.6%	16.0%	-	0.736

1. Hypocalcemia: admission n=84; 48hrs post admission n=34. 2. Normocalcemia: admission n=32; 48hrs post admission n=50.
3. Hypercalcemia: admission n=0; 48hrs post admission n=6.

Table 15: Correlations between serum calcium and specific clinical parameters

	Corrected Ca^{2+} at Admission (n=116)		Corrected Ca^{2+} 48hrs post admission (n=90)	
	Pearson Correlation	P value	Pearson Correlation	P value
Age	***-0.477****	***0.012***	-0.045	0.779
Time from injury to presentation (hrs)	0.039	0.840	0.152	0.319
Pre-hospital use of IV fluids	0.217	0.259	-0.003	0.986
Pre-hospital use of Mannitol	-0.010	0.960	-0.010	0.947
Mechanism of injury	-0.066	0.733	0.145	0.343
Systolic BP	***-0.394****	***0.034***	0.006	0.969
Diastolic BP	-0.306	0.107	0.144	0.346
Heart rate	-0.023	0.908	***-0.368****	***0.014***
Respiratory rate	0.111	0.588	-0.024	0.879
Temperature	0.245	0.219	-0.021	0.901
Saturation O2	0.143	0.485	0.022	0.900
Pupil examination	-0.230	0.229	***0.354****	***0.017***
Total GCS Score	-0.047	0.808	0.055	0.720
Injury Severity Score	***-0.406****	***0.029***	0.037	0.811

4.4.3 ASSOCIATION BETWEEN SERUM CALCIUM & RADIOLOGIC PARAMETERS

Radiological parameters did not show any statistically significant association with serum calcium values (Table 16). There were also no significant correlations identified (Table 17).

Table 16: Association between serum calcium and radiologic parameters

		Hypocalcemia[1]	Normal[2]	Hypercalcemia[3]	p value
Subdural hematoma Thickness (mm)	*Admission*	8.3±4.1	12.5±8.7	-	*0.204*
	48hrs post admission	13.0±6.7	9.0±3.2	-	*0.133*
Midline shift (MLS) >5mm	*Admission*	42.9%	50.0%	-	*0.730*
	48hrs post admission	64.7%	36.0%	-	*0.051*
Presence of Epidural hematoma	*Admission*	33.3%	12.50%	-	*0.262*
	48hrs post admission	41.2%	16.0%	-	*0.105*
Presence of Subdural hematoma (SDH)	*Admission*	38.10%	50%	-	*0.561*
	48hrs post admission	29.4%	48.0%	-	*0.179*
Presence of Traumatic Subarachnoid haemorrhage	*Admission*	28.6%	50%	-	*0.278*
	48hrs post admission	23.5%	60.0%	33.3%	*0.060*
Rotterdam CT Score	*Admission*	3.5±1.2	4.1±1.4	-	*0.830*
	48hrs post admission	3.6±1.3	4.0±1.1	3.3±1.5	*0.489*

1. Hypocalcemia: admission n=84; 48hrs post admission n=34.
2. Normocalcemia: admission n=32; 48hrs post admission n=50.
3. Hypercalcemia: admission n=0; 48hrs post admission n=6.

Table 17: Correlations between serum calcium and specific radiologic parameters

	Corrected Ca^{2+} at Admission (n=116)		Corrected Ca^{2+} 48hrs post admission (n=90)	
	Pearson Correlation	*P - value*	*Pearson Correlation*	*P – value*
Midline shift (mm)	0.084	0.739	-0.315	0.103
Epidural Hematoma	0.311	0.101	0.321	0.132
Subdural hematoma	0.250	0.191	0.009	0.955
Traumatic SAH	-0.057	0.769	0.122	0.423
Contusion hemorrhages	0.191	0.321	0.019	0.900
SDH Thickness (mm)	0.234	0.514	-0.093	0.743
Rotterdam CT Score	0.017	0.931	-0.011	0.942

4.4.4 ASSOCIATION BETWEEN SERUM CALCIUM & ACID-BASE PARAMETERS

Up to 59 (70.2 per cent) of patients with hypocalcemia at admission had either compensated respiratory alkalosis or respiratory alkalosis. Patients who had hypocalcemia at admission had significantly lower bicarbonate ions (Table 18). Significant statistical correlations were observed between pCO2 and corrected Ca2 + levels at admission (Table 19). The other parameters did not show any significant differences between the three groups nor did they show any significant correlations.

Table 18: Comparison between serum calcium ion levels and acid-base parameters

		Hypocalcemia[1]	Normal[2]	Hypercalcemia[3]	p value
pH	Admission	7.39±0.10	7.36±0.15		0.289
	48hrs post admission	7.45±0.05	7.42±0.07	7.37±0.09	0.117
pCO_2	Admission	4.67±1.16	4.13±0.63		0.203
	48hrs post admission	4.68±0.79	4.73±0.99	5.74±0.94	0.185
HCO_3	Admission	17.35±3.91	20.11±2.31		***0.039****
	48hrs post admission	23.86±2.78	22.58±4.35	24.13±2.28	0.512
Base deficit	Admission	-4.21±3.37	-3.05±4.41		0.158
	48hrs post admission	0.18±2.60	-1.40±4.30	-1.23±3.67	0.420

[1.] Hypocalcemia: admission n=84; 48hrs post admission n=34.
[2.] Normocalcemia: admission n=32; 48hrs post admission n=50.
[3.] Hypercalcemia: admission n=0; 48hrs post admission n=6.

Table 19: Correlation between serum calcium ion levels and acid-base parameters

	Corrected Ca^{2+} at Admission (n=116)		Corrected Ca^{2+} 48hrs post admission (n=90)	
	Correlation coefficient	*p-value*	*Correlation coefficient*	*p-value*
pH	0.189	0.326	-0.057	0.714
pCO_2	***-0.371****	***0.048***	0.131	0.396
HCO_3	-0.113	0.560	0.080	0.606

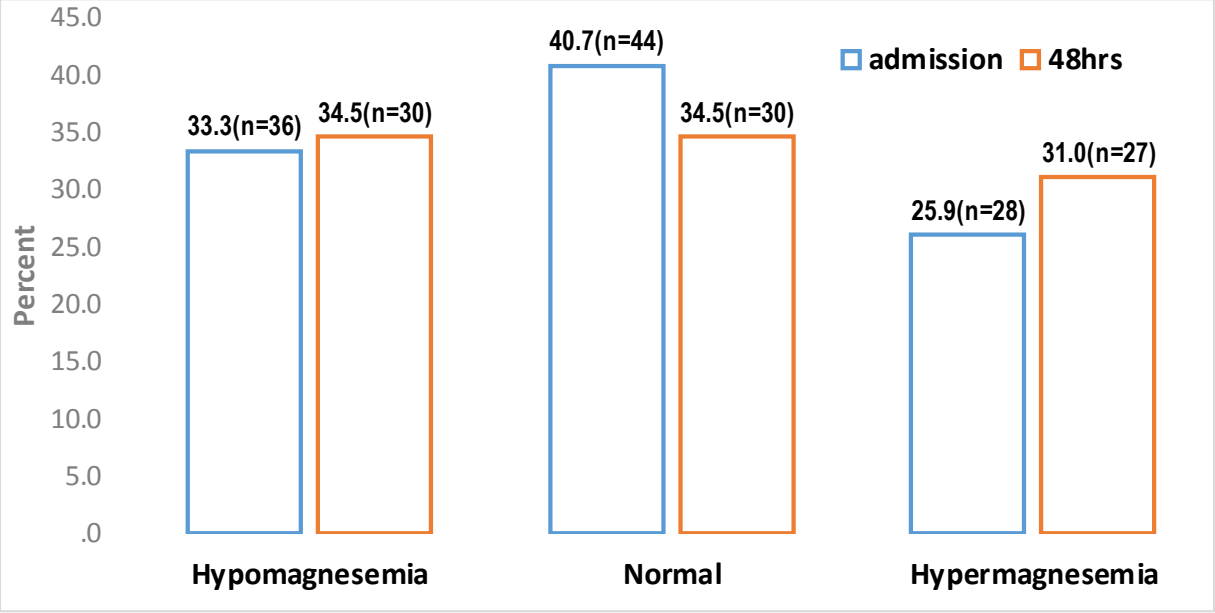
Base deficit	0.034	0.861	0.047	0.761

4.5 SERUM MAGNESIUM ION ABNORMALITIES

4.5.1 PREVALENCE OF MAGNESIUM ION ABNORMALITIES

The mean serum corrected magnesium levels were 0.92±0.44mmol/l and 1.08±0.42mmol/l at admission (n=108) and 48hrs after admission (n=87) respectively (p=0.152). Hypomagnesemia was the most common abnormality, reported in 36(33.3%) and 30(34.5%) of the cases at admission and 48hrs post admission respectively (Figure 10). Hypermagnesemia was reported in 28(25.9%) and 27(31.0%) of the cases at admission and 48hrs post admission respectively. Paired T-test did not reveal any statistically significant differences between the admission and 48hr post admission values (p=0.356).

