PREDICTORS OF OUTCOME OF TREATMENT FOLLOWING SEVERE HEAD INJURY AT MOI TEACHING AND REFERRAL HOSPITAL, (MTRH). ELDORET, KENYA.

BY:

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DECLARATION

Declaration by the Candidate

This thesis is my personal original work and has not been presented for a degree in any other University. No part of this thesis may be reproduced without the prior written permission of the author and/or Moi University.

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DEDICATION

To my wife, Alice and my children Ashley and Bernice for being so wonderful and understanding during the genesis of this work.

ABSTRACT

Background: Severe head injury (SHI) is one of the leading causes of morbidity, disability and mortality among trauma patients. SHI is a dual assault condition mainly primary and secondary. The primary assault results from the anatomic changes caused by the injury. The secondary assault results when the already injured brain tissue is subjected to further injury from hypoxia, hypotension, hypothermia, acidosis and raised intracranial pressure. These are the factors that can be modified to influence the outcome. MTRH receives most of the trauma patients from the larger Western Kenya and North Rift regions. There is no data on outcomes and factors influencing the outcome of these patients at MTRH.

Objective: To establish the predictors of the outcome following severe head injury among patients treated at MTRH.

Methods: A prospective study was conducted at MTRH for 12months between November 2013 and October 2014. Consecutive hospital-based sampling method was used. Multiple variables associated with outcome were identified. These were age, admission GCS, pupil size and its reaction to light, time interval between accident and admission, hypotension, hypothermia, hypoxia, acidosis and associated injuries. Each variable was analyzed and its effect on outcome documented. Those that showed significant associations at bivariate level were further analyzed using logistic regression. The statistical significance was at 95% confidence interval. The outcomes were favorable and unfavorable based on the functional disability.

Results: A total of 84 patients were enrolled, their ages ranged between 1year and 80years, median age of 29.5 years. Majority were Males 72 (85.7%). A total of 62 (73.8%) patients were referred and 22 (26.2%) brought directly from the accident scene. Pre- hospital care lacked in both groups. Significant predictors of unfavorable outcomes were: old age $p = 0.046$, admission GCS of ≤ 6 $p = 0.022$ and unequal pupil size with non-reaction to light (anisocoria) $p = 0.003$. Non-significant predictors of outcome were blood pressure, pulse, hypoxia and other associated injuries with $p = > 0.05$. The outcomes were: favorable ranging from no disability 1.1% to severe disability 2.3% and unfavorable outcomes comprising of extremely severe disability 4.5% and death. The Case mortality rate was at 38.6%. Most patients with severe TBI required ICU care; however, only 6 patients accessed it.

Conclusion: The study showed that the unfavorable outcome of severe head injuries at MTRH was associated with old age (> 60 yrs.), admitting GCS of below 6 and unequal pupil dilation with no reaction to light.

Recommendations: The standard of care protocols for severe TBI patients managed at MTRH should be reviewed to include admission of; elderly patients (≥ 60 years) with severe TBI, those with a low GCS of below 6 and those with unequal pupil dilation with no reaction to light to ICU. This study should be confirmed in future using multicenter hospitals.

DISCLOSURE

I did not receive any outside funding or grants in support of this study. Neither I nor a member of my immediate family received any payments or any other benefits or commitments or agreed to the providence of such benefits from any commercial entity.

Sign…… Date ……

KULOBA BURUDI DOUGLAS

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OPERATIONAL DEFINATIONS.

Head injury - any trauma to the head (scalp, skull or brain)

Traumatic brain injury – is a non-degenerative, non-congenital insult to the brain from an external mechanical force, possibly leading to permanent or temporary impairment of cognitive, physical and psychosocial functions, with an associated diminished or altered state of consciousness.

Acidosis- the accumulation of acid or hydrogen ions or depletion of alkaline reserve (bicarbonate content in the blood and body tissues, resulting in a decrease in PH.

Amnesia - loss of memory may be partial or total.

Anisocoria. - UN equal pupil sizes.

Coma- a state of deep, unarousable unconsciousness.

Concussion- is a clinical syndrome characterized by immediate and transient alteration in brain function, including alteration of mental status and level of consciousness resulting from mechanical force or trauma.

Contusion- is a bruise on the cerebral cortex associated with brain trauma of sufficient force to bruise the brain surface and cause extravasation of blood without rupturing the pia and arachnoid matter.

Hypoxia - is a condition in which the body or a region of the body is deprived of adequate oxygen supply at the tissue level.

Hypotension - a systolic blood pressure of less than 90mmhg and a diastolic blood pressure of less than 60mmhg. This varies in children based on their respective age.

Hypertension - a systolic blood pressure of 140 mmhg and above or a diastolic blood pressure above 90 mmhg**.** This varies in children based on their respective age.

Hypothermia - a low core body temperature of 35^0 C and below. Normal core body temperature is between $36.6\ ^0$C – $37.7\ ^0$C.

Hypoglycemia - a condition characterized by abnormally low levels of blood sugar (glucose) is associated a variety of symptoms including clumsiness, confusion, loss of consciousness, seizures or death.

ABBREVIATIONS AND ACRONYMS

A/ E.	Accident and Emergency.
AMPATH	Academic model for providing access to health
ATP	Adenosine triphosphate.
BBB.	Blood Brain Barrier.
BP.	Blood Pressure.
CBF.	Cerebral Blood Flow.
CPP.	Cerebral perfusion pressure.
CSF.	Cerebral spinal fluid.
CT.	Computerized Tomography.
GCS.	Glasgow Coma Scale.
ICU.	Intensive Care Unit.
JOORTH.	Jaramogi Oginga Odinga Teaching and Referral Hospital.
KNH.	Kenyatta National Hospital.
MTRH.	Moi Teaching and Referral Hospital.
TBI.	Traumatic Brain Injury.

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CHAPTER ONE

INTRODUCTION

1.1 Background information.

Head injury is a broad term that implies any trauma to the head other than superficial injuries to the face. Traumatic brain injury is defined as a non-degenerative, non-congenital insult to the brain from an external mechanical force leading to permanent or temporary impairment of cognitive, physical and psychosocial functions with an associated diminished or altered state of consciousness. In this study severe head injury (SHI) implies severe traumatic brain injury (TBI). The Glasgow Coma Scale (GCS) is a tool that defines the severity of a TBI within 48hrs. Severe TBI denotes trauma to the brain with an associated GCS of ≤ 8.

Traumatic brain injury is a dual insult condition comprising of the primary and the secondary insult processes.

The primary insult is the physical or anatomic damage caused at the time of injury producing injured cells (neurons). Two mechanisms are known to cause primary insult and these are contact (e.g. when an object strikes the head or the brain strikes the inside of a skull) and acceleration – deceleration (Gurdjian, Lissner, Hodgson, & Patrick, 1966). The secondary injury / insult is not mechanically induced; it may be delayed from the moment of impact and may superimpose injury on a brain already injured by a mechanical event. These secondary insults are systemic factors which include hypothermia, hypoxia, acidosis, hypercapnia, hypocapnia, hyperglycemia, hypoglycemia and increased intracranial pressure. When present these factors further injure an already injured brain. These factors can be prevented or modified to influence the outcome. When present, these factors raise the mortality rate to 36% (Jeremitsky,

Omert, Dunham, Protetch, & Rodriguez, 2003; Marshall et al., 1991; Opondo & Mwangombe, 2007).

Head injuries are of significance because of the fact that many patients who die or who are disabled belong to the young age groups. They account for 1% of all deaths, one fourth of the deaths due to trauma and are responsible for half of all deaths from road traffic accidents. Majority of the patients are young adult males. Head injury is a frequent cause of emergency department attendance, accounting for approximately 3.4% of all presentations with an incidence of around 450 cases per 100,000 population per year.

It has been estimated that traumatic brain injuries affect over 10 million people annually leading to either mortality or hospitalization (Hyder, Wunderlich, Puvanachandra, Gururaj, & Kobusingye, 2007).

