FACTORS ASSOCIATED WITH MORTALITY OF PATIENTS ADMITTED WITH TRAUMATIC BRAIN INJURY AT THE MAIN INTENSIVE CARE UNIT, UNIVERSITY TEACHING HOSPITALS, LUSAKA – ZAMBIA

By

DR. IMRAAN AHMED

A dissertation submitted to the University of Zambia in partial fulfillment of the requirements for the award of the degree of
Master of Medicine in Anaesthesia and Intensive Care

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DECLARATION

I, Dr Imraan Ahmed, hereby declare that this dissertation represents my own work and has not been presented either wholly or in part at the University of Zambia or any other university.

Candidate signature _____

DR IMRAAN AHMED

BSc. HB. MB.ChB.

Supervisor signature _____

DR NAOMI SHAMAMBO

BSc. Biological Sciences BSc. HB. MB. ChB. MMed (Anaesthesia & Critical Care)

Consultant Anaesthesiologist & Critical Care Specialist

University Teaching Hospitals, Lusaka, Zambia

CERTIFICATE OF APPROVAL

This dissertation of Dr. Imraan Ahmed has been approved as fulfilling part of the requirements for the award of Master of Medicine in Anaesthesia and Critical Care by the University of Zambia.

Signed by:

NAME	**SIGNATURE**	**DATE**
_____	_____	_____
(Examiner 1)		
_____	_____	_____
(Examiner 2)		
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(Examiner 3)		
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Board of Examiners (Chairperson)		

ABSTRACT

BACKGROUND Traumatic brain injury (TBI) is a common pathology in the main intensive care unit (MICU) at University Teaching Hospitals (UTH), with patients being admitted for airway protection, stabilisation, and close monitoring of vitals, thus helping prevent secondary brain injury. Mortality of these patients was previously found to be high at 66%, however, it is not known whether physiological factors on admission of these patients to MICU are associated mortality. It is important to study these factors to develop proper admission criteria for these patients being admitted to MICU. This study aimed to evaluate the current mortality rate of patients admitted with TBI in MICU at UTH and to explore neuro physiological factors associated with their mortality.

METHODS This was a cross-sectional study done in MICU at UTH in Lusaka, Zambia. 78 participants were enrolled, but one was excluded after transfer to another facility. Upon admission to MICU, the following data was collected: age, gender, mechanism of injury, admission vital signs (mean arterial pressure, body temperature, random blood sugar), admission Glasgow Coma Scale, presence, or absence of convulsions and anisocoria, and the time interval between injury and arrival at UTH. Participants were followed up till either discharge from MICU or death. Statistical analysis was done using Stata.

RESULTS The mean age of the participants was 30.9, majority of the participants being male (84%). Out of the 77 participants in the analysis, 25 (32%) were discharged from MICU and 52 (68%) died. There was no significant difference in the mean MAP, mean body temperature or mean random blood sugar on admission to MICU between the group discharged from MICU and the group which died. An admission GCS of between 3 and 8 was significantly associated with higher mortality ($p<0.001$), as well as presence of convulsions during admission ($p=0.028$). Only 2% of the participants reached UTH within an hour of injury, and a delay of more than 12 hours between injury and arrival at UTH was significantly associated with higher mortality.

CONCLUSIONS The current mortality rate of patients admitted with TBI in the MICU at UTH remains high and there is need for improvement in timely admission and management of these patients in MICU. Majority of the patients delayed reaching reasonable care at UTH and this significantly impacted mortality. Increased severity of TBI and presence of convulsions were also associated with higher mortality.

DEDICATION

This work is dedicated to my parents and siblings, who have always been my constant pillar of support throughout my education and career and have shown so much patience with me.

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ABBREVIATIONS

CBF	Cerebral blood flow
CT	Computed tomography
GCS	Glasgow coma scale
HDU	High dependency unit
ICP	Intracranial pressure
ICU	Intensive care unit
LMIC	Low- and middle-income countries
MAP	Mean arterial pressure
MICU	Main intensive care unit
MMed	Master of Medicine
NTDB	National Trauma Data Bank
RBS	Random blood sugar
RTA	Road traffic accident
SBP	Systolic blood pressure
TBI	Traumatic brain injury
UNZA	University of Zambia
UNZABREC	University of Zambia Biomedical Research Ethics Committee
USA	United States of America
UTH	University Teaching Hospitals
WHO	World Health Organisation

1 INTRODUCTION

Traumatic brain injury (TBI) is a common pathology seen in the Main Intensive Care Unit (MICU) at the University Teaching Hospitals (UTH) in Lusaka. It accounts for 20% of all admissions to the MICU (2018 audit). Patients with TBI, commonly following road traffic accidents (RTA) or physical assault, present to the hospital with a depressed level of consciousness and impairment of neurological function, which may be temporary or permanent. At the MICU, these patients are admitted for securing the airway and mechanical ventilation. In addition, these patients may need hemodynamic stabilisation in the form of inotropic support. Many of the TBI patients may require neurosurgical interventions and these patients are admitted to MICU for post-operative stabilisation and recovery. In the developing world, mortality of TBI patients in an intensive care unit (ICU) is quite high (Kinyanjui, 2016), ranging between 52% and 66%. In more advanced settings, such as the United States of America (USA), the mortality of these patients is significantly less at 10.2% (Krishnamoorthy et al, 2015).

Several factors have been studied and shown to have been associated with mortality of these patients both in developed and developing countries. The severity of TBI was shown to be significantly associated with mortality globally (Gerber et al, 2013). Unstable admission blood pressure and hypotension also correlated with increased mortality both in the developed countries (Krishnamoorthy et al, 2015) as well as the developing countries (Opondo & Mwangombe, 2007) (Qureshi et al, 2013). Other factors that have been found to significantly increase mortality are abnormal vital signs on admission; particularly hyperglycaemia (Opondo & Mwangombe, 2007), hypoxia (Sharda et al, 2014) and abnormal pupil size and reactivity (Khajavikhan et al, 2016).

Patients with TBI typically present with a depressed level of consciousness following history of trauma but may also have other clinical features such as convulsions, anisocoria (difference in size of the two pupils) and absent pupillary reflexes. Patients with severe TBI are managed in a high dependency unit (HDU) or an intensive care unit (ICU), where they can be mechanically ventilated, closely monitored and commenced on hemodynamic

support when necessary. Some patients may also undergo surgical intervention for evacuation of a hematoma as part of the management.

The evolution of TBI is divided into two periods: primary and secondary brain injury. The primary injury is the physical damage that happens to the brain parenchyma during the traumatic event and the secondary injury ensues in the following hours and days. Prevention of secondary brain injury in an ICU setting leads to better outcomes of these patients (Dinsmore, 2013).

The Main Intensive Care Unit (MICU) at the University Teaching Hospitals (UTH) in Lusaka is a 20-bed unit with the capacity to mechanically ventilate as well as continuously monitor admitted patients. It is an open ICU setting, admitting patients with both medical and surgical problems. Trauma patients are also admitted to this ICU. According to the patient turnover audits done between January and December 2018, TBI accounted for 20% of MICU admissions at UTH. The mortality rate of patients admitted with TBI to MICU has been studied previously and has been found to be very high. A study done between November 2012 and December 2013 found that 72.1% of patients admitted to MICU with TBI died (Mwala et al, 2015). Another study done at the MICU in 2016 showed that the mortality rate for patients admitted with TBI at the MICU at UTH was 66% (Shamambo, 2016). However, both these studies did not investigate the factors that may have been associated with such high mortality rates. The ICU is a very resource intensive unit and can be very resource draining especially in resource limited settings. It is important therefore, to have guidelines and protocols for management of ICU patients to reduce mortality.

This was a cross-sectional study which aimed to evaluate the current outcomes of patients admitted to MICU with TBI at UTH in terms of survival or death and aimed to explore factors that may be associated with the outcomes of these patients. The factors that were explored in this study were the neuro physiological factors that were thought to cause a secondary brain injury and not the pre-existing or co-morbid factors inherent in the patients.

2 LITERATURE REVIEW

Traumatic brain injury (TBI) is the leading cause of death and disability in young adults in the developed world, with the World Health Organization (WHO) predicting that TBI and road traffic accidents will soon be the third greatest cause of disease and injury worldwide (Dinsmore, 2013). In the developing world, the burden is felt more; in addition to having the least resources, these countries have a disproportionately high prevalence of TBIs, primarily due to the substantially higher incidence of road traffic accidents (Kinyanjui, 2016).