Figure 10: Serum magnesium levels at admission and 48hrs later



4.5.2 ASSOCIATION BETWEEN SERUM MAGNESIUM & CLINICAL PARAMETERS

Patients with hypermagnesemia had statistically significant lower systolic blood pressure compared to those with hypomagnesemia both at admission and 48 hours after admission (Table

20). At admission, the only statistically significant correlations were the age of the patient and systolic BP (Table 21). Mortality risk associated with hypomagnesemia at admission and 48hrs post-admission was OR 2.4 (95 percent CI: 0.39-14.88, p=0.35) and OR 0.3 (95 percent CI: 0.03 to 2.69, p=0.27) respectively. Hypermagnesemia was associated with a lower mortality risk OR 0.9 (95 percent CI: 0.13 to 6.08, p=0.91) and OR 0.5 (95 percent CI: 0.09 to 2.84, p=0.43) at admission and 48 hours post-admission, respectively.

Table 20: Comparison between serum magnesium levels and clinical parameters

		Hypomagnesemia[1]	Normal[2]	Hypermagnesemia[3]	p-value
Age	Admission	38.9±11.1	28.1±16.9	24.3±11.6	0.117
	48hrs post admission	25.2±13.8	34.6±11.6	32.1±13.4	0.444
Time injury to presentation (hrs)	Admission	32.1±33.5	16.6±21.8	35.1±41.3	0.405
	48hrs post admission	32.1±49.1	6.0±4.7	26.4±33.3	0.195
Pre-hospital use of IV fluids	Admission	55.6%	45.5%	28.6%	0.557
	48hrs post admission	40%	70%	46.2%	0.418
Pre-hospital use of Mannitol	Admission	44.4%	0%	34.3%	0.137
	48hrs post admission	20%	40%	7.7%	0.173
Systolic BP	Admission	142.8±18.3	145.2±22.7	115.3±23.4	***0.019****
	48hrs post admission	137.2±18.9	141.1±15.7	120.6±25.4	***0.045****
Diastolic BP	Admission	75.6±16.9	82.6±18.3	64.3±9.7	0.083
	48hrs post admission	78.2±13.1	82.8±15.2	71.5±19.9	0.314
Heart rate	Admission	84.8±23.5	81.9±17.9	83.7±16.6	0.947
	48hrs post admission	76.0±11.9	92.8±24.1	86.9±15.4	0.276
Respiratory rate	Admission	20.8±3.3	21.5±3.8	21.2±4.02	0.915
	48hrs post admission	22.8±4.9	20.9±3.5	21.8±3.5	0.713
Total GCS Score	Admission	7.2±0.7	6.8±1.3	6.4±1.5	0.415
	48hrs post admission	7.7±0.1	6.0±1.8	6.6±1.4	0.061
ISS Score	Admission	18.6±4.1	21.7±8.2	19.6±3.4	0.499
	48hrs post admission	15.8±3.2	21.7±5.4	23.9±9.9	0.155

[1.] Hypomagnesemia: admission n=36; 48hrs post admission n=30. [2.] Normomagnesemia: admission n=44; 48hrs post admission n=30. [3.] Hypermagnesemia: admission n=28; 48hrs post admission n=27.

Table 21: Correlations between serum magnesium and clinical parameters

		Corrected Mg^{2+} at Admission (n=108)	Corrected Mg^{2+} 48hrs post admission(n=87)
Age	Pearson Correlation	***-0.404****	0.155
	Sig. (2-tailed)	***0.045***	0.448
Time from injury to presentation (hrs)	Pearson Correlation	0.015	0.034
	Sig. (2-tailed)	0.942	0.862
Pre-hospital use of IV fluids	Pearson Correlation	0.205	0.027
	Sig. (2-tailed)	0.304	0.890
Pre-hospital use of Mannitol	Pearson Correlation	0.327	0.199
	Sig. (2-tailed)	0.096	0.310
Mechanism of injury	Pearson Correlation	-0.281	0.155
	Sig. (2-tailed)	0.155	0.430
Systolic BP	Pearson Correlation	***-0.413****	-0.352
	Sig. (2-tailed)	***0.032***	0.066
Diastolic BP	Pearson Correlation	-0.227	-0.208
	Sig. (2-tailed)	0.254	0.287
Heart rate	Pearson Correlation	-0.027	0.148
	Sig. (2-tailed)	0.894	0.462
Respiratory rate	Pearson Correlation	0.052	-0.047
	Sig. (2-tailed)	0.809	0.828
Temperature	Pearson Correlation	0.337	0.106
	Sig. (2-tailed)	0.093	0.606
Saturation O_2	Pearson Correlation	0.277	-0.207
	Sig. (2-tailed)	0.180	0.355
Pupil examination	Pearson Correlation	-0.018	-0.016
	Sig. (2-tailed)	0.927	0.937
Total GCS Score	Pearson Correlation	-0.266	-0.221
	Sig. (2-tailed)	0.180	0.258
ISS Score	Pearson Correlation	0.084	0.356
	Sig. (2-tailed)	0.677	0.063

4.5.3. ASSOCIATION BETWEEN SERUM MAGNESIUM & RADIOLOGIC PARAMETERS

None of the radiological parameters showed statistically significant differences among the three groups (Table 22). Similarly, no statistically significant correlations were observed between the radiological parameters and the magnesium level at admission and 48 hours later (Table 23).

Table 22: Comparisons between serum magnesium levels and radiologic parameters

		Hypomagnesemia[1]	Normal[2]	Hypermagnesemia[3]	p-value
Compressed/absent Basal cisterns	Admission	88.9%	63.7%	74%	0.680
	48hrs post admission	80%	98%	69.3%	0.208
Midline shift (mm)	Admission	12.50±4.18	9.40±7.20	7.50±7.58	0.422
	48hrs post admission	12.50±3.54	10.29±6.87	9.38±9.43	0.886
Presence of epidural Hematoma	Admission	33.3%	36.4%	0%	0.189
	48hrs post admission	20%	20%	30.8%	0.824
Presence of subdural hematoma	Admission	44.4%	36.4%	57.1%	0.688
	48hrs post admission	20%	60%	30.8%	0.246
Presence of Traumatic SAH	Admission	33.3%	27.3%	42.9%	0.792
	48hrs post admission	20%	50%	61.5%	0.288
Presence of contusion hemorrhage	Admission	33.3%	45.5%	42.9%	0.853
	48hrs post admission	20%	60%	69.2%	0.163
SDH Thickness (mm)	Admission	10.00±5.00	6.67±2.89	12.50±8.66	0.528
	48hrs post admission	10.00±0.001	11.00±8.22	10.00±0.01	0.976
Rotterdam CT Score	Admission	4.00±1.32	3.18±1.08	4.00±1.63	0.302
	48hrs post admission	3.40±1.14	4.40±0.97	3.62±1.39	0.218

[1.] Hypomagnesemia: admission n=36; 48hrs post admission n=30. [2.] Normomagnesemia: admission n=44; 48hrs post admission n=30. [3.] Hypermagnesemia: admission n=28; 48hrs post admission n=27.

Table 23: Correlations between serum magnesium and radiologic parameters

	Corrected Mg^{2+} at Admission (n=108)		Corrected Mg^{2+} at 48hrs (n=87)	
	Correlation coefficient	p-value	Correlation coefficient	p-value
Basal cisterns	-0.163	0.417	-0.163	0.407
Midline shift (mm)	-0.337	0.185	-0.125	0.633
EDH volume (ml)	0.063	0.919	0.675	0.528
SDH Thickness (mm)	0.203	0.573	-0.036	0.927
Rotterdam CT Score	-0.025	0.903	-0.034	0.865

4.5.3. ASSOCIATION BETWEEN SERUM MAGNESIUM & ACID-BASE PARAMETERS

None of the acid base parameters showed statistically significant differences between the three groups (Table 24). Similarly, there were no statistically significant correlations between acid-base parameters and magnesium levels (Table 25).

Table 24: Comparison between serum magnesium ion levels and acid-base parameters

		Hypomagnesemia[1]	Normal[2]	Hypermagnesemia[3]	p-value
pH	Admission	7.40±0.10	7.35±0.10	7.42±0.15	0.459
	48hrs post admission	7.41±0.06	7.45±0.07	7.41±0.10	0.612
pCO2	Admission	4.55±1.26	4.78±1.20	4.05±0.53	0.400
	48hrs post admission	5.08±1.37	4.36±0.73	5.04±1.00	0.261
HCO3	Admission	20.26±3.04	18.95±1.60	19.39±4.27	0.616
	48hrs post admission	24.26±7.97	21.98±2.52	23.56±3.46	0.582
Base deficit	Admission	-3.70±3.60	-5.91±2.56	-4.37±6.77	0.509
	48hrs post admission	-0.20±7.65	-1.50±2.97	-0.62±4.13	0.857

[1.] Hypomagnesemia: admission n=36; 48hrs post admission n=30. [2.] Normomagnesemia: admission n=44; 48hrs post admission n=30. [3.] Hypermagnesemia: admission n=28; 48hrs post admission n=27.