The cost of unfavorable outcome from traumatic brain injury is measured not only in personal terms but also socio – economic costs of neurological rehabilitation, long term nursing and supportive care and lost income generation(Bailey, Bulstrode, & Love, 2008)

1.2 Statement of the problem

Severe traumatic brain injury (TBI) is associated with high morbidity and mortality rates. Traumatic brain injury has been termed as “a silent global epidemic” accounting for up to 30% of all trauma related deaths and is the leading cause of death in young males in the developed countries (Hyder et al., 2007), while in the medium and low income countries this number is much higher.

Severe head injury results in physical, cognitive, social, emotional and behavioral symptoms. Outcomes often range from complete recovery to permanent disability or death.

In Kenya, Studies previously done at KNH have put the mortality rate as high as 56% (Mwang'ombe & Kiboi, 2001), Bugando medical Centre in Tanzania at 78.2%(Chalya, Kanumba, Mabula, Giiti, & Gilyoma, 2011) and Mulago in Uganda at 72%(Tran et al., 2015)

Severe TBI commonly affects the low and middle-income earners; it is increasing due to an increase in urbanization, motorization, civil violence and criminal activities. Poor or nonexistent pre-hospital care and inadequate number of trauma centers contributes to a high number of unfavorable outcomes.

MTRH handles almost all severe TBI patients referred from hospitals within the neighboring counties and within Uasin Gishu County we sought to identify the factors associated with their outcome.

1.3 Justification

This study will provide information that will be useful for patient education, educating both MTRH staff and the referring facilities.

This study will also provide information that will aid the hospital in planning and resource utilization.

This study serves as a baseline upon which future studies can be conducted.

1.4 Research question

How do the pre and post injury factors influence the outcome of treatment of severe head injury patients at MTRH?

1.5 Broad objectives

1. To determine the outcome of treatment of severe head injury patients managed at MTRH.
2. To determine factors that influence outcome of treatment of severe head injury in patients managed at MTRH.

1.6 Specific objectives

1. To determine pre-injury factors that influence the outcome of treatment of patients with severe head injury at MTRH.
2. To determine post injury factors that influence the outcome of treatment of patients with severe head injury at MTRH.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Introduction

Head injury refers to injuries affecting not only the brain but also other structures of the head such as the scalp and skull. Traumatic brain injury (TBI) is defined as damage to the brain also known as intracranial injury. These may result from external mechanical force such as rapid acceleration or deceleration, impact, blast waves or penetration by a projectile (Maas, Stocchetti, & Bullock, 2008). Brain function is temporarily or permanently impaired and structural damage may or may not be detectable with the current technology (Parikh, Koch, & Narayan, 2007). The two terms are often used interchangeably. In this study severe head injury will be used to signify severe traumatic brain injury (TBI).

Head injury can be classified as either open or closed depending on whether the skull was fractured with the resultant leakage of cerebral spinal fluid. Glasgow coma scale (GCS) is an assessment tool that is used to grade Head injury into three, mild (13 -15), moderate (9 – 12) and severe head injury ≤ 8.

Severe head injury is defined as trauma to the head with a resulting in a GCS of 8 or less (Badjatia et al., 2008). Primary head injuries occur at the time of impact and this include extradural, subdural hematoma, and intracerebral hematoma, cerebral contusions and diffuse axonal injuries. Insults such as hypoxia, hypotension or hyperpyrexia result in further cerebral damage causing secondary brain damage.

Every year about 1.5 million affected people die and several million receive emergency treatment ((US) & Surgeons, 2000). Kenya has experienced a rapid increase in the number of traffic related injuries and their consequences in terms of mortality, morbidity and disability (Assum, 1998).

The incidence of TBI is high. Towards the end of the last century UK had about 1 million of the emergency department attendees in a year that had TBI. The highest incidence is seen in males aged between 15-24 years; about 90% had minor head injury, with a low case fatality of between 0.04% and 0.29%, almost exclusively caused by intracranial hemorrhage (epidural or subdural hematomas). After more severe head injury, case fatality was noted to be much higher (up to 4%) (van Dijk, 2011)

In the past 10-20 years, prevention of road traffic accidents has received more attention from both National and local governments, making traffic less dangerous, encouraging cyclists to wear helmets, enforcing seat belts etc. and the incidence of head injury has fallen as a consequence. However , in the developing countries, TBI from road traffic accidents are escalating (van Dijk, 2011).

Patients with severe TBI have a high mortality rate (30-50%) and many survivors will have persistent neurological disabilities. Prompt identification and appropriate early management of TBI is essential to improve outcome (Thornhill et al., 2000). The burden of mortality and morbidity that traumatic brain injury imposes on society is manifested throughout the world and is especially prominent in the low and middle-income countries which face a high preponderance of risk factors for the causes of

severe head injury and have inadequately prepared health systems to address the associated health outcomes.

2.2 Causes of severe head injury

Common causes of severe head injury include: -

1. Vehicle related crashes: - collisions involving cars, motor cycles or bicycles and pedestrians involved in such accidents are a common cause of traumatic brain injury. Severity will depend on a couple of factors such as drunken driving, speeding, failure to use protective wear and poor state of roads.
2. Falls: - falling out of bed, slipping in the bathroom, falling down steps, falling from ladders, falling off a roof top and related falls are the most common cause of severe TBI overall, particularly in older adults and young children.
3. Violence: - about10 % of traumatic brain injuries are caused by violence such as gunshot wounds, domestic violence or child abuse, a blow to the head by a blunt object. Shaken baby syndrome is traumatic brain injury caused by violent shaking of an infant that damages brain cells.
4. Sports related injuries: - Traumatic brain injuries may be caused by injuries from a number of sports including soccer, boxing, baseball, hockey and other high impact sports.
5. Explosive blasts and other combat injuries: - explosive blasts are a common cause of traumatic brain injury in active – duty military personnel. Traumatic brain injury also results from penetrating wounds, severe blows to the head with shrapnel or debris and falls or bodily collisions with flying objects following a blast.

2.3 Pathophysiology of traumatic brain injury

TBI may occur via two (2) mechanisms

1. Focal brain damage due to contact injury types resulting in contusions, lacerations and intracranial hematoma (Werner & Engelhard, 2007).
2. Diffuse brain damage due to acceleration / deceleration injury types resulting in diffuse axonal injury or brain edema (Werner & Engelhard, 2007).

TBI is a dual insult injury: -

1. **Primary insult**: - also known as primary damage or mechanical damage which occurs at the time of impact. This type of injury is preventable at the community and personal level.
2. **Secondary insult**: - also known as delayed non-mechanical damage which represents consecutive pathological processes initiated at the time of injury with delayed clinical presentation e.g. cerebral ischemia and intracranial hypertension. These are usually sensitive to therapeutic interventions. These lesions include the following
    a) Hypoxia.
    b) Hypotension.
    c) Raised intracranial pressure.
    d) Reduced cerebral perfusion pressure.
    e) Pyrexia.
    f) Seizures

The first stage of cerebral injury after TBI is characterized by direct tissue damage, impairment or both with resultant impaired regulation of CBF and metabolism. The "ischemia like state" leads to accumulation of lactic acid due to anaerobic glycolysis,

increased membrane permeability and subsequent edema formation. The anaerobic metabolism is inadequate to maintain cellular energy requirements leading to the depletion of ATP stores and failure of energy dependent membrane ion pumps.

The second stage of pathophysiological cascade is characterized by membrane depolarization along with excessive release of excitatory neurotransmitters e.g. glutamate, aspartate, activation of N-Methyl-D-aspartate, α-amino-3-hydroxy-5-methyl-4-isoxazolpropionate, and voltage dependent calcium ($Ca^{2+)}$ and sodium (Na^{+}) channels. The consecutive Calcium and sodium influx lead to self-digesting intracellular processes. Calcium activates lipid peroxidases, proteases and phospholipases which increase the intracellular concentration of free fatty acids and free radicals.

Activation of caspases, translocases, and endonucleases initiates progressive structural changes of biological membranes and the nucleosomal DNA (DNA fragmentation and inhibition of DNA repair). These events lead to membrane degradation of vascular and cellular structures and untimely necrosis or apoptosis.