The severity of TBI can be determined by the Glasgow Coma Scale (GCS), which was first described by Jennette and Teasdale in 1974. It is a score which is calculated from three components of neurological assessment: eye opening, motor response and verbal response of the patient. It has a minimum score of 3 and a maximum of 15. Traditionally, the GCS classified TBIs as mild (GCS 14–15), moderate (GCS 9–13) or severe (GCS 3–8). (Mena et al, 2011)

The primary brain injury can be complicated into secondary brain injury by many factors including hypotension, hypoxia, hypocapnia, hypercapnia, hypothermia, hyperthermia, hypoglycaemia, and electrolyte derangements (Haddad & Arabi, 2012). This evolution from primary to secondary brain injury can ensue within hours of the injury. The key principle of management in TBI is prevention of the secondary brain injury. This is usually done in an HDU or ICU setting by prevention of secondary insults to the already injured brain. In such settings, patients can be mechanically ventilated to prevent hypoxia and hypo/hypercapnia. In addition, continuous monitoring and intervention tries to prevent cardiovascular, metabolic and electrolyte derangements. Interventions can include administration of inotropic drugs to maintain a stable blood pressure. It is the prevention of these secondary insults and hence prevention of secondary brain injury that leads to better patient outcomes in TBI.

The acute phase is the most crucial period in preventing the morbidity and mortality by interventions to prevent secondary brain injury (Dinsmore, 2013). Factors that may lead to development of secondary brain injury can be investigated to see if they are associated

with outcomes in these patients. Outcomes in ICU patients can be studied in terms of mortality or survival. A more objective way of measuring outcome in ICU patients is to measure their functional status after discharge from ICU.

The evolution from the primary injury to secondary brain injury gradually occurs because of ongoing cellular events that cause further damage (Prins et al, 2013). Cerebral blood flow (CBF) is one of the determinants of maintenance of brain tissue integrity. Blood flow to the brain is a function of the blood pressure, specifically the mean arterial pressure (MAP). In a normal brain, the CBF is auto regulated over a wide range of MAP between 50 mmHg and 150 mmHg (Rangel-Castilla et al, 2008), and so CBF remains constant over this range of MAP. However, once subjected to trauma, this mechanism of autoregulation is impaired and the CBF becomes directly dependent on MAP. Thus, a lower MAP results in reduced cerebral blood flow and subsequent ischemia, whereas a very high MAP may increase CBF, increasing cerebral blood volume and in turn intracranial pressure (ICP), which is also detrimental to the brain (Werner & Engelhard, 2007).

Cerebral oxygenation also impacts the primarily injured brain. A critical threshold of blood oxygenation has been studied, below which infarction of brain tissue occurs. The duration and extent of brain tissue hypoxia correlate with poor outcome (Werner & Engelhard, 2007). To prevent this hypoxia, timely intubation and ventilation of the patient is necessary.

Timely neurosurgical intervention is also key in prevention of secondary brain injury. In addition to the actual radiological finding on computed tomography (CT) imaging of the brain, it is also the timely neurosurgical intervention that is necessary to improve outcome. Patients with TBI may have a hematoma in the brain which causes a mass effect and increase in the ICP. Due to the rigidness of the skull, increased intracranial pressure is not well compensated for, and this may lead to obstruction of blood flow within the cranial vault and further ischemia to the brain. Patients who have delayed neurosurgical intervention have a worse mortality than those who have immediate intervention (Tierney et al, 2016). In an observational study done at a trauma centre in New York, USA it was found that patients with severe TBI who were directly transferred from the scene of injury

had a significantly lower mortality (19.3%) as compared to patients who were secondarily transferred to the trauma centre (35.8%) (Prabhakaran et al, 2017).

Globally, there have been various studies done to investigate the factors that may influence mortality in patients admitted to intensive care units following TBI. In a retrospective cohort study done in the United States of America (USA), data was collected from across the country using the National Trauma Data Bank (NTDB) and it was found that in-hospital mortality following isolated severe TBI was 10.2% (Krishnamoorthy et al, 2015). This study found a significant association between admission hypotension and mortality, however a systolic blood pressure (SBP) reading was used to define hypotension rather than the mean arterial pressure (MAP). It is really the MAP that ultimately determines perfusion to the brain which prevents secondary brain injury (Dinsmore, 2013). In another study, done at the University of Michigan, it was concluded that patients over 80 years of age have a higher risk for post-operative complications and significantly longer ICU and hospital stay after undergoing surgical evacuation of hemorrhage following head trauma (Lau et al, 2012). Increasing age as well as severity of the injury were also shown to be associated with poor outcomes in TBI patients from data collected at one of the major trauma centres in West Midlands, United Kingdom (Hawley et al, 2017).

A retrospective analysis of patients admitted to ICU with severe TBI at a Greek hospital between 1999 and 2013, showed a total mortality of 27.38% and this study also found that the admission Glasgow Coma Scale (GCS) was highly correlated with mortality rate (Grigorakos et al, 2016), patients with lower admission GCS had a higher mortality rate. This study also attributed age and Computed Tomography Scan (CT Scan) findings as predictors of outcome in TBI patients. CT Scan finding of subdural hematoma showed the highest mortality. However, it is not clear from this study what statistical tests were used to analyze their data and draw the conclusions made. Similarly, the admission GCS and age were also investigated to be significantly correlated to outcomes of patients with TBI at the Imam Khomeini Hospital in Iran (Khajavikhan et al, 2016). The outcomes investigated in this study included several functional outcomes which all showed significant correlation with age and admission GCS. In contrast, this Iranian study evaluated the mortality rate of TBI patients at 46.2%, significantly higher than the Greek

study. In addition, length of ICU stay, mechanical ventilation and pupil reactivity were found to be significantly correlated with outcomes of ICU patients following severe TBI at the Imam Khomeini Hospital (Khajavikhan et al, 2016).

Hypoxia and hypotension are insults to the brain that can bring about secondary brain injury and lead to poor outcomes, and this was investigated at Hospital Kuala Lumpur in Malaysia. This prospective cohort study concluded that hypoxia and unstable blood pressure were independent predictors of poor outcome in patients with severe TBI who underwent decompressive craniectomy, the strongest predictor being unstable blood pressure (Sharda et al, 2014). Decompressive craniectomy is a surgical intervention that is done for evacuation of a brain hematoma following trauma. A similar study done in Egypt opined that age and initial GCS were the most important factors in determining the postoperative clinical outcome and decompressive craniectomy provided favourable clinical results in nearly 45% of patients who were otherwise most likely to die (Lotfy et al, 2010).

Studies have also been carried out in the Sub-Saharan region of Africa and have investigated the outcomes of patients with TBI. Generally, it was found that mortality in ICU following admission with severe TBI was quite high. At a south-Nigerian teaching hospital, a five-year review of all patients admitted with TBI to the ICU showed a high mortality rate of 52.2%. This was a retrospective case-control study and showed that those patients who required mechanical ventilation had a higher mortality than those who did not (Tobi et al, 2016). In addition, it was concluded from this analysis that those patients who received blood transfusion on the ICU had a better outcome.

Regionally, mortality from severe TBI in ICU has also shown to be high. In Kenya, 54% of patients with TBI at the Kenyatta National Hospital ICU died between April and September 2005. Higher mortality was found in patients who had a GCS of less than 5 as well as those patients with a blood sugar of more than 10 mmol/L. Those patients who had hypotension stayed longer in the ICU and 75% of these hypotensive patients died (Opondo & Mwangombe, 2007). These investigators showed that hypotension, as defined by them as a mean arterial pressure of less than 70mmHg, predicted a poorer outcome in patients

with TBI. Similarly, hypotension was shown to be an independent factor associated with mortality in TBI patients at a national trauma referral centre in Tanzania (Boniface et al, 2017). Extremes of systolic blood pressure were also found to be significantly correlated with mortality at a tertiary hospital in Malawi, where it was found that TBI patients with systolic blood pressures of less than 90 mmHg and greater than 150 mmHg had a significantly higher mortality (Qureshi et al, 2013).

From the studies done, various neurological, clinical, and metabolic factors have been shown to be associated with a higher mortality in patients admitted with TBI. Among these factors, admission hypotension, hypoxia, blood glucose derangements and admission neurological status of patients are factors that strongly influence mortality of these patients.

Locally, TBI presents a major burden to the health institutions as well. A study done at the University Teaching Hospitals in Lusaka found a case fatality rate of 25.6% of patients admitted to the hospital (Mwala et al, 2015). This compares better to statistics from neighbouring Malawi, where overall mortality of patients with TBI was 30.9% (Eaton et al, 2017), but comparison globally shows that mortality is significantly higher. The prospective clinical cohort study done by Mwala et al between December 2012 and November 2013 also showed that admission to the main intensive care unit (MICU) was associated with a risk of unfavourable outcomes. However, it is not known from this study whether this increased risk of mortality was because of the severity of the TBI or there were other factors that may have influenced outcomes. Mwala and colleagues also explored the radiological findings on CT scan of patients with TBI at UTH and showed that the most frequently reported findings were brain contusion.

The outcomes of patients admitted to MICU at UTH has also been studied in terms of their mortality. At least two studies have been done which have shown significantly high mortality of 72.1% (Mwala et al, 2015) and 66% (Shamambo, 2016). Comparing these figures to studies done within the sub-Saharan African region mentioned previously, mortality at the UTH MICU is significantly higher. However, these two studies at UTH did not investigate what factors may be associated with the poor outcome of patients admitted with TBI in the main intensive care unit.