Table 25: Correlations between serum magnesium ion levels and acid-base parameters

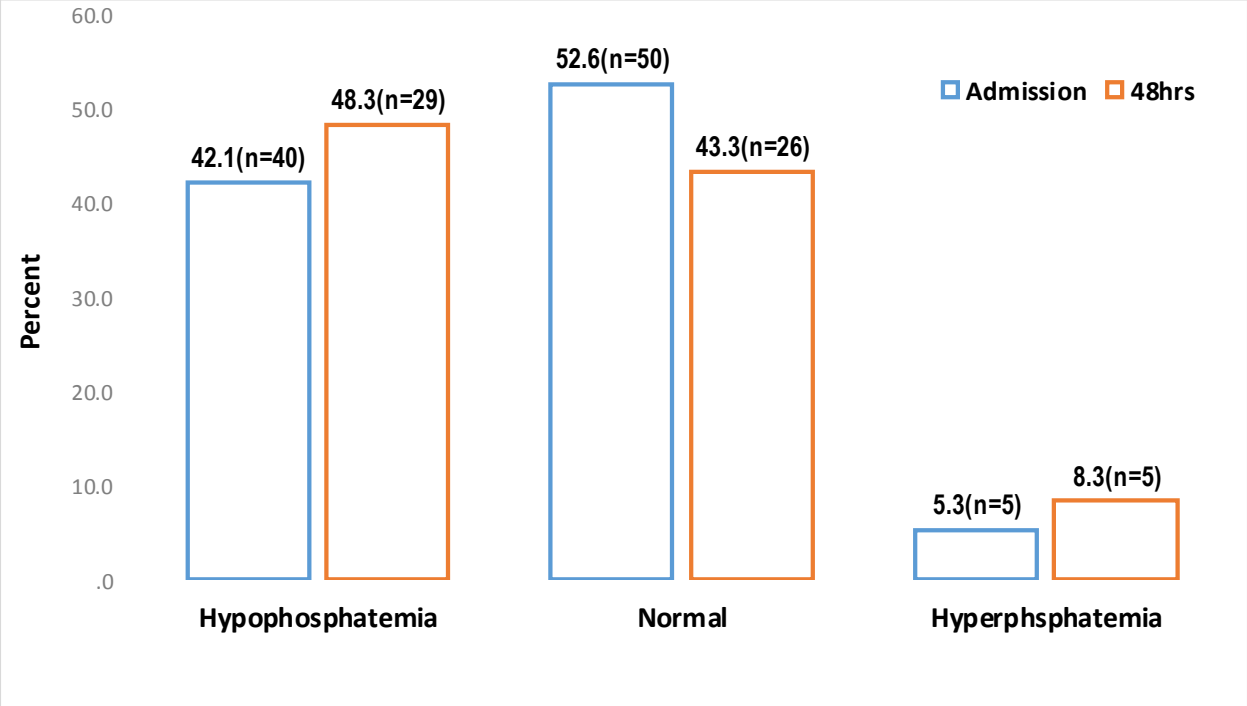
	Corrected Mg^{2+} at Admission (n=108)		Corrected Mg^{2+} 48hrs post admission(n=87)	
	Correlation Coefficient	*p-value*	*Correlation Coefficient*	*p-value*
pH	0.042	0.835	-0.129	0.523
pCO2	0.011	0.955	0.065	0.746
HCO3	-0.020	0.922	0.028	0.888
Base deficit	0.072	0.720	-0.016	0.937

4.6 SERUM PHOSPHATE ION ABNORMALITIES

4.6.1. PREVALENCE OF PHOSPHATE ION ABNORMALITIES

The mean serum phosphate ion levels were 1.03±0.39 mmol / l (n=95) and 1.17±0.53 mmol / l (n=60) at admission and 48hrs after admission. Hypophosphatemia was the predominant abnormality reported in 40 (42.1%) and 29 (48.3%) of the admission and 48 hours post-admission cases, respectively (Figure 11). Hyperphosphatemia was seen in 5 (5.3 per cent) cases at admission and in 5 (8.3 per cent) cases 48 hours after admission. The paired T test did not show any statistically significant differences between admission and post-admission serum phosphate ion levels (p=0.568).

Figure 11: Serum phosphate ion levels at admission and 48hrs later



4.6.2. ASSOCIATION BETWEEN SERUM PHOSPHATE & CLINICAL PARAMETERS

The use IV fluids and mannitol, diastolic blood pressure, respiratory rate and oxygen saturation were significantly correlated with the admission serum phosphate levels (Table 26). On the other hand, post-admission phosphate ion levels were significantly correlated with the GCS score. No statistically significant differences were observed between the clinical parameters and the three serum phosphate groups (Table 27). Mortality risk was higher in hypophosphatemia occurring 48 hours after admission OR 7.5 (95 percent CI: 1.08-90.24, p=0.098) compared to hypophosphatemia at admission (OR 4.12 (95 percent CI: 1.14-14.83, p=0.031). Mortality rates for those with hyperphosphatemia were OR 3 (95 percent CI 0.09-90.97, p=0.53) and OR 3 (95 percent CI 0.15-59.89, p=0.47) at admission and 48 hours post-admission respectively.

Table 26: Correlations between serum phosphate and specific clinical parameters

	Phosphate Admission (n=95)		**Phosphate after 48hrs (n=60)**	
	Correlation coefficient	P value	Correlation coefficient	P value
Age	-0.208	0.409	0.022	0.938
Time from injury to presentation (hrs)	-0.187	0.442	0.230	0.409
Pre-hospital use of IV fluids	**-0.473***	**0.041**	0.198	0.479
Pre-hospital use of Mannitol	**-0.442**	**0.048**	0.271	0.328
Systolic BP	-0.146	0.552	0.044	0.878
Diastolic BP	**-0.469***	**0.043**	-0.192	0.492
Heart rate	0.273	0.259	0.021	0.940
Respiratory rate	**0.493***	**0.044**	-0.253	0.383
Temperature	0.357	0.175	0.014	0.967
Saturation O2	**-0.615***	**0.011**	0.049	0.885
Pupil examination	-0.342	0.152	-0.177	0.527
Total GCS Score	0.102	0.676	**0.547***	**0.035**
ISS Score	0.006	0.981	0.030	0.916

Table 27: Comparison between serum phosphate ion levels and clinical parameters

		Hypophosphatemia[1]	Normal[2]	Hyperphosphatemia[3]	p-value
Age	Admission	37.5±14.5	29.6±14.7	35.0±0.1	0.543
	48hrs post admission	34.6±14.9	28.3±7.9	35.5±13.5	0.690
Time from injury to presentation (hrs)	Admission	28.4±29.7	19.7±34.6	17.0±0.1	0.838
	48hrs post admission	18.8±15.7	9.5±7.7	47.2±17.7	0.358
Pre-hospital use of IV fluids	Admission	56.5%	30.0%	25%	0.115
	48hrs post admission	42.9%	30%	35%	0.804
Pre-hospital use of Mannitol	Admission	60.5%	50%	12.5%	0.142
	48hrs post admission	28.6%	25.0%	-	0.559
Systolic BP	Admission	116.0±2.1	137.6±19.1	134.8±32.7	0.133
	48hrs post admission	126.0±21.8	134.0±9.6	129.0±20.0	0.802
Diastolic BP	Admission	64.5±18.5	82.4±16.1	89.0±0.1	0.094
	48hrs post admission	76.9±15.2	90.5±9.3	83.5±18.0	0.251
Heart rate	Admission	81.4±20.1	85.8±19.1	101.0±5.3	0.627
	48hrs post admission	81.1±13.4	99.0±29.1	82.0±17.5	0.337
Respiratory rate	Admission	24.0±0.1	20.9±3.8	19.1±2.0	0.096
	48hrs post admission	21.7±2.3	21.0±4.8	20.0±2.3	0.726
Saturation O2	Admission	90.0±0.1	92.9±1.9	96.0±3.6	0.112
	48hrs post admission	92.4±6.9	96.5±2.1	94.5±0.7	0.694
Total GCS Score	Admission	7.1±1.0	6.8±1.4	7.8±0.1	0.617
	48hrs post admission	6.4±1.8	6.8±1.3	7.8±0.1	0.245
ISS Score	Admission	19.5±3.2	22.4±12.1	18.0±0.1	0.769
	48hrs post admission	19.7±3.4	27.8±19.5	22.0±8.4	0.517

1. Hypophosphatemia: admission n=40; 48hrs post admission n=29.
2. Normophosphatemia: admission n=50; 48hrs post admission n=26.
3. Hyperphosphatemia: admission n=5; 48hrs post admission n=5

4.6.3 ASSOCIATION BETWEEN SERUM PHOSPHATE & RADIOLOGIC PARAMETERS

None of the radiological parameters revealed any statistically significant differences between the three groups (Table 28) or showed any significant correlations with serum phosphate ion levels (Table 29).