2.3.1 Cerebral blood flow

Hyper perfusion and hypoperfusion.

Cerebral ischemia after TBI is associated with poor neurological outcomes (Bouma et al., 1992; Inoue et al., 2005; Werner & Engelhard, 2007). Cerebral ischemia leads to metabolic stress and ionic disturbances while the head trauma exposes the brain tissue to shear forces with consecutive structural injury of neuronal cell bodies , astrocytes , microglia and cerebral micro vascular and endothelial cell damage (DeWitt & Prough, 2003; Lewelt, Jenkins, & Miller, 1980; Rodríguez□Baeza, Reina□de la Torre, Poca, Martí, & Garnacho, 2003; Werner & Engelhard, 2007). Post traumatic ischemia occurs

due to morphological injury e.g. vessel distortion due to mechanical displacement , hypotension in the presence of autoregulatory failure , inadequate availability of nitric oxide or cholinergic neurotransmitters and potentiating of prostaglandin induced vasoconstriction (DeWitt & Prough, 2003; McIntosh et al., 1996; McLaughlin & Marion, 1996; Werner & Engelhard, 2007).

Cerebral hyper perfusion can occur in the early stages of injury as evidenced by hyperemia (Kelly et al., 1996). This is equally as catastrophic as hypoperfusion because an increase in CBF beyond matching metabolic demands leads to vasoparalysis with consecutive increase in cerebral blood volume leading to raised intracranial pressure (Kelly et al., 1997).

2.3.2 Cerebrovascular autoregulation and carbon dioxide (CO2) reactivity

Adequate CBF is maintained via cerebral vascular autoregulation and CO_2 reactivity. Both patterns form the basis for management of CPP (cerebral perfusion pressure) and ICP. Impairment of these regulatory mechanisms leads to increased risk of secondary brain damage (secondary insult).

TBI impairs CBF autoregulation which can occur immediately following injury or after some time in a transient or persistent manner (Enevoldsen & Jensen, 1978), (Hauerberg, Xiaodong, Willumsen, Pedersen, & Juhler, 1998). Autoregulatory vasoconstriction is more resistant as compared to autoregulatory vasodilatation, hence patients are more prone to damage from low rather than high Cerebral perfusion pressure (DeWitt & Prough, 2003). Severe TBI patients who develop an impaired CO2 reactivity in the early stages of trauma tend to have poor outcomes.

2.3.3 Cerebral vasospasms

Post traumatic vasospasm is an important cause of secondary cerebral insult leading to poor outcomes (Lee et al., 1997). This occurs between the 2nd and 15th post traumatic days, as a result hypo perfusion ensues. Cerebral vasospasm occurs due to chronic depolarization of smooth vascular muscles due to reduced potassium (K^+) channel activity, release of endothelin and reduced availability of Nitric oxide, cyclic GMP ($_C$GMP) depletion of vascular smooth muscle, potentiating of prostaglandin – induced vasoconstriction and free radical formation (DeWitt & Prough, 2003; McLaughlin & Marion, 1996).

2.3.4 Cerebral metabolism dysfunction

Cerebral metabolism is reflected by cerebral oxygen and glucose consumption, cerebral energy states reflected by tissue concentrations of phosphocreatine and ATP or indirectly by (acetate / pyruvate ratio which are reduced after TBI and present with considerable temporal and spatial heterogenicity (Cunningham et al., 2005). The severity of the trauma is directly proportional to the degree of metabolic failure and hence worse outcomes in patients with very low metabolic rates. The primary trauma that relates to the decrease in cerebral metabolic rate leads to mitochondrial dysfunction with decreased respiratory rates and ATP production, decreased availability of nicotinic co-enzyme pool, and intramitochondrial calcium levels (Ca^{2+}) overload (Tavazzi et al., 2005; Verweij et al., 2000). The decrease in cerebral metabolic demand may or may not be matched with the decrease in CBF.

2.3.5 Excitatory and Oxidative stress

Severe TBI is associated with massive release of excitatory amino acid neurotransmitters especially glutamate. Excessive extracellular glutamate affects neurons and astrocytes resulting in overstimulation of ionotropic and metabotropic glutamate receptors with consecutive calcium (Ca^{2+}), Sodium (Na^{+}) and Potassium (K^{+}) influxes (Ross Bullock et al., 1998; Floyd, Gorin, & Lyeth, 2005; Yi & Hazell, 2006). This triggers catabolic processes e.g. the breakdown of Brain blood barrier (BBB), cellular compensatory mechanisms to try and correct this the ionic gradients increase Na^{+} / K^{+} ATPase activity and in turn metabolic demand creating a vicious cycle of flow – metabolism uncoupling to the cell.

Oxidative stress leads to the generation of reactive oxygen radicals (oxygen free radicals and associated entities including superoxide, hydrogen peroxide, nitric oxide, and peroxinitrite) in response to TBI.

These excessive production of reactive oxygen species (radicals) due to excitotoxicity and exhaustion of endogenous antioxidant system (superoxide dismutase, glutathione peroxidase and catalase) induces peroxidation of cellular and vascular structures, protein oxidation, cleavage of DNA and inhibition of mitochondrial electron transport chain (Bayır et al., 2005; Werner & Engelhard, 2007). This process leads to immediate cell death, early or late apoptosis (Chong, Li, & Maiese, 2005).

2.3.6 Brain Edema

Primary (1^{o}) and secondary (2^{o}) cerebral insults cause structural damage or water and osmotic imbalances resulting in edema. The brain edema can be vasogenic or cytotoxic.

1. Vasogenic brain edema is caused by mechanical or autodigestive disruption or functional breakdown of the endothelial cell layer (BBB). The disruption of the vascular endothelial wall allows for uncontrolled ion and protein transfer into the extracellular (interstitial) brain compartment leading to edema.

2. Cytotoxic brain edema is characterized by intracellular H_2O accumulation in the neurons, astrocytes and microglia irrespective of the integrity of the vascular endothelial wall. This is caused by increased cell membrane permeability for ions, ionic pump failure due to energy depletion and cellular reabsorption of osmotically active solutes. These two types of brain edema lead to a raised intracranial pressure.

2.3.7 Inflammation

Both primary and secondary cerebral insults result in the release of cellular mediator's e.g. pro inflammatory cytokines, prostaglandins, free radicals and the activation of the complement system. This processes induce chemokines and adhesion molecules which in turn mobilize immune and glial cells in a parallel and synergistic manner (Lucas, Rothwell, & Gibson, 2006; Obrenovitch & Urenjak, 1997).

Following injury, activated polymorphs infiltrate the lesion together with macrophages and T lymphocytes, these is facilitated by the up regulation of cellular adhesion molecules e.g. P – Selectin, intracellular adhesion molecules (ICAM-1) and vascular adhesion molecules (VCAM-1) leading to the destruction or elimination of the damaged tissues within hours, days or even weeks.

Pro inflammatory enzymes e.g. TNF, interleukin 1β and interleukin 6 are upregulated within hours from injury. This progression of tissue damage relates to direct release of neurotoxic mediators or the release of nitric oxide and cytokines, vasoconstrictors (prostaglandins, leukotrienes), obliteration of microvasculature through adhesion of leucocytes, platelets, the BBB lesion and edema formation further reduces tissue perfusion consequently aggravating secondary brain damage.

Two types of cell death may occur after TBI i.e. necrosis and apoptosis

1. Necrosis in response to severe mechanical or ischemic / hypoxic tissue damage with excessive release of excitatory amino acid neurotransmitters and metabolic failure. Subsequently phospholipases, proteases and lipid peroxidases autolyze biological membranes.
2. Apoptosis, cells undergoing apoptosis remain structurally intact immediately or even hours after the trauma but later begin to systematically disintegrate.

2.3.8 Intracranial hematoma

Extradural / epidural hematoma: the blood clot collects between the dura and the inner table of the skull, commonly in the middle cranial fossa as a result of tearing of the middle meningeal vessels (vein and artery). Approximately 20 – 25 % of extradural hematomas can occur at the frontal, parietal regions of the vertex or in the posterior cranial fossa. Injury / rapture of the Dural venous sinuses or a large diploic venous channel may be responsible. The presentation depends on the source of the bleed, as hyper acute when it develops very rapidly or slowly over a period of hours to a few days (chronic lesion); these are associated with a fractured skull.