3 STATEMENT OF THE PROBLEM

Patients admitted with traumatic brain injury (TBI) to the main intensive care unit (MICU) at the University Teaching Hospitals (UTH) have high mortality. Having a high mortality of patients in an ICU defeats the purpose of an ICU, which is supposed to reduce short term mortality of patients. An intensive care unit (ICU) at any hospital is very resource straining, more so in resource limited settings, and it becomes imperative to use these limited resources to ensure good outcomes of patients.

From the studies that have been conducted at UTH previously, it is not known what factors may be associated with the high mortality of TBI patients in MICU. It is not known whether patients with TBI in the MICU have a high mortality due to the severity of the injury or because of the physiological and clinical derangements. It is also not known whether these patients are admitted promptly to ICU to prevent mortality. It is the aim of this study to explore these possible factors that may be associated with this high mortality.

4 STUDY JUSTIFICATION

This study will provide data on what factors are associated with poor outcomes of TBI in the MICU at UTH. The data will also help to determine if there are any modifiable factors that can help to improve outcome of patients in the MICU and whether any improvement in management of TBI patients is needed in the unit. It will also provide details on factors that can influence selection of patients with TBI being admitted to MICU to appropriately use the limited resources of the unit to improve outcomes of patients being admitted with TBI.

5 RESEARCH QUESTION

What factors are associated with mortality of patients admitted with TBI in the MICU at UTH?

6 OBJECTIVES

6.1 GENERAL OBJECTIVE

To explore the factors associated with survival or death of patients admitted with TBI in the MICU at UTH.

6.2 SPECIFIC OBJECTIVES

1. To evaluate the current mortality rate of patients admitted with TBI in the MICU at UTH.
2. To determine the effect of admission vital signs on the mortality of patients admitted with TBI to MICU at UTH.
3. To determine the effect on the duration of time between time of injury to admission to MICU on the mortality of patients admitted with TBI in MICU at UTH.

7 RESEARCH METHODOLOGY

7.1 STUDY DESIGN

The study was a cross-sectional study.

7.2 STUDY SETTING

The study was conducted at the Main Intensive Care Unit (MICU) of the University Teaching Hospitals (UTH) in Lusaka, Zambia.

7.3 STUDY TIMEFRAME

The study took place over a period of six consecutive months, 1st August 2019 till 31st January 2020, after approval was sought from the University of Zambia Biomedical Research Ethics Committee (UNZABREC) and permission sought from the management of UTH and MICU.

7.4 STUDY POPULATION

The study population was the patients admitted with traumatic brain injury to the MICU, UTH.

7.5 INCLUSION CRITERIA

- Patients presenting with a Glasgow Coma Scale below 15, and
- Patients who were admitted to the MICU at UTH with a clinical or radiological diagnosis of traumatic brain injury (TBI), and
- Patients who had consented to take part in the study.

In this study, a diagnosis of TBI was made clinically as patients who presented to UTH with a GCS below 15, following a confirmed history of trauma involving the head in the immediate 24 hours prior to presentation to UTH. A radiological diagnosis was not used as a criterion because of unavailability of a consistently functional CT Scan machine at the UTH.

7.6 EXCLUSION CRITERIA

- Patients who were discharged from MICU less than four hours after admission.
- Patients who were transferred to another health facility or left MICU against medical advice.

7.7 SAMPLING AND DATA COLLECTION

The sample size was derived using the prevalence formula and then was corrected for a finite population. Openepi version 3 was used to calculate the sample size and the following formulae were used:

$$n = \frac{Z^2 \times P(1-P)}{E^2} = 345$$

Correction for a finite population was done as follows,

$$n' = \frac{345}{1 + \frac{Z^2 \times P(1-P)}{E^2 N}} = 60$$

Z, being 1.96, which was the statistic corresponding to a confidence interval of 95%

P, being 66%, which was the assumed mortality rate of patients admitted with TBI as determined in the previous study done in MICU at UTH

E, being the precision at +/- 5%

N, the population, based on the number of patients admitted with TBI in MICU for the year 2018 which was 72.

After calculation, the sample size was found to be 60.

Consecutive method of sampling was used. All consecutive patients who met the inclusion criteria over the six-month timeframe of data collection were recruited. Data was collected using a structured data collection sheet (Appendix 3). Data was obtained from the notes in the patients' files.

7.8 STUDY VARIABLES

The data obtained from the patients' records was as follows, which constituted the independent variables:

- Age
- Gender
- Mechanism of injury
- Glasgow coma scale (GCS) immediately before intubation
- Presence or absence of anisocoria, defined as difference in size of pupils of 1mm or more

- Mean arterial pressure (MAP) on admission to MICU
- Random blood sugar (RBS) on admission to MICU
- Body temperature on admission to MICU
- Time taken between injury to presentation to UTH
- Whether any neurosurgical intervention was done or not. (Neurosurgical intervention was defined, in this study, as any surgical procedure done following trauma which was aimed at relieving pressure on the brain, e.g., decompressive craniotomy, burr holes or placement of an intra cranial drain)
- Time taken between injury and neurosurgical intervention
- Presence or absence of extra-cranial injuries, defined as injuries involving other parts of the body apart from the brain.
- Presence or absence of convulsions during the period of admission in MICU.

The outcome variable was defined as either discharge from MICU or death.

7.9 DATA ANALYSIS

All data was coded and stored in tabular format using Microsoft Excel for Office 365 and was analyzed using Stata version 13.0.

Continuous variables were summarized using means and categorical variables were summarized using percentages.

The mortality rate of patients admitted with TBI in MICU was calculated. Univariate analysis was done using t-test for continuous variables and for categorical variables the Pearson chi-square test or Fisher's exact test (when the frequency of any variable was less than 5) was used. A p-value of less than 0.05 was considered as statistically significant.

8 ETHICAL CONSIDERATIONS

An informed consent (Appendix 1 & 2) was obtained from either the participants of the study or, where this was not possible as in the case of critically ill participants, from their

next of kin. The details of the study were explained to the participants or their next of kin using the language they were familiar with.

This study was purely observational and did not introduce any new intervention or deviate from the normal standard of care of management of TBI in MICU and this was explained to the participants of the study. Aside from the normal care that participants received in MICU, no additional procedures were done on them by virtue of this study. As such, participants were exposed to very minimal risk by participating in this study. If a participant was observed with deteriorating vital signs which could endanger the life of the participant, the standard appropriate care or help was facilitated.

Participants were free to refuse to participate or withdraw from the study at any point in time, without any consequences to them or the care they received in MICU. No participant names were included during data collection and participants were only identified by numbers. Paper records of the data collected were always stored securely under lock and key in a cupboard. Computer records of the data were securely kept on a password protected computer. All data was treated with respect and confidentiality during the study. Participants were free to contact the investigator to access the results if they wished to know the outcome of the study.

Permission was sought from the management of UTH and MICU before commencing the study (Appendix 5). Ethical approval for the research was granted by the University of Zambia Biomedical Research Ethics Committee (UNZABREC), reference number 135-2019 (Appendix 4).

9 RESULTS

A total of 78 participants met the inclusion criteria and were recruited into the study over the period of data collection. However, 1 participant was evacuated abroad for continued medical care and so withdrew from the study. As such, the total number of participants who were included for data analysis was 77.

Amongst the 77 participants included in the analysis, 25 (32%) were discharged from the main intensive care unit (MICU), while 52 (68%) died on MICU. Hence, the current mortality rate of patients admitted with traumatic brain injury (TBI) in MICU at UTH was evaluated to be 68%.

Table 1 Summary of Age and Gender Distribution

VARIABLE	**DISTRIBUTION**
Age	Range 3 – 64 (Mean age 30.9)
Gender, n (%)	Males, 65 (84%) Females, 12 (16%)

Table 1 summarizes the age and gender distribution of the participants in the study.

The study participants represented a significantly young cohort of population with a mean age of 30.9 years, with males constituting the majority of participants admitted with TBI in the MICU.