Table 28: Comparison between serum phosphate and radiologic parameters

		Hypophosphatemia[1]	Normal[2]	Hyperphosphatemia[3]	p-value
Compressed/absent Basal cisterns	*Admission*	85%	70%	92.5%	0.208
	48hrs post admission	87.5%	85%	75%	0.312
Midline shift (mm)	*Admission*	11.0±4.2	10.4±9.1	15.0±0.01	0.842
	48hrs post admission	8.8±6.3	8.8±4.8	5.0±7.1	0.728
Presence of epidural Hematoma	*Admission*	37.5%	30%	50%	0.427
	48hrs post admission	14.3%	5%	5%	0.600
Presence of subdural hematoma	*Admission*	12.5%	40%	60%	0.164
	48hrs post admission	28.6%	50%	50%	0.746
Presence of Traumatic SAH	*Admission*	50%	40%	65%	0.554
	48hrs post admission	65%	25%	50%	0.144
Presence of contusion hemorrhages	*Admission*	37.5%	60%		0.440
	48hrs post admission	57.1%	75%	50%	0.794
SDH Thickness (mm)	*Admission*	5.0±0.01	8.3±2.9	15.0±0.01	0.238
	48hrs post admission	10.0±0.01	10.0±7.1	10.0±0.01	0.998
Rotterdam CT Score	*Admission*	3.9±0.8	3.4±1.2	5.0±0.01	0.297
	48hrs post admission	4.6±1.0	4.0±0.8	3.5±1.3	0.279

1. Hypophosphatemia: admission n=40; 48hrs post admission n=29.
2. Normophosphatemia: admission n=50; 48hrs post admission n=26.
3. Hyperphosphatemia: admission n=5; 48hrs post admission n=5

Table 29: Correlations between serum phosphate and radiologic parameters

		Phosphate at admission (n=95)	Phosphate 48hrs post-admission (n=60)
Midline shift (mm)	*Pearson Correlation*	-0.326	0.117
	Sig. (2-tailed)	0.475	0.783
Epidural Hematoma	*Pearson Correlation*	0.249	-0.006
	Sig. (2-tailed)	0.193	0.970
Subdural hematoma	*Pearson Correlation*	-0.351	-0.179
	Sig. (2-tailed)	0.263	0.579
Traumatic SAH	*Pearson Correlation*	0.173	-0.245
	Sig. (2-tailed)	0.591	0.443
Contusion	*Pearson Correlation*	-0.308	0.149
hemorrhages	*Sig. (2-tailed)*	0.331	0.644
EDH volume (mls)	*Pearson Correlation*	0.249	-0.006
	Sig. (2-tailed)	0.193	0.970
SDH Thickness (mm)	*Pearson Correlation*	0.701	-0.163
	Sig. (2-tailed)	0.506	0.793
Rotterdam CT Score	*Pearson Correlation*	-0.152	-0.415
	Sig. (2-tailed)	0.637	0.180

4.6.4 ASSOCIATION BETWEEN SERUM PHOSPHATE & ACID-BASE PARAMETERS

Thirty out of forty (75 per cent) of patients with hypophosphatemia at admission had either respiratory alkalosis or compensated respiratory alkalosis ($p<0.001$). Hypophosphatemia at admission was associated with statistically significant higher pH and lower pCO2 levels compared to hyperphosphatemia (Table 30). Admission pH and pCO2 showed significant correlations with serum phosphate ion levels (Table 31).

Table 30: Comparison between serum phosphate ion levels and acid-base parameters

		Hypophosphatemia[1]	Normal[2]	Hyperphosphatemia[3]	p-value
pH	Admission	7.46±0.11	7.33±0.13	7.18±0.01	**0.041***
	48hrs post admission	7.43±0.07	7.44±0.07	7.41±0.08	0.784
pCO_2	Admission	4.25±0.53	4.79±0.35	7.34±0.01	**0.046***
	48hrs post admission	4.80±0.93	5.14±0.79	4.92±0.85	0.830
HCO_3	Admission	20.70±3.29	19.22±2.94	20.10±0.02	0.610
	48hrs post admission	23.36±3.07	25.30±1.96	23.30±2.87	0.502
Base deficit	Admission	-3.04±4.91	-5.26±4.53	-8.70±0.01	0.420
	48hrs post admission	-0.49±3.27	1.13±2.43	-0.65±2.19	0.611

1. Hypophosphatemia: admission n=40; 48hrs post admission n=29.
2. Normophosphatemia: admission n=50; 48hrs post admission n=26.
3. Hyperphosphatemia: admission n=5; 48hrs post admission n=5

Table 31: Correlations between serum phosphate ion and acid-base parameters

	Phosphate at admission (n=95)		Phosphate 48hrs post-admission (n=60)	
	Correlation coefficient	p-value	Correlation coefficient	p-value
pH	-0.416	**0.046**	-0.260	0.350
pCO_2	0.447	**0.045**	0.134	0.633
HCO_3	-0.218	0.371	-0.032	0.909
Base deficit	-0.357	0.134	-0.109	0.699

CHAPTER 5: DISCUSSION

5.1 SERUM SODIUM ION ABNORMALITIES

In the current study, most patients (79.5 per cent) had normal serum sodium ion levels at admission. However, after 48hrs of admission, hypernatremia was predominant (63.9%). Paired T-test samples showed statistically significant differences between admission and 48hr post-admission sodium levels ($p<0.001$). Previous studies also reported similar trends in early normonatremia followed by hypernatremia in severe traumatic brain injury (30,66). A retrospective study of 588 severe TBI patients by Vedantam et al. (30) reported a 79.3 per cent incidence of hypernatremia diagnosed within the first week of admission, with the highest incidence reported within 72hrs. Another retrospective study of 130 extreme TBI patients recorded 2.3 percent of admission hypernatremia, but hypernatremia cases increased to 51.5 percent during ICU stay (66). Hypernatremia was also reported by Rafiq et al. in 65.1 per cent of all severe TBI patients (15).

Due to the coexistence of predisposing factors such as weakened sensorium, altered appetite, central diabetes insipidus with polyuria, increased insensitive losses, and the use of hyperosmolar therapies such as mannitol and hypertonic saline (25,26,67), serious traumatic brain injury patients are at high risk of developing hypernatremia throughout their ICU stay. Although these mechanisms may have contributed to the occurrence of the delayed hypernatremia reported in the current study, either in isolation or combination, the sequelae of primary brain injury is more likely to have contributed to this finding. In support of this, GCS admission, Injury Severity Score, Rotterdam CT Head Score, basal cistern compression degree, and subdural hematoma presence were significantly correlated ($p<0.001$) with serum sodium ion levels 48hrs after admission.

The relationship between sodium abnormalities and clinico-radiological parameters has been identified by few studies. Li et al. reported a linkage between GCS admission and hypernatremia severity (68). These authors reported a significantly lower GCS for extreme hypernatremia group 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, GCS score, abbreviated injury score (head), and the amount Injury Severity Score were the clinical parameters that have significant associations with sodium ion levels , particularly 48hr post-admission. A study conducted by Paiva et al. in 2011 found that the presence of subdural and intracerebral hematomas was associated with sodium disorders in severe TBI patients (69). The only mass lesion strongly associated with sodium anomalies in the present study was the presence of a subdural hematoma. Additionally, the Rotterdam CT head score and basal cistern status showed statistically significant positive correlations with the sodium ion levels.

In the current study, a high mortality rate of 73.3 per cent was associated with hypernatremia. Previous studies identified hypernatremia among TBI patients as an independent risk factor for mortality (30,66–68). Hypernatremia in severe TBI patients is associated with a threefold increase in ICU death (66). Li et al. reported mortality rates of 20.6 percent, 42.4 percent, and 86.8 percent respectively for the mild , moderate, and extreme hypernatremia groups, while the normonatremia group reported 2.0 percent (68). Vedantam et al. also reported that hypernatremia was a major mortality indicator in TBI patients and that mortality rates increased with hypernatremia severity (hazard ratios for mild , moderate, and serious hypernatremia were 3.2, 5.1, and 7.9 respectively) (30).

5.2 SERUM POTASSIUM ION ABNORMALITIES

The most common serum potassium abnormality reported in the current study was hypokalemia, seen in 21.4 percent and 23.9 percent of admission and 48 hours post-admission cases, respectively. Earlier studies have also shown that hypokalemia is the most common abnormality of potassium in patients with head injury. The prevalence rate of hypokalemia in TBI is 21.5–68.3 per cent (14–16). The main mechanism of post-traumatic hypokalemia is postulated to be the result of potassium shifts in the intracellular compartment due to epinephrine surge caused by injury (39). Post-traumatic surge in catecholamines leads to stimulation of the β-2-adrenergic receptor and activation of the sodium-potassium pump, resulting in an intracellular K+ shift (70). Studies have also shown that there is an increase in cardiac output, blood pressure, pulse rate and pulmonary shunting, along with decreased or normal systemic and pulmonary vascular resistance, consistent with increased circulating catecholamines (71). This may explain the finding in the current research that there was a statistically significant association between admission heart rate and serum potassium levels.

Although not observed in this study, there was a strong correlation between [K+] and GCS in a previous study (72). In a study of 46 patients, the level of hypokalaemia was found to be proportional to the decrease in GCS (72). The concentration of serum catecholamine is related to ICP in the brain injury setting and the relationship between the two is dynamically dependent on ICP (46). Insulin, known to cause hypokalaemia, is not increased in patients with traumatic brain injury (40). Hypokalemia is associated with life-threatening cardiac arrhythmias and is a major risk of death in patients with TBI (38,39). In the current study, hypokalemia was associated with 4-fold and 5-fold increased risk of death at admission and 48 hours post-admission, respectively.