Subdural hematoma: this is the accumulation of blood between the dura and the arachnoid mater. These occur due to disruption of the cortical vessels or brain laceration. The patients who sustain an acute subdural hematoma tend to lose consciousness immediately. Those who present with subacute subdural hematoma will present 10 -14 days after the injury. Patients with chronic subdural hematoma will be elderly patients with a history of trivial or minor head injury usually weeks or months before presentation.

Subarachnoid hematoma: in this case bleeding is direct into the subarachnoid space hence mixing with CSF.

Intracerebral hematoma: - this occurs within the brain parenchyma and can also cause mass effects.

2.4 Outcome of severe head injury

The Glascow outcome scale (GOS) has been used widely to determine the functional outcome after head injury, despite its widespread use questions have been raised about its reliability, sensitivity, validity and its relevance. The reliability of GOS on assigning outcomes is based on a number of considerations. The criteria for differentiating between outcome is not clearly defined however, it is generally accepted that severe disability implies total dependence. These was proved by various studies (Brooks, Hosie, Bond, Jennett, & Aughton, 1986; Maas, Braakman, Schouten, Minderhoud, & van Zomeren, 1983). These has resulted in variations in outcome following severe head injury where GOS was used by different observers using the same data or even by the same observer on different occasions, the modified Rankin scale has tried to address these variations by clearly defining each score based on their ability to perform Daily activities of living (DAL). The clinical outcomes were evaluated at the time of discharge / death according to the modified Rankin scale. The Modified Rankin scale is a commonly used scale for measuring the degree of disability or dependence in daily activities of life for people who have suffered a stroke or other causes of neurological disability. It is a widely used measure of clinical outcome. It was introduced in 1957 by Dr John Rankin of Stobhill hospital, Glasgow, Scotland. It was then modified to its current form by Professor C. Warlow's group at Western general hospital in England (Rankin, 1957).

The scale runs from 0-6 ranging from perfect health without symptoms to death. Persisting disability after brain damage comprises both mental and physical handicap. The mental component is often the more important in contributing to the overall social

disability. Lack of an objective scale leads to vague and over optimistic estimates of outcome which obscure the ultimate results of early management. The seven (7) point scale was used to analyze the outcome (Wilson et al., 2002). The duration considered was immediate outcomes upon discharge from the hospital.

The outcomes were further grouped as follows: -

1. Favorable outcome: -
    - Modified Rankin scale ranges between 0 and 4.
2. Unfavorable outcome: -
    - Modified Rankin scale of 5 and 6

Patients with severe disability were those who were bedridden, incontinent and were fully dependent on a care giver. Those who died were also grouped as having an unfavorable outcome.

2.4.1 The modified Rankin scale (mRS)

Table 1: Modified Rankin Scale

Scale	Symptom
0	**No symptom**
1	**No significant disability**. Able to carry out all usual activities, despite some symptoms.
2	**Slight disability**. Able to look after own affairs without assistance, but unable to carry out all previous activities.
3	**Moderate disability**. Requires some help, but able to walk unassisted.
4	**Moderately severe disability.** Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
5	**Severe disability.** Requires constant nursing care and attention, bedridden, incontinent
6	**Dead**

2.5 Factors influencing the outcome of severe head injury

Identification of reliable prognostic indicators for patients with severe TBI is of importance to the practicing neurosurgeon or health worker. Such information provides

the neurosurgeon with an objective basis for family counseling and for appropriate allocation of treatment resources and rehabilitation. This information provides the clinician with insight into the pathophysiology of TBI(Narayan et al., 1981). Factors influencing the outcome of severe head injury can be influenced by several non-neurological factors such as somatic injuries or medical complications (Bowers & Marshall, 1980).

A study conducted at Kenyatta National Hospital (Mwang'ombe & Kiboi, 2001) established that factors influencing the outcome of severe head injury patients who were treated there were age, admitting GCS, admitting BP (Systolic), pupillary reaction to light and the presence of other associated injuries. Factors influencing the outcome of severe head injury patients can be grouped as pre-injury factors, mechanism of injury and post injury factors.

The post injury factors can also be broadly grouped as demographic variables, clinical variables and radiological (Computerized tomography) findings.

2.5.1 Mechanism of injury and presence of comorbidities.

Traumatic brain injury occurs when the brain is damaged as a result of physical trauma, this can be caused by a penetrating (open) head injury in which an object pierces the skull and enters the brain tissue. Closed Head injury occurs when the skull is not breached despite the occurrence of severe head injury. Closed head injury often results in long term disability among the survivors (Hasar & Bir, 2009). Penetrating head injury as a result of gunshot wound (GSW) has a high morbidity and mortality rate.

Gunshot wounds can be classified as tangential, perforating or penetrating(MOUSA & ABED, n.d.). The penetrating injuries are the most devastating type of missile injury to the head. Mortality increases based on several factors such as involvement of three (3)

or more lobes, involvement of the 3rd ventricle, trans ventricular involvement, brainstem involvement and hemispheric involvement.

Closed head injury as a result of high velocity impact is associated with a high mortality.

2.5.2 Prehospital care

Prehospital care is aimed at minimizing patient morbidity by protecting the brain from secondary brain insults while recognizing and stabilizing associated injuries. This is by protecting and maintaining the airway open, preventing and correcting hypoxia, hypotension and increased intracranial pressure, immobilizing the spine, identifying and stabilizing associated injuries (Abbott, Brauer, Hutton, & Rosen, 1998). Several North American studies have established an improvement in the functional outcome of patients with severe head injury who received prehospital care with the critical care teams (Abbott et al., 1998; Celli, Fruin, & Cervoni, 1997; Garner, Crooks, Lee, & Bishop, 2001). The critical care teams are highly skilled and are able to carry out several specialized emergency interventions such as airway management options such as cricothyroidotomy, use of neuromuscular blocking agents to facilitate intubation, they can administer drugs such as mannitol, sedatives and barbiturates among others.

Prehospital hypoxia and hypotension have been demonstrated to significantly affect the outcome of severe head injury patients (Garner et al., 2001; Piek et al., 1992; Stocchetti, Furlan, & Volta, 1996). Timely response, identification and prevention of hypoxia and hypotension is associated with favorable outcomes.

2.5.3 Age

The proportion of survivors with a poor outcome (severe disability or vegetative state) increases with age and the proportion of patients with favorable outcomes decline with

advancing age (Hukkelhoven et al., 2003). The prognosis for recovery from trauma as one ages is a function not only of the aged brain but the type of injury associated with SHI in each age group. A decline in health as one ages may predispose the aged brain to systemic complications after TBI.

The reaction of the aged brain to trauma becomes apparent in head CT scan of the patient. Increasing age is associated with increasing size of hematomas with the largest intracranial hematoma observed in the oldest age groups. The chances of survival in patients with intracranial hematomas decreases with advancing age (Alberico, Ward, Choi, Marmarou, & Young, 1987).

2.5.4 Glasgow Coma Scale (GCS)

The neurological examination has traditionally been regarded by the clinicians as the most reliable basis for predicting outcome in severe head injury. The significance of various clinical signs both singly or in combination such as measured by the Glasgow Coma Scale (GCS) have been very important. The GCS was developed by Teasdale and Jennet in 1974 as an objective measure of level of consciousness (Teasdale & Jennett, 1974).

The Glasgow Coma Scale permits a repetitive and moderately reliable standardized method of reporting and recording ongoing neurologic evaluation even when performed by a variety of health care providers.

A patient is assessed against a criterion of a scale and the resulting points give a patient a score of between 3 (indicating deep unconsciousness) and 15. The scale is composed of three values namely eye opening, verbal response and best motor response. The three values separately as well as their sum are considered. The lowest possible GCS of 3 (deep coma /death) while the highest score of 15 (fully awake).