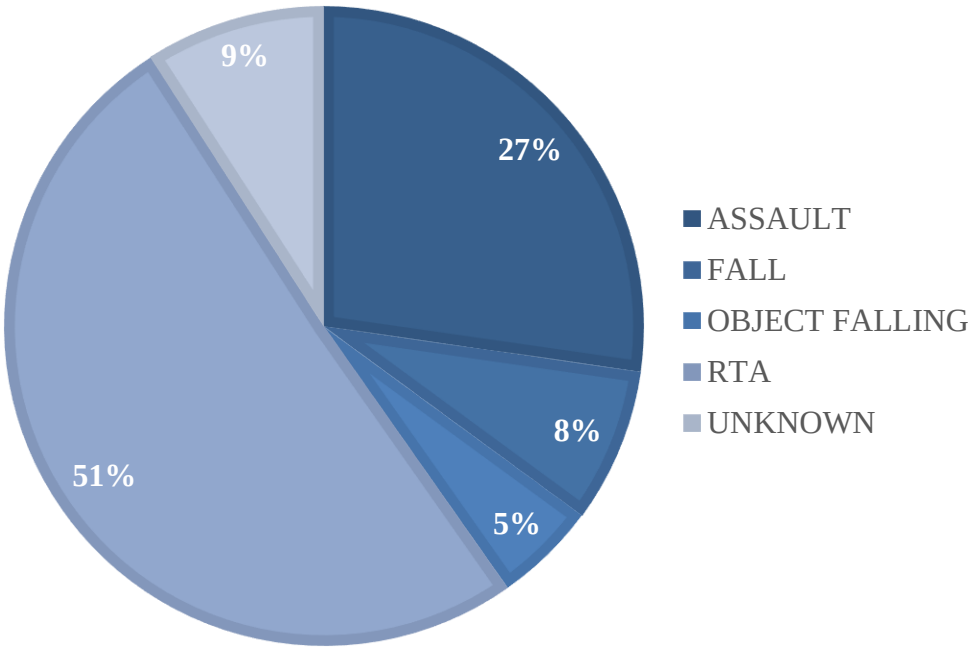

Figure 1 Summary of Mechanism of Injury

Figure 1 shows the proportions of participants with TBI according to the mechanisms of injury that caused trauma in them.

Majority of TBI patients admitted to MICU were involved in road traffic accidents (RTA), constituting 51% of the participants. This was unsurprising as it was a common finding in other studies done locally (Mwala et al, 2015) and regionally as well (Boniface et al, 2017) (Qureshi et al, 2013).

Table 2 Comparison of Socio-Demographic Characteristics Between Outcome Groups

VARIABLE		**OUTCOME**		**p-value (Fisher's exact test)**
		DISCHARGED N=25	**DIED N=52**	
AGE (years)	<16	3 (12%)	8 (15.4%)	1.000
	16 - 50	20 (80%)	41 (78.8%)	
	>50	2 (8%)	3 (5.8%)	
GENDER	Male	19 (76%)	46 (88.5%)	0.188
	Female	6 (24%)	6 (11.5%)	
MECHANISM OF INJURY	RTA	11 (44%)	28 (53.8%)	0.399
	Assault	10 (40%)	11 (21.2%)	
	Fall	2 (8%)	4 (7.7%)	
	Object falling	0 (0%)	4 (7.7%)	
	Unknown	2 (8%)	5 (9.6%)	

Table 2 shows a comparison of age, gender, and mechanism of injury of the participants between the two outcome groups.

The age of the participants was categorized as follows: less than 16 years, between 16 and 50, and greater than 50 years. Most of the participants (79%) were in the age group between 16 and 50, and this group also recorded most of the mortality (78.8%). However,

on univariate analysis, there was no statistical difference between the age groups as regards to mortality of the TBI patients (p=1.000). Males constituted the majority of the participants who died with TBI on MICU (88.5%), however, the female gender was not significantly associated with survival (p=0.188).

As the majority of the patients admitted with TBI were involved in RTAs, more than half of the participants who died (53%) were victims of RTAs, however, there was no statistically significant difference between those who survived and those who did not across all the mechanisms of injury (p=0.399).

Table 3 Comparison of Neurological Parameters Between Outcome Groups

VARIABLE		**OUTCOME**		**p-value (Fisher's exact test/Chi-square test)**
		DISCHARGED N=25	**DIED N=52**	
ADMISSION GLASGOW COMA SCALE	3 - 8	14 (56%)	49 (94.2%)	<0.001
	9 - 13	11 (44%)	3 (5.8%)	
ANISOCORIA	Present	9 (36%)	18 (34.6%)	0.905
	Absent	16 (64%)	34 (65.4%)	
CONVULSIONS	Present	1 (4%)	14 (26.9%)	0.028
	Absent	24 (96%)	38 (73.1%)	
NEUROSURGICAL INTERVENTION	Done	12 (48%)	14 (26.9%)	0.067
	Not Done	13 (52%)	38 (73.1%)	

Table 3 shows a comparison of the admission GCS, presence, or absence of convulsions and anisocoria and whether neurosurgical intervention was done or not between the participants in the two outcome groups.

Participants who were admitted with severe TBI, with a Glasgow Coma Scale (GCS) of 8 or less, had a significantly higher mortality on MICU than those admitted with moderate TBI, with a GCS of 9-13 ($p<0.001$), hence, severity of TBI correlated with increased mortality. Presence of convulsions prior to admission and during admission in MICU was also found to be significantly associated with mortality in these participants ($p=0.028$).

It was surprising to find that there was no significant difference in outcome between participants who underwent neurosurgical intervention and those who did not (p=0.067). This, as discussed below, could be due to other confounding factors such as the severity of injury and delay in admission to hospital after the injury. Neurosurgical intervention was defined, in this study, as any surgical procedure done following trauma which was aimed at relieving pressure on the brain, e.g., decompressive craniotomy, burr holes or placement of an intra cranial drain.

Table 4 Comparison of Admission Vital Signs Between Outcome Groups

VARIABLE	**OUTCOME**		**p-value (t-test)**
	DISCHARGED N=25	**DIED N=52**	
MEAN ARTERIAL PRESSURE (mmHg)	Mean MAP = 92	Mean MAP = 90	0.674
BODY TEMPERATURE (°C)	Mean temp = 36.5	Mean temp = 36.4	0.679
RANDOM BLOOD SUGAR (mmol/L)	Mean RBS = 9.0	Mean RBS = 9.2	0.847

Table 4 shows a summary of the admission vital signs i.e., mean arterial pressure (MAP), body temperature and random blood sugar (RBS) and their comparison between the two outcome groups.

The mean admission vital signs were all comparable between participants in the two outcome groups and none of these vital signs showed any statistically significant difference, as illustrated above. This showed that none of these admission vitals were associated with mortality of participants with TBI in MICU. It was also a worthy finding that the means of all the admission vitals in both outcome groups fell within the acceptable normal ranges targeted in TBI patients. This is discussed more in detail below.

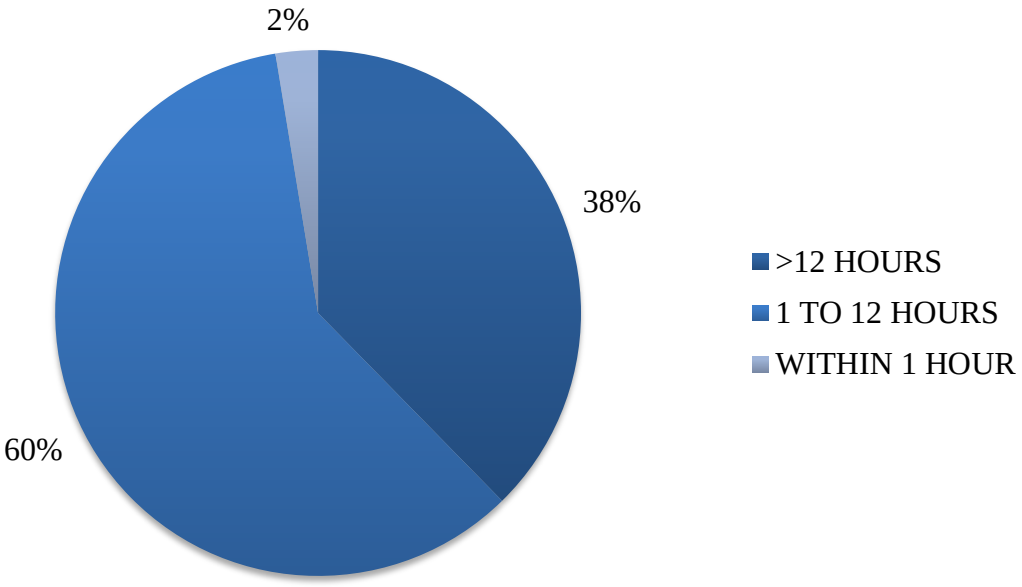

Figure 2 Duration Between Time of Injury and Presentation to UTH

Figure 2 summarizes the proportions of participants according to the time taken for them to reach UTH after the time of injury.

It was found that only a small proportion of participants reached UTH within an hour after injury occurred, and all the participants falling within this category survived. Delay in presentation to UTH of more than an hour, subsequently delayed neurosurgical intervention in those who required it.

Table 5 Comparison of Time Intervals Between Outcome Groups

VARIABLE		**OUTCOME**		**p-value (Fisher's exact test)**
		DISCHARGED	**DIED**	
TIME INTERVAL BETWEEN INJURY AND UTH (hours)	<1	2 (100%)	0 (0%)	0.041
	1 – 12	17 (37%)	29 (63%)	
	>12	6 (21%)	23 (79%)	
TIME INTERVAL BETWEEN INJURY AND NEUROSURGICAL INTERVENTION (hours)	<12	4 (67%)	2 (33%)	0.365
	>12	8 (40%)	12 (60%)	

Table 5 summarizes the comparison of the time intervals between injury and presentation to UTH and between injury and neurosurgical intervention between the two outcome groups.