The present study reported hyperkalemia in 6.8 percent of admission cases and 48hrs post-admission cases. Previous research found a prevalence rate of 0.9-17.7% (14–16). Post-traumatic hyperkalemia is caused by extensive tissue damage and aggressive transfusion (39). Alternatively, potentially, acute hemorrhagic shock leads to hyperkalemia due to changes in the structure of the cell membrane. Mannitol and anaesthetic agents such as succinylcholine and barbiturates are other causes of hyperkalemia in TBI (70,73–76). Although hyperkalemia in TBI is rare, it should be managed timely, as it is also associated with life-threatening cardiac arrhythmias that can lead to death (38,39). In the present study, hyperkalemia was associated with the risk of OR 0.34 and OR 2.20 mortality at admission and 48 hours post-admission respectively.

5.3 SERUM CALCIUM ION ABNORMALITIES

Hypocalcemia was the most common calcium ion abnormality found in the current study, seen in 72.4% and 37.8% of admission patients and 48hrs post-admission respectively. Previous studies also reported hypocalcemia as the most common calcium ion abnormality following head injury (14,16,77). Hypocalcemia is greatest in severe traumatic brain injury, ranging from 62.3%-64% (50,77).

The key pathomechanisms for post-TBI hypocalcemia are the sudden influx of intracellular ionized calcium and chemical ionized calcium binding to proinflammatory proteins / molecules (49). TBI leads to traumatic deformation of the cell membrane leading to rapid intracellular calcium inflow with subsequent release of exciting neurotransmitters such as glutamate (48,78,79). This inhibits mitochondrial enzymatic activities and activates lipases and caspases resulting in apoptotic cell death (48,49,80). Hypocalcemia can also result from calcium depletion due to increased chelation to pro-inflammatory molecules / proteins released into the extracellular space following direct trauma (49,50,81). This leads to a decrease in intracellular calcium levels with the consequent release of Ca2+ from the sarcoplasmic reticulum, thus activating caspases and resulting in cell death (82). Increased intracranial pressure as a result of cerebral oedema and loss of cerebrovascular self-regulation as a result of neuroinflammation may lead to under-perfusion of neuronal tissue resulting in lactate accumulation (50,78,83). Lactate increases calcium chelation with additional hypocalcemia (49,50,81,84)

Hypocalcemia is an independent prognostic factor for mortality and morbidity in traumatic brain injury (14,49,50,84). In the present study, hypocalcemia was associated with a high risk of mortality (odds ratio 5.70, p= 0.033). Pin-on et al. reported hypocalcemia associated with 3.52 mortality risk within 24hrs of TBI (14). An ambispective study of 122 Mexican patients with

moderate/severe TBI, showed significantly lower serum calcium levels on the third day of admission between the survivors and non-survivors with an OR of 5.2 (95% CI 4.48- 6.032, p 0.026) (50). In addition, hypocalcemia is associated with poor GOS in patients who survive. Kuhna et al. reported that 60.8 percent ($p<0.001$) of all patients who had GOS ≤ 3 had hypocalcemia (84). Manuel et al. also reported hypocalcemia being significantly associated with weak GOS on day 3 following TBI (odds ratio 6.6, $p<0.009$) (49).

Neurodegenerative processes mentioned above are likely to cause poor outcomes in hypocalcemia. Calcium is required for normal cell function, neural transmission, membrane stability, bone structure, blood clotting, and intracellular signals (80,82,85). Most neuronal cells die following brain injury (82,86). Many that recover have a sustained alteration in their physiology, and this after a traumatic insult may lead to functional disability (87,88). Prolonged intracellular signal transduction disruption can alter the normal response to neurotransmitters such as glutamate and acetylcholine leading to detrimental effects on the regulation of excitability of the neuronal membrane, intercellular communication, and synaptic plasticity (82,87,89). Such modifications lead to cognitive dysfunction and reduction in brain injury-related seizure threshold (89). While hypocalcemia is normal after TBI and has detrimental effects, calcium administration has not been shown to have possible neuronal death impact (90).

Significant negative correlations between serum calcium ion levels and systolic blood pressure and heart rate have been observed in the current study. Calcium ions are important intracellular signals and muscle contraction, which can explain the findings of the cardiovascular parameters (91). Ca2 + disorders have been associated with cardiac arrhythmias and prolonged QT interval and may be associated with poor outcomes (92).Pupillary examination findings and injury severity also exhibited a significant negative correlation with calcium ion levels. This means that worse

ISS and pupil findings were seen more in patients with hypocalcemia. Other studies (93,94) have documented similar results. Although these studies indicated that acidosis was associated with hypocalcemia, the majority of patients in the current study had compensated for respiratory alkalosis. Therefore acidosis is less likely to have led to the hypocalcemia reported in this study.

5.4 SERUM MAGNESIUM ION ABNORMALITIES

Hypomagnesemia was the most common abnormality, reported in 33.3% and 34.5% of admission and 48hrs post-admission cases respectively. Magnesium loss has been found both in animal models and in human blood following brain injury (95). Prevalence of hypomagnesemia among TBI patients at admission from previous studies is 28.5%-58% (14,57,96). Thirty patients with head injury (12 mild, 8 moderate, and 10 severe TBI) were followed up by Kahraman et al. (97), who monitored average magnesium levels for five days. They identified a statistically significant difference in serum ionized magnesium concentrations between the three groups, with lowest levels of Mg2 + among severe TBI patients. These authors also stated that on the first day after trauma, serum ionized Mg2 + concentrations showed a decline and then increased on subsequent days.

Magnesium plays an important role in the homeostatic regulation of brain injury pathways (98). Magnesium is a predominant intracellular ion that inhibits the action of the exciting neurotransmitter glutamate by blocking the N-methyl - D-aspartate (NMDA) glutamate receptor calcium channel, thereby controlling calcium entry into the postsynaptic neuron (99). Increased intracranial pressure following TBI activates the sympathetic nervous system leading to Mg2+ efflux from subsequent urinary loss cells (95,97,100). Using osmotic diuretics like mannitol may also cause increased urinary loss of magnesium ions (53). The resulting post-TBI hypomagnesemia leads to excessive glutamate and calcium flow into the post-synaptic neuron leading to excitotoxicity, increased free radical generation, proteolysis, apoptosis cell death, and neuro-inflammation (56,57,98). This leads to secondary brain injury with consequent neuronal loss.

Mortality and severe morbidity have also been correlated with hypomagnesemia. In the current study, the odds ratio for 30-day hypomagnesemia-related mortality was 2.4 and 0.3 at admission

and 48 hours post-admission, respectively, but was not statistically significant. Pin-on et al. (14), reported risk ratio 2.52 (p=0.05) to death within 24hrs of TBI in patients with hypomagnesemia. Compared to normomagnesemia, hypomagnesemia is associated with increased need for mechanical ventilation, extended ICU stay and mechanical ventilation, sepsis and poor outcome scores (96,101). Neuromuscular signs including muscle weakness, arrhythmias, tremors, seizures and depression are usually associated with hypomagnesemia (101,101,102). Muscle fatigue is a significant factor causing difficulties in withdrawing these patients from the ventilator (102). In experimental studies, magnesium has also been linked to antidepressant effects because it affects the functioning of monoaminergic and serotonergic neurotransmitter systems that are disrupted as part of the secondary injury cascade following TBI and alters the activity of the hypothalamic-pituitary-adrenocortical system (103).

While experimental animal studies have shown neuroprotective effects of magnesium following brain trauma, inconsistent results have been documented in human trials (56,98,103,104).. Dhandapani et al. (105) reported that parenteral magnesium sulphate administered within 12 hours of severe TBI resulted in less brain swelling and lower mortality than magnesium-free patients. A double-blind study involving 499 with mild to extreme traumatic brain injury tested the effects of two doses of magnesium (low or high) or placebo intravenous administration within 8 h of injury and continued for 5 days (106). Magnesium use in that study did not demonstrate any major positive impact on survival, seizure frequency or neurobehavioral functioning. Further analysis of 8 randomized controlled trials in a total of 786 patients (394 magnesium sulphate groups and 392 controls) was conducted in a meta-analysis (107). This meta-analysis showed that there was no significant difference between the mortality groups (mortality rates of 19.94 per cent in the treatment group and 20.56 per cent in the placebo group). Nonetheless, significant improvement

in patient GOS scores ($p=0.05$) and a significant improvement in GCS scores in patients treated with magnesium sulphate ($p<0.001$) were observed. Hence, these findings have concluded that no evidence actually exists to support the prophylactic use of magnesium in patients with acute traumatic brain injury.

Although hypomagnesemia was the predominant magnesium ion abnormality reported in the current study, hypermagnesemia was reported in 25.9 per cent and 31 per cent of patients on admission and 48 hours later. There is a paucity of data on hypermagnesemia occurring post-TBI. The prevalence of hypermagnesemia in critically ill patients is 10-15% (108,109). Hypermagnesemia in patients admitted to intensive care units is often seen in those with trauma (110). Hypermagnesemia may result from reduced renal excretion, cell lysis (rhabdomyolysis and hemolysis), or extracellular shift due to acidosis (108,109). The exact cause of high levels of hypermagnesemia in the present study needs to be explored further. Compared to hypomagnesemia, hypermagnesemia was associated with a lower risk of mortality of 0.9 Vs. 2.4. This may support the findings of previous studies which have shown that hypermagnesemia can be beneficial in TBI (98).