The GCS can be affected by pre- and post-traumatic factors that may impair neurologic response. Reversible conditions such as hypoglycemia or narcotic overdose should be recognized and treated immediately with appropriate antidote such as glucose and naloxone. Hypoxia and hypotension can alter the GCS negatively hence the need for stabilizing the patient before scoring.

2.5.5 Pupillary response / light reflex

The pupillary examination is an essential component of post-traumatic neurological examination. It consists of assessment of the size, symmetry and reaction to light in both pupils. The light reflex depends on a properly functioning lens, retina, optic nerve, brainstem and oculomotor nerve (3rd cranial nerve). The direct pupil responses assess unilateral function of the third cranial nerve, the consensual response assesses the function of the contralateral 3rd cranial nerve. Absence or asymmetry of the reflexes may indicate a Herniation syndrome or ischemia of the brain stem hence, a predictor of poor outcome (Riggio & Jagoda, 2004).

Pupillary constriction is mediated via parasympathetic pathways which require integrity of the 3rd cranial nerve and its nuclei. The 3rd cranial nerve palsy initially causes mydriasis followed by the loss of reactivity to light usually on the contralateral side. An ipsilateral 3rd cranial nerve palsy may be caused by either the compression of the nerve on the free edge of the tentorium, kinking of the nerve over the clivus or buckling of the brain stem due to an increased supra-tentorial pressure causing the brain to herniate (Larner, 2003). During unilateral 3rd cranial nerve palsy the consensual light reflex is usually maintained.

In some instances, examining the 3rd cranial nerve following head injury may cause a challenge. When the optic nerve is injured as occurs in association with frontal bone fractures both direct and indirect light reflexes are impaired leading to fixed or

sluggishly reacting pupils which may often display a spasmodic, rhythmic but regular dilating and contracting pupillary movements (hippus).

Pupillary asymmetry of less than 1mm is normal and may not have a pathological significance (Riggio & Jagoda, 2004). Raised intracranial pressure resulting in uncal Herniation compresses the 3rd cranial nerve resulting in a reduction of parasympathetic tone to the pupillary constrictor fibers producing a dilated pupil with decreased reactivity. Destruction of the nerve also results in a dilated and fixed pupil.

Bilaterally dilated and fixed pupils are consistent with direct brainstem injury as well as with raised intracranial pressure. Metabolic and cardiovascular disturbances such as hypoxemia, hypothermia and hypotension may be associated with dilated pupils with an abnormal reaction making it necessary for one to resuscitate the patient before assessing pupillary function. Pupillary function is a guide for immediate medical and surgical attention both in an acute setting and as a prognostic factor in the long term. Impaired pupillary responses and eye movements have a well-documented association with a poor outcome (Miller et al., 1981).

2.5.6 Hypoxia

Hypoxemia is a strong predictor of outcome in a traumatic brain injured patient (Randall M Chesnut et al., 1993). The primary goal in the initial management of the patient is to assess the airway and ensure adequate oxygenation. There is evidence to show that severe TBI patient with persistently low oxygen saturation despite oxygen therapy benefits from intubation (Winchell & Hoyt, 1997). Hypoxemia (oxygen saturation of <90%) should be avoided and should be corrected immediately upon identification.

Pre-hospital airway management is very important; a single episode hypoxemia during this period can damage the brain permanently. Health care providers attending to such patients should be well trained on endotracheal intubation skills.

Recent studies show pre-hospital intubation of traumatic brain injured patients may not be beneficial in a patient able to maintain an oxygen saturation of > 90 % with supplemental oxygen alone (D. P. Davis et al., 2004). A partial pressure of oxygen of 60% on arterial gases in patients in emergency department has a detrimental effect on the patient's outcome particularly when associated with hypotension (Randall M Chesnut et al., 1993). Hypoxemia can be corrected using supplemental oxygen and varying combinations of bag and mask ventilation, endotracheal intubation and other adjuncts including combi tubes and laryngeal mask airways (Miller et al., 1981).

2.5.7 Hypotension

Hemorrhage following trauma decreases cardiac preload when compensatory mechanisms are overwhelmed. Hypotension becomes evident leading to decreased peripheral perfusion and oxygen delivery.

Fluid therapy is used to replete preload, supporting cardiovascular function and peripheral oxygen delivery. Hypotension has been shown to produce significant secondary brain injury and is associated with unfavorable outcome.

In adult's hypotension is defined as a systolic blood pressure of < 90mmhg. In children hypotension is defined as a systolic pressure less than the 5th percentile for age or by clinical signs of shock. The usual values are as follows: -

< 60mmhg in term neonates (0 – 28 days.)

<70mmhg in infants (1month – 12months.)

<70mmhg + 2x age in years for children (1 – 10 years)

<90mmhg in children > 10 years.

The goal of fluid resuscitation is to support oxygen delivery and optimize cerebral hemodynamics. The commonly used fluids are normal saline 0.9% and ringers' lactate.

The underlying cause of hypotension in severe traumatic brain injury is usually blood or fluid losses. Intravascular repletion is the most effective way of restoring blood pressure. Michaud et al found out that hypotension in the pre-hospital setting and in the emergency department was significantly related to a higher mortality in children (Michaud, Rivara, Grady, & Reay, 1992).

2.5.8 Cerebral Herniation

This is the displacement of a portion of the brain through an opening or across a separating structure into a region that it does not normally occupy.

Cerebral herniation is caused by a number of factors that cause a mass effect and increased intracranial pressure such as traumatic brain injury and intracranial hemorrhage (Barr, Gean, & Le, 2007). This is a potentially deadly effect of very high intracranial pressures.

There are two types of cerebral herniation: -

a) Supratentorial herniation.
    i. Uncal trans tentorial herniation.
    ii. Central tentorial herniation.
    iii. Subfalcine herniation.
    iv. Transcalvarial herniation.
b) Infratentorial herniation.
    i. Upward trans tentorial herniation (reverse coning)
    ii. Foraminal or tonsillar herniation (coning)

The uncontrolled increased ICP and progression to herniation causes compression of the 3rd cranial nerve, ipsilateral post cerebral artery resulting in ischemia of the ipsilateral primary visual cortex and contralateral visual field deficits in both eyes (contralateral homonymous hemianopsia)

Compression of the contralateral cerebral crus containing descending corticospinal and some corticobulbar tracts leading to ipsilateral hemiparesis causing false localizing sign (Kernohan's notch)

Management of severe head injury is directed at maintaining cerebral perfusion.

This herniation can be easily identified on radiology by a head Computerized tomography (CT) scan of the patient.

2.5.9 Neuroprotective measures

Neuroprotective measures are instituted at the prehospital setting and in the hospital before definitive neurosurgical treatment. The main aim of neuroprotective measures is to prevent early brain swelling (edema), preventing and correcting hypoxia by providing adequate oxygenation, correcting hypotension and minimize subsequent neurologic damage. Management of elevated intracranial pressure in order to maintain adequate cerebral perfusion pressure (C.P.P) and identifying and stabilizing associated injuries has led to favorable outcomes (Abbott et al., 1998)

2.6 Computerized Tomography (CT) Scan

Craniocerebral injuries are a common cause of hospital admission following trauma and are associated with significant long-term morbidity and mortality. CT scan remains essential for detecting lesions that require immediate neurosurgical intervention as well as those that require in hospital observation and medical management.

CT scan advantages for evaluation of the TBI patient include its sensitivity for demonstrating mass effect, ventricular size and configuration, bone injuries and acute hemorrhage. CT offers widespread availability, rapidity of scanning and compatibility with medical devices. Its limitations include insensitivity in detecting small and non-hemorrhagic lesions such as contusions, particularly adjacent to bony surfaces. Likewise, diffuse axonal injuries (DAIs) that result in small brain lesions go undetected on CT.

CT scan is relatively insensitive for detecting increased intracranial pressure or cerebral edema and for early demonstration of hypoxic- ischemic encephalopathy (HIE) that may accompany TBI. Potential risks of exposure to ionizing radiation warrant judicious patient selection for CT scan as well as radiation dose management (P. C. Davis, 2007).