It was found that a delay of more than one hour between injury and presentation to UTH was significantly associated with mortality of the participants (p=0.041). However, it was also found that there was no significant difference in outcome of the participants who had neurosurgical intervention within 12 hours and those who had intervention more than 12 hours after injury (p=0.365). This could be because the golden one-hour period within which the intervention should have been done had already elapsed and this resulted in the poor outcomes.

10 DISCUSSION

This study found the mortality rate of patients admitted with traumatic brain injury (TBI) in the main intensive care unit (MICU) at the University Teaching Hospitals (UTH) to be 68%, which is slightly higher than a previous study done at the same setting, which evaluated the mortality at 66% (Shamambo, 2016). The bed capacity at the MICU has doubled since the previous study, hence, this means an increased number of patients being admitted to MICU. This increase in the mortality is of noteworthy concern, as it showed that there has not been an improvement within the four years since the previous study.

The mortality rate in our setting was compared to other studies done in the region and was found to be higher than the mortality rate in Kenya, which was 54% (Opondo & Mwangombe, 2007), as well as in Nigeria, which was 52.2% (Tobi et al, 2016). However, it was significantly lower than the 78.2% mortality rate which was found in Tanzania (Elahi et al, 2019). This shows that our mortality rate of patients admitted to MICU with traumatic brain injury is comparable with other low- and middle-income countries (LMIC) in Africa (The World Bank Group, 2019). However, our mortality rate was found to be much higher than that in most published studies done in higher income countries (Krishnamoorthy et al, 2015) (Grigorakos et al, 2016) (Khajavikhan et al, 2016). This was unsurprising, considering the limited resources and staffing in our ICU setting. It was also due to late presentation of patients in our setting, as was shown in our study that 38% of the participants reached UTH more than 12 hours after injury. Also, in higher income settings, better admission criteria to ICU results in better selection of patients admitted to ICU and this results in better outcomes (Gerber et al, 2013).

The mean age of the participants in this study was 30.9, which showed that the patients admitted with traumatic brain injury (TBI) to the MICU is a particularly young cohort. A similar finding was documented in almost all published studies which were reviewed. An inference to this finding could be that the younger population is more active and subsequently more likely to be involved in traumatic events. However, age of the patients was not found to be significantly associated with mortality. Another similar finding to other studies published was that majority of the patients admitted with TBI were males,

however, the male gender was not significantly associated with mortality as compared to females. These findings of the younger and male population being the most involved in traumatic events and eventually dying means that it poses a negative impact on the socio-economic welfare of their families, and subsequently on the nation.

Timely hospitalization and subsequent resuscitation are important in the management of patients with traumatic brain injury, especially those with severe TBI. Timely resuscitation leads to better outcomes in patients with TBI (Kannan et al, 2018). A delay of more than 12 hours after injury was found to be significantly associated with mortality ($p=0.041$). Similarly, it was found that most of the patients (67%) who received neurosurgical intervention within 12 hours of injury survived and most of the patients who had neurosurgical intervention more than 12 hours after injury died (60%). As a result of the delay in admission to UTH, neurosurgical interventions were also delayed in these patients. A very small window period is available for management of severe TBI patients, which made up the majority of those admitted to MICU and hence, in an ideal situation, these patients need to be transferred to MICU in the shortest possible time. The first hour after injury, sometimes referred to as the "golden hour" largely determines a critically injured patient's likelihood of survival (Rogers et al, 2015). This study found that only 2% of the patients reached reasonable care within the "golden hour" after injury. The reason for this could be weaknesses in the emergency response protocol at the site of trauma as well as in the emergency medical care in the pre-hospital period. In a previous study done at UTH, which looked at trauma patient admissions, it was found that only 5.6% of all trauma patients were transported to UTH by emergency transportation services. Most of the trauma patients were either transported by private vehicles (51.8%) or public transport (37.1%) (Seidenberg et al, 2014). Most of the first responders as well the personnel who transport (private and public transport) these patients to UTH would have had no training in basic first aid, let alone training in approaching a trauma patient. In addition, it usually takes a lot of time to transport these patients to the hospital, due to long distances that need to be covered sometimes as well as other things that may not be avoidable by public or private transport, like heavy traffic congestion. Therefore, it is important to improve the emergency response system, especially in cases of RTAs, so that the delay in admission of

the TBI patients may be reduced and timely interventions, which are often indicated in the management of patients with severe TBI, can be done (McCafferty et al, 2018). Factors that may have delayed admission to UTH and delayed neurosurgical intervention in TBI patients could be plenty, but this study did not explore these factors.

Patients who had a Glasgow Coma Scale between 3 and 8 (severe TBI) on admission to MICU had a significantly higher mortality than those who had a GCS greater than 8 on admission ($p<0.001$). This was a similar finding to studies not only done regionally in Malawi, Kenya, and Tanzania (Qureshi et al, 2013) (Opondo & Mwangombe, 2007) (Boniface et al, 2017), but also in studies done in more developed countries, such as Iran, Greece, and the United Kingdom, where a lower admission GCS was associated with a higher risk of mortality (Khajavikhan et al, 2016) (Grigorakos et al, 2016) (Hawley et al, 2017). This was an unsurprising finding across most studies, as the more severe the injury to the brain, the less likely it is for recovery of the neuronal damage and hence, the increased likelihood of mortality. Even in those patients who do survive severe TBI, they do not have a favourable outcome and functional status upon discharge from hospital (Khajavikhan et al, 2016). It is important to consider this finding when making admission criteria for patient selection to ICU as it would be futile to admit a severe TBI patient, whose outcome would be poor.

The other neurological factor that was found to be significantly associated with mortality was the presence of convulsions prior to admission of the patients to MICU ($p=0.028$). Convulsions are a likely sign of severe TBI. A probable factor that could explain this increased mortality is that these patients did not receive any anti-convulsant drugs in the pre-hospital period and during the admission in the ICU. Anisocoria, or difference in size between the pupils, was not found to be significantly associated with mortality ($p=0.905$), which was also a similar finding in the study done in Kenya (Opondo & Mwangombe, 2007).

One of the factors that was surprisingly found not to be associated with mortality in TBI patients was the absence of neurosurgical interventions done on these patients. It would be expected that patients who underwent neurosurgical interventions would have a higher

likelihood of survival, but there was no significant difference in outcome in these patients. As discussed above, this finding could be because most of these patients had a significant delay in reaching the hospital, hence, even in those who did undergo neurosurgical intervention, this was much later than the golden hour within which it needed to be done. Another reason for this finding is that most of the patients who underwent neurosurgical interventions initially had severe TBI (GCS below 8), which was an independently a factor that was significantly associated with mortality.

Road traffic accidents (RTA) represented the major cause of trauma and subsequent admission of patients with TBI to MICU. More than half (51%) of the participants in this study were involved in RTAs. With the rapid growth of the road network systems and number of motor vehicles in the country, it is unsurprising that a reflecting increase in motor vehicle accidents ensues. This was also a significant finding in a previous study done at UTH, which looked at all TBI cases admitted to the hospital, regardless of whether they were admitted to MICU or not. It also found that RTAs contributed much (56.9%) to the cause of the TBI patients (Mwala et al, 2015). It also followed that much of the mortality from TBI recorded in our study was due to RTAs. Thus, it would be of much importance that road safety monitoring and education is done to try and reduce the burden of RTAs on our health systems.

It was found that none of the vital signs studied i.e., mean arterial pressure (MAP), random blood sugar (RBS) or body temperature of the patient with TBI upon admission to MICU was significantly associated with mortality. The mean MAP in both groups of patients who survived and died were comparable and were found to be within acceptable range of MAP greater than 80mmHg, which has been shown to prevent brain ischemia (Kinoshita, 2016). The mean RBS in both groups also did not show any significant difference. This was unsurprising, as intensive glycemic control in TBI patients has not been shown to reduce mortality in more recent studies done (Hermanides et al, 2018). Hence, our findings of normoglycaemia in both groups of patients conformed to findings of the above study. Admission body temperature was also found to be within normal ranges in both groups of patients, and hence did not show any significant association with outcomes of the patients. It was previously studied that therapeutic hypothermia had neuroprotective benefits in

management of TBI, but it is now known that aggressive temperature control does not lead to improved clinical outcomes (Sombat & Pornchai, 2017). Thus, normothermia, rather than permissive hypothermia is important in management of TBI patients and this was noted in our study too.

It is worth noting that the vital signs studied were those recorded upon admission only and not subsequent vital signs. The reason for this was that it was these admission vital signs that really affected the subsequent management of these patients in the MICU, and thus it was thought that these vitals were key in affecting survival of these patients. Likewise, in other studies done regionally this was the case too. Like our study, admission blood pressure of the patient was not associated with mortality in a study done in Kenya (Opondo & Mwangombe, 2007), which also studied association of admission blood sugar in TBI patients with their mortality. In contrast, other studies done regionally concluded that there was a significant association between the vital signs of the patients with TBI and mortality. Systolic blood pressure (SBP) of less than 90mmHg was significantly associated with mortality in studies done in Malawi and Tanzania (Qureshi et al, 2013) (Boniface et al, 2017). To explain these variations between similar studies, it would be worth studying the trends of the vital signs of the patients during the entire course of admission and exploring whether there were any significant differences in outcome of patients with regards to these trends.