5.5 SERUM PHOSPHATE ION ABNORMALITIES

Hypophosphatemia was the predominant abnormality, noted in 42.1% and 48.3% of the cases at admission and 48hrs post-admission respectively. Our results are in agreement with findings from previous studies that reported a prevalence rate of hypophosphatemia of 28.5-56% among TBI patients (14,77,96,111). The occurrence of hypophosphatemia seems to be more among the severe head injury patients. A prospective study of 145 patients in Thailand with traumatic brain injury revealed hypophosphatemia in 72(49.6%) patients (14). Of these, 56(77.8%) had severe head injury while 14(19.4%) and 2(2.8%) had moderate and mild TBI respectively. Even among critically ill trauma patients in intensive care units, those with traumatic brain injury have significantly lower phosphate levels (53).

There are three main mechanisms of hypophosphatemia: increased renal excretion, decreased intestinal absorption, and shifts from the extracellular to intracellular compartments (112). The intracellular influx of phosphate is the most common cause of hypophosphatemia in critically ill patients and can be caused by respiratory alkalosis, hyperglycemia, refeeding syndrome, and high catecholamine levels (112,113). All these conditions are common in severe traumatic brain injury (52,53). Renal loss of phosphate is accentuated by metabolic acidosis and drugs such as diuretics, glucocorticoids, and aminoglycosides (51,112). Polyuresis is common in head injury patients and may result from the syndrome of inappropriate antidiuretic hormone secretion, cerebral salt loss, and use of hyperosmolar therapies such as mannitol (52,53,111). Hypophosphatemia may also be dilution due to rapid volume expansion (111). Indeed, in the current study, hypophosphatemia was associated with respiratory alkalosis and admission serum levels of phosphate displayed significant negative correlations with prehospital use of mannitol or intravenous fluids.

Phosphate is a major intracellular anion and is involved in many normal physiologic functions such as acid-base buffering, cell signalling, energy transfer, and information storage and translation in DNA and RNA, and maintenance of muscle tone (113,114). Hypophosphatemia leads to muscle weakness, cardiac dysfunction including hypocontractility, ventricular tachycardia, and cardiac arrest, altered mental status, and seizures (112,113). In the current study, hypophosphatemia was associated with significantly lower diastolic blood pressure and Glasgow Coma Score. The weakness of the respiratory muscles leads to difficulty in weaning from the ventilator as well as increased respiratory infections (16,96). In the present study, low levels of phosphate were associated with reduced oxygen saturation, increased respiratory rate and respiratory alkalosis. Respiratory and cardiovascular complications of hypophosphatemia are associated with a 2- to 4-fold increase in mortality in critically ill patients (113). The odds of death in the current study was 4.12 ($p=0.031$) at admission and 7.5($p=0.198$) at 48hrs post-admission.

Hyperphosphatemia was reported in 8.3% of the cases 48hrs after admission. This concurs with findings from previous studies that reported an incidence rate of 6%-9.8% (16,77). Hyperphosphatemia may be caused by renal insufficiency, excessive phosphorus intake, acidosis, hemolysis, rhabdomyolysis, and hypothyroidism (16,77). Hyperphosphatemia results in acute renal failure and calcification of organs such as the heart and the lungs (54,109). Phosphate chelates with calcium and may lower the biologically active ionized calcium fraction leading to clinical features of hypocalcemia (109). It is an independent risk factor for mortality among critically ill patients, an odds ratio of 3.29, $p<0.001$ (115). No study has however reported the risk of mortality for head injury patients with hyperphosphatemia. In the current study, hyperphosphatemia was associated with a 3-fold increase in mortality compared to normophosphatemic patients.

CONCLUSIONS

Serum sodium, potassium, calcium, magnesium and phosphate ion abnormalities are common in severe traumatic brain injury patients in our setting. Hypernatremia was the predominant serum sodium ion abnormality reported in 56 (63.6 percent) cases 48 hours after admission. It was correlated significantly with mannitol use, lower GCS score, higher Injury Severity Score, presence of subdural hematoma on CT scan, midline change > 5 mm, compressed / absent basal cisterns, higher Rotterdam CT Score, low pCO_2, low HCO_3, and low base deficit. Hypernatremia was associated with a higher risk of mortality rate of 3.55 compared to OR 1.26 for hyponatremia.

Hypokalemia was the most common potassium ion abnormality, reported in 26 (21%) and 21 (23.9%) admission cases and 48hrs post-admission assays respectively. Hypokalemia was significantly associated with the presence of epidural hematoma, higher levels of HCO3 and base deficit. Increased pulse rate and traumatic SAH were seen mainly in patients suffering from hyperkalemia. Mortality risk associated with hypokalemia was significantly increased OR 4.12 and OR 5.12 at admission and 48 hours post-admission, respectively.

Hypocalcemia was the most common calcium ion abnormality in 84(72.4%) patients at admission and in 34(37.8%) patients 48hrs after admission. The age of the patient, severity score of injury, heart rate and systolic blood pressure showed statistically significant negative correlations with calcium ion levels. Hypocalcemia that develops 48hrs after admission is associated with a higher mortality risk (OR 5.70) compared to admission risk (OR 3.2).

Hypomagnesemia was the most common magnesium ion abnormality reported in 36 (33.3 per cent) and 30 (34.5 per cent) of admission and 48 hours post-admission cases, respectively. The risk of hypomagnesemia-related mortality at admission and at 48hrs post-admission was OR 2.4

and OR 0.3. Patient age and systolic BP showed a significant negative correlation with magnesium ion levels. None of the radiological or acid-based parameters exhibited substantial correlations.

Hypophosphatemia was the predominant phosphate ion abnormality reported in 40 (42.1%) and 29 (48.3%) of admission and 48 hours post-admission cases, respectively. Low levels of phosphate were significantly correlated with pre-hospital use of IV fluids, mannitol use, lower diastolic pressure, tachypnoea, hypoxemia and respiratory alkalosis. Hypophosphatemia was associated with a statistically significant high risk of death; OR 4.12 and OR 7.5 at admission and OR 48 hours post-admission respectively.

STUDY LIMITATIONS

- The ideal time would be a much longer time, but the study was limited to four months due to budgetary and time constraints. Nonetheless, we are sure that the findings are correct because we reached the estimated minimum sample size.
- The analysis was confined to Kenyatta National Hospital and therefore the findings may not be the true national image. However, KNH is the area 's primary neurotrauma referral center.
- Several (seven) patients died in the emergency room before imaging tests were performed to assess their injuries. Therefore, radiological parameters were not included in the study for these patients.

RECOMMENDATIONS FOR FUTURE STUDIES

1. A multicenter research involving greater sample size should be performed to validate current study findings.
2. The effect of therapeutic intervention / correction of specific ion abnormalities on the outcome (e.g. duration of ICU stay, Glasgow Outcome Score, etc.) needs to be studied.

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APPENDICES

APPENDIX I: INFORMED CONSENT - ENGLISH

Patient's Study Number: _____ **Date: _____**

STUDY TOPIC: Evaluation of Serum Electrolyte Abnormalities among Severe Head Injury Patients at Kenyatta National Hospital0.

Principal Investigator:

Dr Philip Mwachaka, *Department of Surgery- University of Nairobi*
P0.O0. Box 19676-00202 KNH, Nairobi0. Telephone: 0723353914
Email: pmaseghe@gmail0.com

Supervisors:

10. Prof Nimrod Mwang'ombe *MB ChB, M0.Med, PhD*0
Head, Neurosurgery Unit, Department of Surgery, University of Nairobi
P.O. Box 19676-00202 KNH, Nairobi0. Telephone: 0723353913
Email: nimrod@uonbi0.ac0.ke
20. Prof Angela Amayo, MBChB, MMed (Pathology)
Chairperson, Department of Pathology, University of Nairobi
P.O. Box 19676-00202 KNH, Nairobi0. Telephone: 0727643779
Email: angela0.amayo@uonbi0.ac0.ke
30. Dr Peter Kitunguu, *BSc, MBChB, M.Med (Neurosurgery)*
Neurosurgeon0. Department of Surgery, University of Nairobi
P.O. Box 19676-00202 KNH, Nairobi0. Telephone: 0722881405
Email: pkitunguu@gmail0.com

This Informed Consent Form has three parts:

1) Information Sheet (to share information about the research with you)
2) Statement of Consent (for signatures if you agree to take part)
3) Statement by the researcher/person taking consent

You will be given a copy of the full informed consent form.

PART I: Information Sheet

Introduction

My name is Dr Philip Mwachaka, a postgraduate student in Neurosurgery at the University of Nairobi0. I am researching the "**Evaluation of Serum Electrolyte Abnormalities Amongst Severe Head Injury Patients at the Kenyatta National Hospital (KNH)**"0. The purpose of this consent form is to provide you with the information you will need to assist you in deciding whether you want to participate in the study0. This process is called 'Informed Consent'0. Please read this consent information carefully and ask any questions or seek clarification on any matter concerning the study with which you are uncertain0.

What is the purpose of the study?