The CT scan findings that suggest a poor prognosis and prompt early surgical evacuation include a significant hematoma thickness of ≥15mm, large hematoma volume of ≥ 30cm^3, significant midline shift > 5mm, compression of the basilar cisterns and mixed density of the hematoma which indicates active bleeding (Kim & Gean, 2011).

2.6.1 Indications for a head CT scan

1. History of loss of consciousness / amnesia.
2. Obvious depression on the skull.
3. Compound fracture of the skull.
4. Glasgow coma scale of less than 13 at any point of injury.
5. Any sign of base of skull fracture.
6. Focal neurological signs.
7. More than (1) one episode of vomiting in patients more than 12 years old.
8. Laceration or contusion of the scalp with loss of consciousness.

CHAPTER THREE

3.1 Introduction

This chapter outlines the study site, study design, study population and the study execution, methods of data collection and the inclusion, exclusion criterion that were used.

3.2 Study site

Moi Teaching and Referral Hospital, Eldoret, is a National Teaching and Referral Hospital in the western region of Kenya attending to both rural and urban populace. Eldoret is the administrative center of Uasin Gishu County. Eldoret is among the fastest growing towns in Kenya being the 5th largest town in Kenya today. It lies south of the Cherangani Hills and has a local elevation varying from about 2100 meters above sea level at the airport to more than 2700 meters in nearby areas (7000–9000 feet). With the high altitude, it is dotted with a milliard of training camps for many middle- and long-distance athletes who contribute largely to the town's economic prowess. Eldoret is also one of Kenya's bread baskets as it is endowed with rich agricultural soils and favorable climatic pattern. Other than being a leading sports training hub of the country, the town also hosts numerous learning institutions.

Moi Teaching and Referral Hospital offers a wide range of health services in both Out-Patient and In-Patient sections. The hospital has a bed capacity of 800. The facility boasts of highly trained and specialist medical staff from both the hospital and its associated training institution, the College of Health Sciences, Moi University. It is the only tertiary referral hospital serving the former Western province, Rift valley province, parts of Eastern Uganda and Southern Sudan. The hospital also hosts students from Kenya Medical Training Centre (KMTC), University of East Africa, Baraton, and the

ECN (enrolled community nurse) upgrading program as well as international students on exchange program courtesy of Moi University.

MTRH does not have a separate trauma unit and patients are admitted to the hospital through the A/E department while children are admitted though the outpatient department of the newly constructed children's hospital.

The hospital has a very busy department of surgery which is serviced by other key departments of the hospital e.g. laboratory, physiotherapy, occupational therapy, nutrition, social work, and operating theatres. The hospital has an intensive care unit (ICU) with a six (6) bed capacity. The department of surgery and anesthesiology at the school of medicine has several sub specialties, namely Neurosurgery, Orthopedic surgery, General surgery, Plastic surgery, Urology and Cardiothoracic surgery. The department of surgery experiences a high bed occupancy of between 100 -150 %. The hospital is in the process of constructing an ultra-modern Accident and Emergency (A/E) unit that will assist in the timely management of trauma patients. The hospital is also the home of AMPATH, the fruit of the collaboration involving a consortium of both American universities and Moi university. The Riley mother and baby hospital is a modern facility for the care of expectant mothers and their newborn babies. There are recent developments including the construction of the children's hospital, chronic diseases center and the installation and commissioning of the MRI unit.

3.2 Study population

The study population included all the patients who presented to the A/E departments of MTRH with severe TBI and who met the study's inclusion criteria. The patients presented to the A/E and the sick child outpatient departments where they were assessed, resuscitation commenced as per the ATLS guidelines and later the patients

were admitted to the general wards and ICU depending on the availability of space. Surgery was recommended and performed immediately on those who had indications for urgent surgical intervention.

3.3 Study design

This was a prospective study that was conducted for twelve (12) months from 1st November 2013 to 30th October 2014. Data was collected as patients were admitted and followed up during their admission up to the point of discharge or death when the Modified Rankin Scale was administered.

3.4 Sample size determination

In order to be 95% sure that the proportion of patients with moderate, severe disability or death as an outcome following severe head injury was within, plus or minus 5% of the population prevalence of 70% we had to estimate the sample size using the Daniel (1999) formula for finite population.

$$n = \frac{N\, Z_{\alpha/2}^2 P(1-P)}{d^2(N-1) + Z_{\alpha/2}^2\, P(1-p)}$$

$$n = \frac{120 \times 1.96^2 \times 0.7(1-0.7)}{0.05^2(120-1) + 1.96^2\, 0.7(1-0.7)}$$

n = 88 patients

where

n = Sample size required.

P = is the population proportion of those who had unfavorable outcomes after severe TBI in KNH study taken as 0.7 (70%)

d = was the margin of error equal to 5% used in this case.

Z = Confidence level, Z value (1.96 for 95% confidence level)

N = is the estimated accessible study population in one year taken as 120 (Moi Teaching and Referral Hospital records for the year 2012).

Using the above formula, it gives **88 patients** as a sample size.

This formula is applicable when the population under study is small.

This is the minimum sample size that could be collected. However, only **84** patients were recruited.

3.4.1 Sampling procedure

Non-probability (consecutive) sampling method was used to recruit all eligible patients who presented to the accident and emergency department, sick child clinic. The patients were first resuscitated as per the ATLS guidelines before their recruitment into the study.

3.4.2 Inclusion criteria

1. All patients with a history of trauma and with a GCS of 8 or less.
2. Available relative / guardian gave an informed consent to participate in the study.

3.4.3 Exclusion criteria

1. Patients with a previous head injury that was treated.
2. Relatives / guardians who refused to participate in the study.

3.5 Patient flow chart

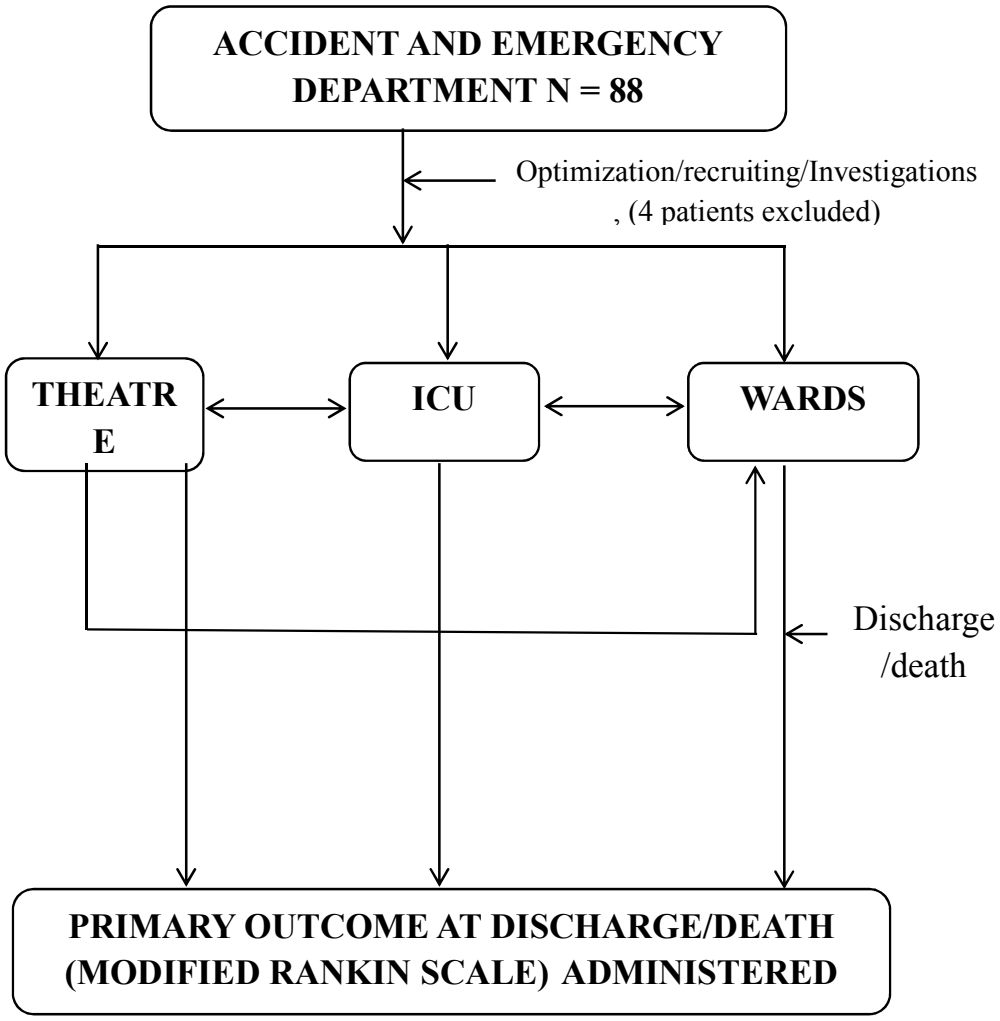


Figure 1: Patient flow chart.