Although this study only explored the patient-related factors that were associated with mortality of patients admitted with traumatic brain injury (TBI) in the main intensive care unit (MICU), there could be other factors, such as resource and staff related issues, that may have an impact on the mortality of these patients. These factors were not studied as they were beyond the scope of this study. It is also important to note that the patient related factors are usually the ones which are studied when it comes to development of criteria and protocols for the admission of patients to an intensive care unit. Ultimately, it is these criteria which will ensure that those patients with the higher likelihood of survival are the ones admitted to ICU, to ensure that a resource-demanding ICU is utilised appropriately.

11 CONCLUSIONS

This study evaluated an updated mortality rate of patients admitted with traumatic brain injury (TBI) in the main intensive care unit (MICU) at the University Teaching Hospitals (UTH). It also gave insight regarding the neuro-physiological factors that were associated with the mortality of these patients.

Severe TBI, with Glasgow Coma Scales (GCS) below 8, was significantly associated with high mortality as well as presence of convulsions during admission to MICU. The admission vital signs of a patient were not found to have an impact on patients' survival.

It was also learnt from this study that the majority of patients presenting with TBI reached UTH for reasonable care more than an hour after injury, and this delay not only delayed neurosurgical interventions, but was also associated with a significant increase in mortality, particularly in those patients who reached UTH more than 12 hours after injury.

The current mortality rate of patients admitted with traumatic brain injury (TBI) in the main intensive care unit (MICU) at the University Teaching Hospitals was found to be high at 68%, and this was slightly higher than found in a previous study done in the same setting. This means that there is need for improvement in the management of these patients.

12 STUDY LIMITATIONS AND STRENGTHS

12.1 STUDY LIMITATIONS

This study only explored the patient-related factors that were associated with mortality of TBI patients in MICU. It did not explore non-patient related factors, such as resources and staffing issues in MICU, which could also have an impact on mortality.

It was found that the number of females recruited was significantly lower than the number of males, so it made it difficult to make any conclusions or inferences.

The study also did not follow up patients after discharge from the main intensive care unit (MICU) to the normal wards, and hence did not consider mortality that may have occurred in the normal wards after discharge from MICU.

The functional status of patients who were discharged from MICU, in terms of what the patients were able to do by themselves upon discharge from MICU, was also not studied in this study. This plays an important role on the socio-economic welfare of the family of the patients.

12.2 STUDY STRENGTHS

The study explored a good number of physiological factors that were likely to be associated with mortality of patients with TBI in MICU. Data was systematically and easily collected, which avoided missing data.

This study added to the knowledge base of the management of patients admitted with TBI in the MICU.

13 RECOMMENDATIONS

There is need to come up with revised criteria and protocols regarding admission of TBI patients to MICU. Of note from the findings of this study is the fact that a patient's GCS below 8 on admission to MICU was associated with a higher mortality. This needs to be addressed in the admission criteria of patients to MICU to prevent futile admissions to MICU. This will also ensure that the limited resources in our ICU are utilised properly.

The delay of patients coming to the University Teaching Hospitals (UTH) after a traumatic injury is too much and there is need to improve both the emergency response to trauma patients at the site of injury as well as the emergency medical care that patients receive before admission to UTH. Further studies need to be conducted to explore what factors may help improving these services. This delay in presentation to UTH after trauma may also need to be considered in the admission criteria of these patients to MICU to prevent unnecessary admissions.

The management protocol of patients admitted to MICU with TBI needs to be revised to emphasize the importance of prevention of convulsions in these patients. It is recommended that all patients with TBI should receive adequate anti-convulsant drugs in the pre-admission period as well as during admission in MICU. It will also be good to review and escalate the current anti-convulsive drugs being used in MICU.

Further studies need to be carried out to explore whether other non-patient related factors also affect the mortality of patients admitted with TBI in the MICU.

14 REFERENCES

Boniface, R. et al (2017). Management and outcome of traumatic brain injury patients at Muhimbili Orthopaedic Institute Dar es Salaam, Tanzania. *Pan African Medical Journal,* [online] Vol. 26(140). Available at: www.panafrican-med-journal.com/content/article/26/140/full

Dinsmore, J. (2013). Traumatic brain injury: An evidence-based review of management. *Continuing Education in Anaesthesia, Critical Care & Pain,* [online] Vol. 13(6), pp. 189-195. Available at: https://academic.oup.com/bjaed/article-abstract/13/6/189/246749

Eaton, J. et al (2017). Epidemiology, management, and functional outcomes of traumatic brain injury in Sub-Saharan Africa. *World Neurosurgery,* [online] Vol. 108(1), pp. 650-655. Available at: https://www.sciencedirect.com/science/article/pii/S1878875017315917?via%3Dihub

Elahi, C. et al (2019). An evaluation of outcomes in patients with traumatic brain injury at a referral hospital in Tanzania: evidence from a survival analysis. *Neurosurgical Focus,* [online] Vol. 47(5). Available at: https://bmcneurol.biomedcentral.com/articles/10.1186/s12883-019-1246-1

Gerber, L. M. et al (2013). Marked reduction in mortality in patients with severe traumatic brain injury. *Journal of Neurosurgery,* [online] Vol. 119(12), pp. 1583-1590. Available at: https://pubmed.ncbi.nlm.nih.gov/24098983

Godoy, D.A., Behrouz, R. & Di Napoli, M. (2016). Glucose control in acute brain injury: does it matter? *Current Opinion in Critical Care,* [online] Vol. 22(2), pp. 120-127. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26866521

Grigorakos, L. et al (2016). Predictors of outcome in patients with severe traumatic brain injury. *Journal of Neuroscience & Clinical Research,* [online] Vol. 1(1). Available at: https://www.scitechnol.com/peer-review/predictors-of-outcome-in-patients-with-severe-traumatic-brain-injury-4oea.php?article_id=5494

Haddad, S.& Arabi, Y. (2012). Critical care management of severe traumatic brain injury in adults. *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine,* [online] Vol.20(12). Available at: http://www.sjtrem.com/content/20/1/12

Hawley, C. et al (2017). Traumatic brain injuries in older adults-6 years of data for one UK trauma centre: retrospective analysis of prospectively collected data. *Emergency Medicine Journal,* [online] Vol. 34(8), pp. 509-516. Available at: https://emj.bmj.com/content/34/8/509.long

Hermanides, J. et al (2018). Glycaemic control targets after traumatic brain injury: a systematic review and meta-analysis. *Critical Care (London, England),* [online] Vol. 22(1), pp. 11. Available at https://doi.org/10.1186/s13054-017-1883-y

Kannan, N. et al (2018). Timely Hemodynamic Resuscitation and Outcomes in Severe Pediatric Traumatic Brain Injury: Preliminary Findings. *Pediatric Emergency Care,* [online] Vol. 34(5), pp. 325-329. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5233691/pdf/nihms771185.pdf

Khajavikhan, J. et al (2016). Outcome and predicting factors following severe traumatic brain injury: A retrospective cross-sectional study. *Journal of Clinical and Diagnostic Research,* Vol. 10(2), pp. 16-19.

Kinoshita, K (2016). Traumatic brain injury: pathophysiology for neurocritical care. *Journal of Intensive Care,* [online] Vol. 4(29). Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4847183/

Kinyanjui, B. (2016). Traumatic brain injury in Kenya: A preliminary review of the literature. *SAGE Open,* [online] Vol. 6(1) pp. 1-7. Available at: https://www.researchgate.net/publication/298425766_Traumatic_Brain_Injury_in_Kenya_A_Preliminary_Review_of_the_Literature

Krishnamoorthy, V. et al (2015). Demographic and clinical risk factors associated with hospital mortality after isolated severe traumatic brain injury: A cohort study. *Journal of Intensive Care*, [online] Vol. 3(1), p. 46. Available at: https://www.ncbi.nlm.nih.gov/pmc/issues/249678/

Lau, D. et al (2012). Postoperative outcomes following closed head injury and craniotomy for evacuation of hematoma in patients older than 80 years. *Journal of Neurosurgery,* Vol. 116(1), pp. 234-245.

Lotfy, M., Said, A. & Sakr, S. (2010). Decompressive craniotomy after traumatic brain injury: Post operative clinical outcome. *Egypt J Neurol Psychiat Neurosurg.,* Vol. 47(2), pp. 255-259.

McCafferty, R. et al (2018). Neurosurgery and Medical Management of Severe Head Injury. *Military Medicine,* [online] Vol. 183(9/10), pp. 67-72. Available at: https://academic.oup.com/milmed/article/183/suppl_2/67/5091155

Mena, J. et al (2011). Effect of the modified Glasgow coma scale criteria for mild traumatic brain injury on mortality prediction: Comparing classic and modified Glasgow coma scale score model scores of 13. *The Journal of Trauma,* [online] Vol. 71(5), pp. 1185-1193. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3217203

Mwala, K., Munthali, J. & Chikoya, L. (2015). Factors associated with outcome in patients admitted with traumatic brain injury at the University Teaching Hospital, Lusaka, Zambia. *Medical Journal of Zambia,* Vol. 42(2), pp. 68-73.