Severe Traumatic brain injury is the leading cause of death and disability both locally and internationally0. Abnormal serum electrolytes occurring after a head injury may contribute to these poor outcomes0. This study aims at determining the prevalence of serum electrolyte abnormalities among severe Traumatic brain

injury patients seen at the KNH0. In addition, we aim at determining the association between the electrolyte abnormalities and specific clinico-radiologic parameters0. This may help clinicians predict patients likely to develop the abnormalities and therefore institute the necessary preventive measures0.

I am going to give you information and invite you to be a participant in this research0. There may be some words that you do not understand or that you may need clarification0. Please ask me to stop as we go through the information and I will explain or clarify0.

What will happen if you decide you want your next of kin to be in this research study?

If you agree for your next of kin to participate in this study, the following things will happen:

You will be interviewed by the investigator in a private area where you feel comfortable answering questions0. The interview will last approximately 15 minutes0. The interview will cover the clinical presentation0. Then the principal investigator will examine your next of kin and record his/her radiological imaging findings as well as serum electrolyte findings0. Any abnormalities noted will be communicated to the physicians managing the patient0. At the point of discharge from the hospital, the investigator will also record the clinical management administered and the outcome of the patient0.

Are there any risks, harms, discomforts associated with this study?

The study carries no extra risk to the patient0. There will be no invasive procedures carried out in the study that may harm the patient0. Refusing to take part in this study will not jeopardize your treatment in any way0.

The information obtained about you will be kept in strict confidence0. We will keep everything you tell us as confidential as possible0. We will use a code number to identify you in a password-protected computer database and will keep all of our paper records in a locked file cabinet0. No specific information regarding you will be released to any person without your written permission0. We will, however, discuss general overall findings of the study regarding all patients assessed but nothing specific will be discussed regarding your patient0.

Are there any benefits of being in this study?

The results obtained from the study will be used as a basis to improve the quality of care offered to patients diagnosed with traumatic brain injury treated at Kenyatta National Hospital0. The information will be shared among treating clinicians and the hospital0.

Will being in this study cost you anything?

Being in this study will cost you nothing0.

Is there reimbursement for participating in this study?

There is no reimbursement for participating in this study0.

What if you have questions in future?

If you ever have any questions about the study or about the use of the results you can contact the principal investigator, **Dr MWACHAKA,** Tel0.0723353913, or his supervisors, **PROF0. MWANG'OMBE**, Tel0.0722788994; **PROF AMAYO**, Tel: 0727643779 and **DR0. KITUNGUU**, Tel0.07228814050. If any queries arise regarding your rights as a research participant you can contact the **Kenyatta National Hospital Ethics and Research Committee (KNH- ERC**) by calling 020-2726300 Ext0. 44355 or email uonknh_erc@uonbi0.ac0.ke0.

What are your other choices?

Your decision to have your next of kin participate in this research is voluntary0. You are free to decline or withdraw participation of your next of kin in the study at any time without injustice or loss of benefits0. Just inform the investigator and the participation of your next of kin in the study will be stopped0. You do not have to give reasons for withdrawing if you do not wish to do so0. Withdrawal of your next of kin from the study will not affect the services he/she is otherwise entitled to in this health facility or other health facilities0.

Part II: Consent Form (Statement of Consent)

The person being considered for this study is unable to consent for him/herself because he/ she has a severe head injury0. You as the next of kin are being asked to give your permission to include him/her in this study0.

Next of kin statement

I have read this consent form or had the information read to me0. I have had the chance to discuss this research study with a study investigator0. I have had my questions answered by him or her in a language that I understand0. The risks and benefits have been explained to me0. I understand that I will be given a copy of this consent form after signing it0. I understand that my participation and that of my next of kin in this study is voluntary and that I may choose to withdraw it any time and this will not in any way alter the care being given to him/her0. The results of the study may be of benefit to other patients with a severe head injury and aid in better care of such patient's outcome in the future0. I understand that all efforts will be made to keep the information confidential0.

By signing this consent form, I have not given up my next of kin's legal rights as a participant in this research study0.

I agree to participate in this research study:	Yes	No
I agree to have blood preserved for later study	Yes	No
I agree to provide contact information for follow-up:	Yes	No

I ……0.0. freely give consent of next of kin (Name ……) to take part in the study conducted by Dr0.Philip Mwachaka, the nature of which has been explained to me by him/ his research assistant0.

…… ……

Signature Date

Statement by a witness if the guardian or proxy is illiterate0.

I have witnessed the accurate reading of the consent form to the participant, and the individual has had the opportunity to ask questions0. I confirm that the individual has given consent freely0.

Name of witness……..……..…… Signature of witness…… Date……	Thumbprint of next of kin

Part III: Statement by the researcher

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has knowingly given his/her consent0.

Name: _____ Date: _____

Signature: _____

Role in the study: _____

APPENDIX II: IDHINI YA KUJIHUSISHA NA UTAFITI

Namba ya utafiti:_____ **Tarehe:_____**

Jina la utafiti: Uchunguzi wa madini ya damu baada ya kuumia Kichwa kwa wangonjwa wanaohudhuria matibabu katika hospitali kuu ya Kenyatta

Mpelelezi mkuu:

Dkt0. Philip Mwachaka, *Chuo Kikuu Cha Nairobi – Kitengo cha upasuaji*
P0.O0. Box 19676-00202 KNH, Nairobi0. Telephone: 0723353914

Wasimamizi:

10. Prof Nimrod Mwang'ombe *MB ChB, M0.Med, PhD*0.
Chuo Kikuu Cha Nairobi – Kitengo cha upasuaji wa ubongo
S0.L0.P 19676-00202 KNH, Nairobi0. Telephone: 0723353913
Barua pepe: nimrod@uonbi0.ac0.ke

20. Prof Angela Amayo, MBCHB, MMed (Pathology)
Mwenyekiti, Kitengo cha Pathologia, *Chuo Kikuu Cha Nairobi*
S0.L0.P 19676-00202 KNH, Nairobi0. Telephone: 0727643779
Barua pepe: angela0.amayo@uonbi0.ac0.ke

30. Dr0. Peter Kitunguu, *BSc, MBChB, M0.Med (Neurosurgery)*
Chuo Kikuu Cha Nairobi – Kitengo cha upasuaji wa ubongo
S0.L0.P 19676-00202 KNH, Nairobi0. Telephone: 0722881405
Barua pepe: pkitunguu@gmail0.com

Hii fomu iko na sehemu tatu:

1) Habari kuhusu utafiti
2) Idhini ya mgonjwa
3) Dhibitisho la mpelelezi

Sehemu ya kwanza: Habari kuhusu utafiti

Utangulizi: Jina langu ni Dk0. Philip Mwachaka, wa Neurosurgery katika Chuo Kikuu cha Nairobi0. Ninafanya utafiti kuhusu "***Uchunguzi wa madini ya damu baada ya kuumia Kichwa kwa wangonjwa wanaohudhuria matibabu katika hospitali kuu ya Kenyatta"0.***

Kusudi la utafiti ni nini?

Kujeruhiwa kwa ubongo ni ugonjwa wa kudhoofisha na unaosababisha ulemavu mkubwa0. Utafiti huu unalenga kutoa taarifa ambayo itasaidia maendeleo ya mikakati ambayo itasaidia kuzuia na kutibu kuumia kwa ubongo katika kanda letu kwa mtazamo wa kuboresha matibabu na matokeo0.

Nitawapa taarifa na kukualika uwe mshiriki katika utafiti huu0. Kunaweza kuwa na maneno ambayo hujui au kwamba unahitaji ufafanuzi0. Tafadhali niulize kuacha tunapopitia maelezo na nitasema au kufafanua0.

Nini kitatokea ikiwa utaamua unataka mjammi wako awe katika utafiti huu wa utafiti?

Ikiwa unakubaliana na mjamii wako kushiriki katika utafiti huu, mambo yafuatayo yatatokea:

Utashughulikiwa na uchunguzi katika eneo la kibinafsi ambako unasikia vizuri kujibu maswali0. Mahojiano itaendelea dakika 150. Mahojiano itakuwa inahusu mambo yaliofanyika mpaka akaletwa hospitalini0. Kisha

mchunguzi mkuu atamtazama mgonjwa na kurekodi matokeo yake ya picha ya radiology na ya madini ya damu0. Wakati wa kutolewa kutoka hospitali, matibabu aliyoyapata pamoja na hali yake yatarekodiwa0.

Je, kuna hatari yoyote, madhara, kutokuwepo na uhusiano na utafiti huu?

Utafiti huu hauna hatari zaidi kwa mgonjwa0. Hakutakuwepo na taratibu za uvamizi zitazofanywa katika utafiti ambazo zinazoweza kumdhuru mgonjwa0. Kukataa kushiriki hakutahatarisha matibabu yako kwa njia yoyote0.

Taarifa unayejitolea au tunayopata itachukuliwa kwa siri na inapatikana kwa uchunguzi mkuu na timu ya utafiti pekee yao0. Jina lako halitatumiwa kamwe0. Taarifa yoyote kuhusu wewe itakuwa nayo nambari badala ya jina lako0. Hatuwezi kugawana utambulisho wa wale wanaoshiriki katika utafiti huu0.

Faida ya kushiriki matokeo ni nini?