Note: Investigations done included laboratory tests (hemogram, urea, electrolyte levels, grouping and cross matching blood), radiological investigations included trauma series (skull x-ray, C-spine, chest and pelvis x-rays), cranial CT scan.

3.6 Data collection instruments and methods

Data was collected and recorded on a coded structured questionnaire. The GCS was used as an assessment tool to determine the patients who qualified for the study and to assess the response of the participant to treatment while in the wards / ICU. The

modified Rankin Scale, was a functional outcome tool which was administered upon discharge from the hospital and upon death of the recruited patients.

3.7 Pretesting the data collection instrument

The coded structured questionnaire was pretested for 3 days at the accident and emergency unit; issues that arose were addressed before the final questionnaires were printed. The participants used for pretesting were not included in the study.

3.8 Data collection, processing and analysis

Data was collected using a coded structured questionnaire by the researcher. At discharge or upon death of the participant efforts were made to ensure that the information collected was complete by counterchecking with the patient's file documentation.

The data that was collected in hard copy was entered into a computer on Microsoft excel by the researcher on a daily basis to maintain quality and accuracy of the data being collected. The data was then cleaned and analyzed using SPSS version 21.

For descriptive statistics; measures of central tendency and dispersion were reported for numerical variables while frequencies and proportions were reported for categorical variables. Chi square was used to assess the association between categorical variables but where the expected count in any cell was less than 5 then Fischer's exact test was reported.

3.9 Presentation of results

The results were generated on frequency tables for categorical variables and means (standard deviations) for continuous variables. Pie charts and tables were also used.

3.10 Measures of morbidity and mortality

The following measures were used in the study: -

Measures of morbidity

- Length of hospital stay.
- Glascow Coma scale.
- Modified Rankin scale.

Measures of mortality

- Case mortality rate.

3.11 Ethical considerations

To carry out the study, approval was sought and granted from the Institutional Research and Ethics Committee (IREC) and MTRH approval Reference number IREC/2013/123. Informed consent was sought from the relative or the legal guardian accompanying the patient before their recruitment into the study. Any risks or benefits accrued due to the research were explained to each relative / legal guardian. Utmost confidentiality with regards to the participants was assured. The legal guardian / relative accompanying the patient had the leeway to withdraw from the study at any stage even after consenting and these did not affect the medical treatment.

3.12 Study limitations

1. The researcher participated in the management of some of the patients hence some findings may appear as biased.
2. Patients on non–operative management were treated within the general surgical wards which had their own challenges such as serious staff shortage, inadequate monitoring equipment and non-conformity to strict monitoring instructions.
3. Patients were followed up for the duration of their hospital stay only, long term outcomes were not assessed.
4. Some patients who met the inclusion criteria were excluded as there was no accompanying relative to consent for their inclusion into the study this resulted in failure to achieve the desired sample size.

CHAPTER FOUR

4.1 Introduction

This chapter presents the findings of the study, it was based on 84 subjects who were interviewed and their medical charts reviewed regularly to obtain the clinical details about the health care services they received upon arrival and as inpatients at MTRH. The Modified Rankin Scale was administered upon death or discharge at any level of care within MTRH

4.2 Demographics

Table 2: Demographics

variable	category	No of patients (n)	Percentage (%)
Age	0 - 13	6	7.14
	14 -25	23	27.38
	26 - 45	42	50.00
	46 – 65	8	9.52
	66 +	5	5.95
Sex	Female	12	14.29
	Male	72	85.71
Occupation	Student	19	22.62
	Peasant	17	20.24
	Casual	14	16.67
	Boda-boda operator	8	9.52
	Unemployed	9	10.71
	Housewife	5	5.95
	Driver	3	3.57
	Business	3	3.57
	Teacher	3	3.57
	Security guard	2	2.38
	Prison warden	1	1.19

4.2.1 Age

The age group that was most affected with severe head injury were those between 26 – 45 years.

4.2.2 Gender

Male to female ratio was at 6.3 :1 Males n = 72 (85.7%), Females n = 12 (14,3%)

Table 3: Gender and assault as the mechanism of injury.

Sex	Injury cause	Alive	Died	Total
Female	Assault	1	1	2
	Others	7	3	10
Male	Assault	13	12	25
	Others	29	18	47
Total		**50**	**34**	**84**

4.2.3 Occupation

The majority of the patients who sustained severe TBI were students 19 (21.59%) followed by farmers 17 (19.32%) and casual workers 16 (18.18%).

Table 4: Occupation and outcome.

Occupation	Alive	Died	Total
Student	16	3	19
Peasant	12	5	17
Casual	9	5	14
Unemployed	4	5	9
Boda-boda operator	2	6	8
Housewife	3	2	5
Driver	2	1	3
Business	1	2	3
Teacher	1	2	3
Security guard	0	2	2
Prison warden	0	1	1
Total	**50**	**34**	**84**

4.3 Causes of severe head injury

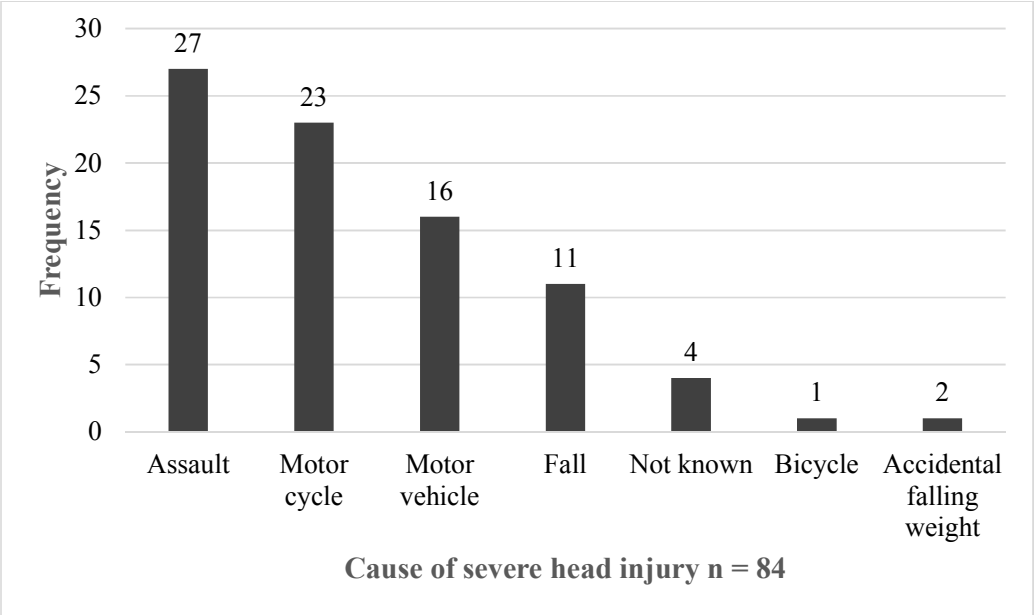


Figure 2: Causes of severe head injury

Table 5: Causes of SHI with their outcome

Causes	Alive	Died	Total
Assault	14 (51.8%)	13 (48.1%)	27
Motor cycle	14 (60.9%)	9 (39.1%)	23
Motor vehicle	8 (50%)	8 (50%)	16
Fall	9 (81.8%)	2 (18.2%)	11
Not known	2 (50%)	2 (50%)	4
Bicycle	1 (100%)	0	1
Accidental falling weight	2 (100%)	0	2
Total	**50 (59.5%)**	**34 (40.5%)**	**84**

Assault was the most common cause of severe head injury n = 27(32.1%), bicycle accidents was the least.