Opondo, E. & Mwangombe, N. (2007). Outcome of severe traumatic brain injury at a critical care unit: A review of 87 patients. *The Annals of African Surgery,* Vol. 1(1), pp. 3-9.

Prabhakaran, K. et al (2017). Mortality rates of severe traumatic brain injury patients: impact of direct versus nondirect transfers. *Journal of Surgical Research,* [online] Vol. 219(11), pp. 66-71. Available at: https://pubmed.ncbi.nlm.nih.gov/29078912

Prins, M. et al (2013). The pathophysiology of traumatic brain injury at a glance. *Disease Models & Mechanisms,* [online] Vol. 6(1), pp. 1307-1315. Available at: http://dmm.biologists.org/content/6/6/1307

Qureshi, J. et al (2013). Head injury triage in a sub Saharan African urban population. *International Journal of Surgery,* [online] Vol. 11(1), pp. 265-269. Available at: http://dx.doi.org/10.1016/j.ijsu.2013.01.011

Rangel-Castilla, L. et al (2008). Cerebral pressure autoregulation in traumatic brain injury. *Neurosurgical Focus,* [online] Vol. 25(4), pp.1-8. Available at: https://pubmed.ncbi.nih.gov/18828705

Rogers, F.B., Rittenhouse, K. J. & Gross, B. W. (2015). The golden hour in trauma: dogma or medical folklore? *Injury,* Vol. 46(4), pp. 525-527.

Seidenberg, P. et al (2014). Epidemiology of injuries, outcomes, and hospital resource utilisation at a tertiary teaching hospital in Lusaka, Zambia. *African Journal of Emergency Medicine,* [online] Vol. 4(3), pp. 115-122. Available at: https://www.sciencedirect.com/science/article/pii/S2211419X14000329

Shamambo, N. (2016). *Critical Care at University Teaching Hospital, Zambia: Mortality and Quality of Life Outcomes: Cross Sectional Study.* MMed (Anaesthesia and Critical Care). UNZA.

Sharda, P., Haspani, S. & Idris, Z. (2014). Factors prognosticating the outcome of decompressive craniectomy in severe traumatic brain injury: A Malaysian experience. *Asian Journal of Neurosurgery,* [online] Vol. 9(4), pp. 203-212.

Shi, J. et al (2016). Review: Traumatic brain injury and hyperglycaemia, a potentially modifiable risk factor. *Oncotarget,* [online] Vol. 7(43), pp.71052-71061. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5342608/

Sombat, M. & Pornchai, Y. (2017). 'Targeted Temperature Management in Traumatic Brain Injury', in Nikolai, V. G. & Joseph B. L. (IntechOpen) *Traumatic Brain Injury - Pathobiology, Advanced Diagnostics and Acute Management*. Available from: https://www.intechopen.com/books/traumatic-brain-injury-pathobiology-advanced-diagnostics-and-acute-management/targeted-temperature-management-in-traumatic-brain-injury

Tierney, K. J. et al (2016). Neurosurgical intervention in patients with mild traumatic brain injury and its effect on neurological outcomes. *Journal of Neurosurgery,* [online] Vol. 124(2), pp. 538-545. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26406795

Tobi, K., Azeez, A. & Agbedia, S. (2016). Outcome of traumatic brain injury in the intensive care unit: A five-year review. *Southern African Journal of Anaesthesia and Analgesia,* [online] Vol. 22(5), pp. 135-139. Available at: https://doi.org/10.1080/22201181.2016.1206293

The World Bank Group, (2019). *Low & middle income | Data*. [online] Available at: https://data.worldbank.org/income-level/low-and-middle-income

Werner, C. & Engelhard, K. (2007). Pathophysiology of traumatic brain injury. *British Journal of Anaesthesia,* [online] Vol. 99(1), pp. 4-9. Available at: https://academic.oup.com/bja/article/99/1/4/269306

APPENDIX 1 INFORMATION SHEET FOR PARTICIPANT OR NEXT OF KIN

TITLE OF STUDY

FACTORS ASSOCIATED WITH MORTALITY OF PATIENTS ADMITTED WITH TRAUMATIC BRAIN INJURY AT THE MAIN INTENSIVE CARE UNIT, UNIVERSITY TEACHING HOSPITALS, LUSAKA – ZAMBIA

INTRODUCTION

My name is Dr Imraan Ahmed, and I am a student at the School of Medicine, University of Zambia. I am currently training to acquire a specialist degree called the Master of Medicine in Anaesthesia and Critical Care. A part of my training requires me to undertake a study. You/your relative have been invited to be part of this study, but before you decide whether to take part in the study or not, I would like to explain to you the details of the study.

BACKGROUND/RATIONALE OF THE STUDY

Traumatic brain injury (TBI) is a common condition that is managed in the main intensive care unit (MICU). It is a condition which results from injury to the brain, and which can cause significant morbidity in patients such as paralysis, coma, and seizures. This study is being done to look at what clinical factors affect outcome of patients admitted with Traumatic Brain Injury (TBI) at the Main Intensive Care Unit (MICU) at University Teaching Hospitals (UTH), Lusaka. The results of this study may help to improve the management of patients with TBI in MICU.

PROCEDURES

If you agree to take part in this study, you will be asked to sign a consent form in the presence of a witness. The study will then involve collecting information from your/your relatives' hospital file when admitted to MICU. The information collected will purely be demographic and clinical details. This information will be collected using a data sheet and it will not involve collecting any personal details such as names, identity or contact details. By agreeing to participate in this study you will not be required to give any additional

information besides the information which is already in the hospital notes and file. This study is non-experimental and you/your relative will always receive the normal standard care from the staff in MICU. No additional procedures will be performed on you/your relative because of this study. You/your relative will not be required to stay in MICU or the hospital any further than the time that will be determined by the medical staff taking care of you/your relative.

CONFIDENTIALITY

All the information that will be collected will always be treated with strict confidentiality. No personal details such as name or identity will be collected at any time during the study and none of the information that will be collected can be traced back to you/your relative. During the entire period of the study, all the information will be kept securely in a locked cabinet and on a password protected computer.

POSSIBLE RISKS

You/your relative will not be exposed to any additional risks by participating in this study. You/your relative will always be under the care of medical personnel in MICU and will receive the normal standard of care by the MICU staff as received by all other patients. This study will not add or remove any type of management and no extra procedures will be performed on you/your relative during to the study.

POSSIBLE BENEFITS

The information obtained during the study may help in your/your relatives' care and may also help in the management of patients admitted with TBI to MICU in the future.

RESULTS DISSEMINATION

The results and outcome of this study will be made freely available to you if you so wish. You may contact me at any time to enquire about the results of the study. The results of this study will also be made known to the Department of Anaesthesia & Critical Care as well as the management of MICU and UTH to know how to improve management of

patients. However, no personal details or identification will be disseminated, and no data can be traced back to you.

COSTS

You/your relative will not be required to pay anything during the study nor will you/your relative receive any financial benefit by participating in this study.

PARTICIPATION IN STUDY

Your/Your relative's participation is purely voluntary and should be out of your free will. It is not mandatory to participate in this study. You may refuse to take part in the study if you so wish and there will be no consequences on the care given to you/your relative and you will still receive the normal care in MICU. You/Your relative may withdraw from the study at any time and there will be no consequences.

Thank you for your time and consideration in participation in this study.

If you have any queries, concerns, or clarifications regarding your rights as a participant in this study, please contact me or the University of Zambia Biomedical Research Ethics Committee as follows:

Dr Imraan Ahmed
Department of Anaesthesia & Critical Care,
University Teaching Hospitals, P/Bag RW1X, Lusaka
Mobile number: +260-97-7504836
E-mail: imraan.ahmed.89@gmail.com

The Chairperson,
University of Zambia Biomedical Research Ethics Committee,
Ridgeway Campus,
P.O. Box 50110, Lusaka, Zambia
Telephone: +260-211-256067
E-mail: unzarec@unza.zm

APPENDIX 2 CONSENT FORM

I, _____, hereby confirm that the details of this study have been adequately explained to me. I have been informed of what is being done during the study and the procedures that are involved. I am aware that participation in this study will not alter my/my relatives' normal medical care. I am aware of the risks and benefits of participating in this study and I am participating in the study voluntarily. I am also aware that I may withdraw from this study at any time without any consequences. I am adequately satisfied that the information collected from this study will be confidential and it will be used for the purposes of this study only. I have been given enough time to seek clarification. I understand that by signing this form, I do not waive any of my legal rights but merely agree that I have been adequately informed about the study that I voluntarily agree to participate in. I have also received an information sheet as well as a signed copy of this consent form.