Maarifa tunayopata kutokana na utafiti huu yatashirikiwa na watunga sera katika Wizara ya Afya, KNH na madaktari kupitia machapisho na mikutano0. Maelezo ya siri hayatashirikiwa0.

Je kuna gharama na fidia?

Hakutakuwa na gharama ya ziada iliyopatikana kwa kushiriki katika utafiti huu wala kuna fidia inayotolewa0. Hata hivyo, wakati wako utahitaji kushiriki katika mahojiano0.

Ikiwa uko na matatizo au maswali?

Ikiwa una maswali yoyote kuhusu utafiti au juu ya matumizi ya matokeo unaweza kuwasiliana na mpelelezi mkuu, **Dr MWACHAKA**, Tel0.**0723353913**, au wasimamizi wake, **PROF0. MWANG'OMBE**, Tel0.0722788994, au **DR0. KITUNGUU**, Tel0.07228814050. Ikiwa una maswali yoyote kuhusu haki zako kama mshiriki wa utafiti unaweza kuwasiliana na **Kenyatta National Hospital Ethics and Research Committee (KNH- ERC)** kwa kupiga **2726300 Ext0. 443550.**

Ushiriki wa hiari: Wewe ni huru kushiriki au la0. Ikiwa unachagua kushiriki au la, huduma zote unazopata katika hospitali hii itaendelea na hakuna kitu kitakachobadilika0. Ikiwa unachagua kushiriki katika mradi huu wa utafiti, utapewa matibabu ambayo hutolewa mara kwa mara katika hospitali hii kwa hali yako0. Una haki ya kukataa au kuondoa ushiriki wako katika utafiti huu wakati wowote0.

Sehemu ya pili – Idhini ya mgonjwa

Nimeisoma habari hapo juu, au imesomewa0. Nimekuwa na fursa ya kuuliza maswali kuhusu hilo na maswali yoyote niliyoyaomba yamejibiwa kwa kuridhika kwangu0. Ninakubali kwa hiari kushiriki kama mshiriki katika utafiti huu0.

Jina la Mshiriki: _____

Sahihi la Mshiriki: _____ Tarehe _____

Nimeona usomaji sahihi wa fomu ya kibali kwa mshiriki mwenye uwezo, na mtu huyo amepata fursa ya kuuliza maswali0. Ninathibitisha kwamba mtu huyo ametoa ridhaa kwa uhuru0.

Jina la Mshiriki: _____ Thumb print of participant

Sahihi la Mshiriki: _____

Tarehe: _____

Sehemu ya tatu: Dhibitisho la mtafiti

Nimeeleza kikamilifu maelezo muhimu ya utafiti huu kwa mshiriki jina lake hapo juu na kuamini kuwa mshiriki ameelewa na amepeana idhini yake0. Ninathibitisha kwamba mshiriki huyo alitolewa fursa ya kuuliza maswali kuhusu utafiti huo, na maswali yote aliyoulizwa na mshiriki amejibu kwa usahihi na kwa uwezo wangu mkubwa0. Ninathibitisha kwamba mtu huyo hakulazimishwa kutoa idhini, na ridhaa imetolewa kwa uhuru na kwa hiari0.

Jina la mtafiti: _____

Sahihi la mtafiti: _____

Tarehe: _____

APPENDIX III: DATA COLLECTION SHEET

1. **Study Number** *

_____

2. **Age** *

_____

3. **Gender**
Mark only one oval.

- ◯ Female
- ◯ Male

4. **Date and time of presentation to KNH** *

_____
Example: December 15, 2012 11:03 AM

5. **Date and time of injury**

_____
Example: December 15, 2012 11:03 AM

6. **Brought to hospital by** *
Mark only one oval.

- ◯ Ambulance staff
- ◯ Police/ Firefighters
- ◯ Rescuers/Bystanders
- ◯ Relatives/Relations/ Neighbors

7. **Referral details** *
Mark only one oval.

- ◯ Direct
- ◯ Private Hospital
- ◯ Government Hospital

8. **Pre-hospital care/ First aid** *

Mark only one oval per row.

	Yes	No
Intubation	◯	◯
IV fluids	◯	◯
Mannitol	◯	◯

History

9. **Mechanism of injury**

Mark only one oval.

- ◯ Assault
- ◯ Fall from height
- ◯ Pedestrian hit by car
- ◯ Pedestrian hit by a motorcycle
- ◯ Motorcycle rider/passenger
- ◯ Motor vehicle occupant
- ◯ Unknown

10. **History** *

Mark only one oval per row.

	Yes	No
Vomiting	◯	◯
Otorrhea	◯	◯
Rhinorrhea	◯	◯
Seizures	◯	◯
Lucid interval	◯	◯
Diabetes	◯	◯
Hypertension	◯	◯
Tobacco- smoking/smokeless	◯	◯
Illicit drug use	◯	◯
Use of alcohol at injury	◯	◯

Physical examination findings

11. **Systolic BP** *

12. **Diastolic BP** *

13. **Heart rate**

14. **Respiratory rate**

15. **Temperature**

16. **Saturation O2** *

17. **GCS Motor response** *

Mark only one oval.

- 1. No response
- 2. Extensor response
- 3. Flexor response
- 4. Withdrawal from pain
- 5. Localizes to pain
- 6. Obeys commands
- NT = not testable

18. **GCS Verbal response** *

Mark only one oval.

- 1. No verbal response
- 2. Incomprehensible sounds.
- 3. Inappropriate words.
- 4. Confused.
- 5. Oriented.
- Intubated

19. **GCS Eye opening** *

Mark only one oval.

- 1. No opening of the eye
- 2. To pain stimulus.
- 3. To speech.
- 4. Spontaneously
- Not testable

20. **Pupil examination** *

Mark only one oval.

- Anisocoria R>L
- Anisocoria L>R
- BERL
- Pinpoint bilat
- Dilated and fixed
- Not testable
- Option 7

21. **Injury Severity Score**

Mark only one oval per row.

	0 - no injury	1 - minor	2 - moderate	3 - severe (not life-threatening)	4 - severe (life-threatening, survival probable)	5 - severe (critical, survival uncertain)	6 - maximal, possibly fatal
head	◯	◯	◯	◯	◯	◯	◯
face	◯	◯	◯	◯	◯	◯	◯
neck	◯	◯	◯	◯	◯	◯	◯
thorax	◯	◯	◯	◯	◯	◯	◯
abdominal and pelvic contents	◯	◯	◯	◯	◯	◯	◯
spine	◯	◯	◯	◯	◯	◯	◯
upper extremity	◯	◯	◯	◯	◯	◯	◯
lower extremity	◯	◯	◯	◯	◯	◯	◯
external	◯	◯	◯	◯	◯	◯	◯

CT Scan head findings

22. **Basal cisterns** *

Mark only one oval.

- ◯ Normal
- ◯ Compressed
- ◯ Absent

23. **Midline shift (mm)** *

_____

24. **Mass lesion/SAH present?** *

Mark only one oval per row.

	Yes	No
Epidural Hematoma	◯	◯
Subdural hematoma	◯	◯
Intracerebral hematoma	◯	◯
Traumatic SAH	◯	◯
Contusional hemorrhages	◯	◯

25. **Location of mass lesion**

_____

26. **EDH volume (mls)**

_____

27. **SDH Thickness (mm)**

_____

28. **Other abnormal radiology investigations**

_____

_____

_____

Laboratory findings	
At admission	**72hrs post-admission**
30. Sodium levels *	43. Sodium levels
31. Potassium levels *	44. Potassium levels
32. Chloride *	45. Chloride
33. Urea *	46. Urea
34. Creatinine *	47. Creatinine
35. Calcium	48. Calcium
36. Magnesium	49. Magnesium
37. Phosphate	50. Phosphate
38. Albumin	51. Albumin
39. pH	52. pH
40. pCO2	53. pCO2
41. HCO3	54. HCO3
42. Base deficit	55. Base deficit

Management

56. **Management** *

Mark only one oval.

- ◯ Conservative
- ◯ Operative

57. **Non surgical interventions** *

Mark only one oval per row.

	Yes	No
Mannitol	◯	◯
Hypertonic saline	◯	◯
Normal saline	◯	◯
Intubation & mechanical ventilation	◯	◯
Blood transfusion	◯	◯

58. **Cranial Operative interventions**

Check all that apply.

- ☐ Craniotomy and evacuation of hematoma
- ☐ Decompressive craniectomy
- ☐ Elevation of depressed skull fracture
- ☐ Other: _____

59. **Extra-cranial operative interventions**

_____

_____

_____

_____

_____

60. **Time from Admission to Surgery**

_____

Example: 8:30 AM

61. **Length of surgery**

_____

Immediate outcome

62. **Immediate outcome**
Mark only one oval.

- ◯ Dead
- ◯ Alive

63. **In-case of mortality, where did it occur?**
Mark only one oval.

- ◯ While in ER
- ◯ In the OR
- ◯ In ICU

64. **Date and time of death**

Example: December 15, 2012 11:03 AM

65. **If alive, indicate date of discharge from ICU**

Example: December 15, 2012

66. **If alive, indicate the GCS at discharge from ICU**

67. **Duration of mechanical ventilation (days)**

APPENDIX IV: STUDY APPROVALS