_____ _____

NAME OF PARTICIPANT PARTICIPANT SIGNATURE/THUMBPRINT

DATE:_____

_____ _____

NAME OF WITNESS WITNESS SIGNATURE

DATE:_____

_____ _____

NAME OF INTERVIEWER INTERVIEWER SIGNATURE

DATE:_____

Dr Imraan Ahmed
Department of Anaesthesia & Critical Care,
University Teaching Hospitals, P/Bag RW1X, Lusaka
Mobile number: +260-97-7504836
E-mail: imraan.ahmed.89@gmail.com

The Chairperson,
University of Zambia Biomedical Research Ethics Committee,
Ridgeway Campus,
P.O. Box 50110, Lusaka, Zambia
Telephone: +260-211-256067
E-mail: unzarec@unza.zm

APPENDIX 3 DATA COLLECTION SHEET

FACTORS ASSOCIATED WITH MORTALITY OF PATIENTS ADMITTED WITH TRAUMATIC BRAIN INJURY IN MAIN INTENSIVE CARE UNIT, UNIVERSITY TEACHING HOSPITALS, LUSAKA - ZAMBIA

DEMOGRAPHICS

Patient ID No.		Date:	_____/_____/_____
Age:		Gender:	Male Female
Mechanism of injury	RTA Assault Fall Object Falling Unknown		

ADMISSION NEUROLOGICAL STATUS

Glasgow Coma Scale	
Anisocoria	Present Absent
Convulsions	Present Absent
Neurosurgical intervention	Done Not done

ADMISSION VITALS

Mean Arterial Pressure	_____mmHg
Body Temperature	_____ºC
Random Blood Sugar	_____mmol/L

DELAYS			
Injury to UTH	Within 1 hour	1-12hours	>12hours
Injury to neurosurgical intervention	Within 1 hour	1-12hours	>12hours

EXTRA-CRANIAL INJURIES	Present	Absent

OUTCOME	Discharged	Died

APPENDIX 4 ETHICAL CLEARANCE

UNIVERSITY OF ZAMBIA
BIOMEDICAL RESEARCH ETHICS COMMITTEE

Telephone: 260-1-256067
Telegrams: UNZA, LUSAKA
Telex: UNZALU ZA 44370
Fax: + 260-1-250753
Federal Assurance No. FWA00000338

Ridgeway Campus
P.O. Box 50110
Lusaka, Zambia
E-mail: unzarec@unza.zm
IRB00001131 of IORG0000774

1st August, 2019.

REF. No. 135-2019

Dr. Ahmed Imraan,
University Teaching Hospital,
Registrar at Anaesthesia and Critical Care,
P/Bag RW 1X,
Lusaka.

Dear Dr. Imraan,

RE: "FACTORS ASSOCIATED WITH MORTALITY OF PATIENTS ADMITTED WITH TRAUMATIC BRAIN INJURY AT THE MAIN INTENSIVE CARE UNIT, UNIVERSITY TEACHING HOSPITALS, LUSAKA- ZAMBIA" (Ref. No. 135-2019)

The above-mentioned research proposal was presented to the Biomedical Research Ethics Committee on 31st July, 2019. The proposal is **approved**. The approval is based on the following documents that were submitted for review:

a) **Study proposal**
b) **Questionnaires**
c) **Participant Consent Form**

APPROVAL NUMBER : REF. 135-2019
This number should be used on all correspondence, consent forms and documents as appropriate.

- **APPROVAL DATE : 1st August 2019**
- **TYPE OF APPROVAL : Standard**
- **EXPIRATION DATE OF APPROVAL : 31st July 2020**
  After this date, this project may only continue upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the UNZABREC Offices should be submitted one month before the expiration date for continuing review.
- **SERIOUS ADVERSE EVENT REPORTING**: All SAEs and any other serious challenges/problems having to do with participant welfare, participant safety and study integrity must be reported to UNZABREC within 3 working days using standard forms obtainable from UNZABREC.
- **MODIFICATIONS**: Prior UNZABREC approval using standard forms obtainable from the UNZABREC Offices is required before implementing any changes in the Protocol (including changes in the consent documents).
- **TERMINATION OF STUDY**: On termination of a study, a report has to be submitted to the UNZABREC using standard forms obtainable from the UNZABREC Offices.

- **NHRA:** Where appropriate, apply in writing to the National Heath Research Authority for permission before you embark on the study.
- **QUESTIONS**: Please contact the UNZABREC on Telephone No.256067 or by e-mail on unzarec@unza.zm.
- **OTHER**: Please be reminded to send in copies of your research findings/results for our records. You're also required to submit electronic copies of your publications in peer-reviewed journals that may emanate from this study. Use the online portal: unza.rhinno.net for further submissions.

Yours sincerely,

Sody Mweetwa Munsaka, BSc., MSc., PhD
CHAIRPERSON
Tel: +260977925304
E-mail: s.munsaka@unza.zm

APPENDIX 5 PERMISSION TO CONDUCT RESEARCH

Dr. Imraan Ahmed,
Department of Anaesthesia & Critical Care,
University Teaching Hospitals – Adult,
Lusaka, Zambia.

03rd June 2019

Head Clinical Care,
University Teaching Hospitals – Adult,
P/Bag RW1X, Lusaka.

Dear Sir,

RE: PERMISSION TO CONDUCT RESEARCH IN MAIN INTENSIVE CARE UNIT, UNIVERSITY TEACHING HOSPITALS, LUSAKA

I refer to the above mentioned.

I am hereby applying to your office for permission to conduct a study entitled "**FACTORS ASSOCIATED WITH MORTALITY OF PATIENTS ADMITTED WITH TRAUMATIC BRAIN INJURY AT THE MAIN INTENSIVE CARE UNIT, UNIVERSITY TEACHING HOSPITALS, LUSAKA**". The duration of the study will be six (6) months from July to December 2019.

I am a student pursuing a Masters of Medicine degree in Anaesthesia and Critical Care at the University of Zambia, School of Medicine. A partial requirement for the award of this degree is for me to complete research in my area of clinical practice. I am also currently working as a Registrar in the Department of Anaestheisa and Critical Care.

Attached is a copy of the research proposal.

Your consideration will highly be appreciated.

Yours sincerely,

Dr. Imraan Ahmed
+260-977-504836
imraan.ahmed.89@gmail.com

NATIONAL HEALTH RESEARCH AUTHORITY
Paediatric Centre of Excellence, University Teaching Hospital, P.O. Box 30075, LUSAKA
Tell: +260211 250309 | Email: znhrasec@gmail.com | www.nhra.org.zm

Ref No:…… **Date: 20th January, 2020**

The Principal Investigator
Dr. Ahmed Imraan,
University Teaching Hospital,
Registrar at Anaesthesia and Critical Care,
P/Bag RW 1X,
Lusaka.

Dear Dr. Imraan,

Re: Request for Authority to Conduct Research

The National Health Research Authority is in receipt of your request for authority to conduct research titled **"Factors Associated with Mortality of Patients Admitted with Traumatic Brain Injury at the Main Intensive Care Unit, University Teaching Hospitals, Lusaka - Zambia."** I wish to inform you that following submission of your request to the Authority, our review of the same and in view of the ethical clearance, this study has been **approved** on condition that:

1. The relevant Provincial and District Medical Officers where the study is being conducted are fully appraised;
2. Progress updates are provided to NHRA quarterly from the date of commencement of the study;
3. The final study report is cleared by the NHRA before any publication or dissemination within or outside the country;
4. After clearance for publication or dissemination by the NHRA, the final study report is shared with all relevant Provincial and District Directors of Health where the study was being conducted, University leadership, and all key respondents.

Yours sincerely,

Dr. Godfrey Biemba
Director/CEO
National Health Research Authority

APPENDIX 6 GRADUATE PROPOSAL PRESENTATION FORUM

UNIVERSITY OF ZAMBIA
SCHOOL OF MEDICINE

Telephone : +260211252641
Telegram: UNZA, Lusaka
Telex: UNZALU ZA 44370
P.O Box 50110
Lusaka, Zambia
Email: assistantdeanpgmedicine@unza.zm

7 June 2019

Dr. Imraan Ahmed
UNZA, School of Medicine
C/O Department of Surgery
LUSAKA

Dear Dr. Ahmed

RE: GRADUATE PROPOSAL PRESENTATION FORUM

Following the presentation of your proposal entitled **"Factors Associated with Mortality of Patients Admitted with Traumatic Brain Injury at the Main Intensive Care Unit, University Teaching Hospitals, Lusaka"** your supervisor has confirmed that the necessary corrections to your research proposal has been done.

You can proceed and present to the Research Ethics.

Yours faithfully,

Dr. P. Machona
ASSISTANT DEAN, POSTGRADUATE

cc: Head, Department of Surgery

UNIVERSITY OF ZAMBIA
SCHOOL OF MEDICINE
- 7 JUN 2019
ASSISTANT DEAN (PG)
P.O. BOX 50110, LUSAKA.