Table 6: Assault and Occupation with their associated outcome

Occupation	Assault	Others	Total
Peasant	7	10	17
Student	4	15	19
Others	16	32	48
Total	27	57	84

4.3.1 Motor vehicle crashes

Table 7: Motor Vehicle crashes

Person involved	Frequency	Percentages	Case fatality n (%)
Pedestrian.	12	75	7 (58.3)
Passenger.	4	25	1 (25)
Vehicle involved			
Personal car.	7	43.75	4 (57.1)
Lorry.	5	31.25	2 (40)
Matatu. (PSV)	2	12.5	0 (0)
Unknown.	2	12.5	2 (100)

Most of the patients involved in motor vehicle crashes were pedestrians n = 12 (75%) while passengers were n = 4 (25%). Personal motor vehicles n = 7(43.8%) were responsible for most of the accidents, two (2) patients did not know the type of motor vehicle that was involved in the accident.

4.3.2 Motor cycle crashes

Table 8: Motor cycle crashes

Person involved	Frequency(N)	Percentages (%)	Case fatality
Rider (boda-boda)	8	34.7	4 (50%)
Passenger	8	34.7	4 (50%)
Pedestrian	7	30.4	1 (14%)
Cause of accident			
Collusion with a vehicle	14	60.9	8 (57%)
Knocked down	6	26.1	1 (17.0%)
Free fall	2	8.7	1 (50.0%)
Collusion with a motorcycle	1	4.3	0 (0.0)

Motor cycle crashes n = 23 was the cause of severe SHI, riders n = 8 (34.7%), passengers n = 8(34.7%). The most common form of motor cycle crashes being collusion with a motor vehicle n=14 (60.9%).

4.4 Referring Counties

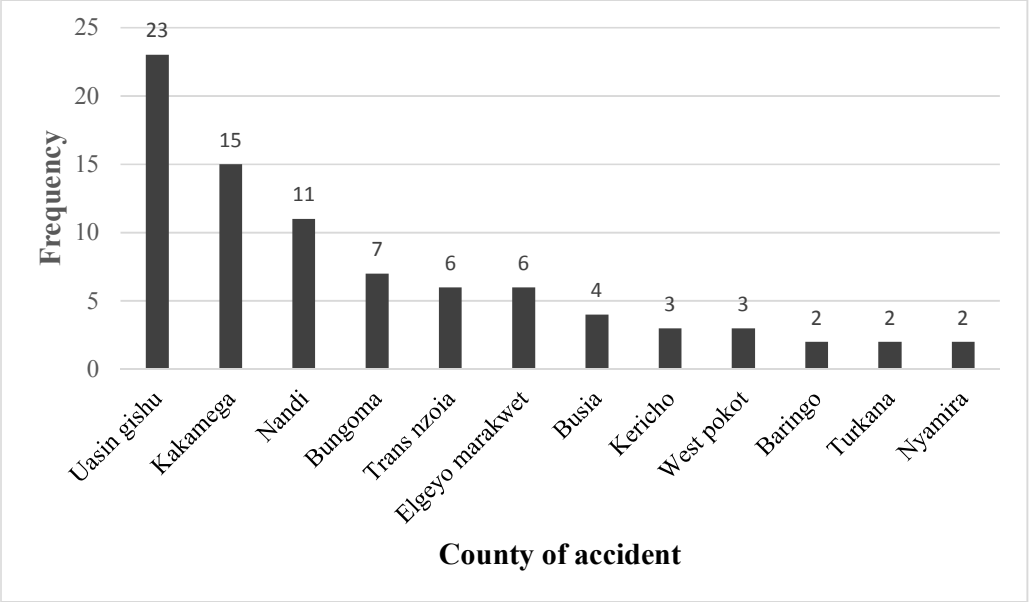


Figure 3: Referring County

A total of 62 patients were referred to MTRH, Kakamega County referred most of the patients n = 13. Uasin Gishu County where MRTH is located contributed n = 18 who included both referrals and those patients who were directly transported to the hospital from the accident site.

4.4.1 Referring institutions

Table 9: Referring institutions

	Frequency	Percentage
Private institution	3	4.84
Public institution	56	90.32
Faith based hospitals	3	4.84
	62	100

The public institutions n = 56(90.32%) referred most of the patients, most of the referral were made by doctors n = 51 (60.7%).

Table 10: GCS of patients at the point of referral

	Frequency	Percent (%)
Severe head trauma	27	43.5
Moderate head trauma	34	54.8
Mild head trauma	1	1.7
Total	62	100.0

Majority of the patients had moderate head trauma n= 34 (54.8%).

4.4.3 Reasons for referral

Table 11: Reasons for referring patients to MTRH

Reason	Frequency	Percentage (%)
For CT-scan and further management	59	95.2
For ICU care.	2	3.2
Deteriorating GCS.	1	1.6

Most of the patients were referred for CT scan of the head and further management n = 59 (95.2%).

4.5 Neuroprotective measures

Table 12: Neuroprotective measures instituted at the referring facility

Measures	Responses	Percentage of cases (%)
Cervical color applied	1	4.3
Endotracheal intubation done	1	4.3
Indwelling urinary catheterization to monitor Renal function and volume replacement	13	56.5
IV fluids running	**21**	**91.3**

The neuroprotective measures were incompletely instituted among the referred patients. Most patients with some neuroprotective measure 21(91.3%) had intravenous fluids running. Most of the referred patients did not have any neuroprotective measure instituted n = 39

4.6 Hospital length of stay

The length of hospital stay ranged from 30 minutes to 150 days with a median of 6 days, (IQR 3,16).

4.7 Factors influencing outcome of severe head injury

Table 13: Factors influencing outcome of severe head injury patients at MTRH

Variable	category	Outcome		P-value
		Alive	Dead	
Age		27.5(17, 37)	33(26, 39)	0.046*
Gender	Female	8	4	0.75†
	Male	42	30	
Time interval	Up to 24hrs	27	27	0.011**
	More than 24hrs	23	7	
Anisocoria	No	28	8	0.003**
	Yes	21	27	
GCS	3-4	2	5	0.022†
	5-6	8	11	
	7-8	40	18	
SBP (mmhg)	90-100	2	4	0.141†
	101-120	10	13	
	>120	35	20	
Pulse rate/min	<60	5	5	0.579†
	60-120	45	25	
	>120	2	2	
Presence of other injuries	No	41	24	0.220**
	Yes	9	10	

'*' Data expressed as median (IQR) & Mann-Whitney U test; † Fisher's Exact test, ** Chi square

Table 14: Pupil size with associated outcome

Variable	category	Outcome		P-value
		Alive	Dead	
Pupil size	Normal	28 (77.8%)	8 (22.2%)	0.022*
	Constricted	3 (50%)	3 (50%)	
	Dilated reacting	11 (50%)	11 (50%)	
	Dilated not reacting	7 (35 %)	13 (65%)	
* Fishers exact test				

Table 15: GCS with associated outcome

GCS	Alive	Died	Total
3 - 4	2 (28.6%)	5 (71.4%)	7
5 - 6	8 (42.1%)	11(57.9%)	19
7 - 8	40 (69%)	18 (31%)	58
Total	**50**	**34**	**84**

P value = 0.022 (Fishers exact test)

The admission GCS is an important indicator of outcome, p - value 0.022. Very low GCS was associated with unfavorable outcomes 5 (71.4%) with a GCS of 3-4.

The time interval between the time of injury and arrival to the hospital (MTRH) ranged from 30 minutes to 6 days with a median of 12 hours.

Patients with raised systolic blood pressure showed an unfavorable outcome, 18 (32%) who had a systolic blood pressure of more than 120mmhg died.

Most Patients who developed unequal pupil size (anisocoria) had an unfavorable outcome, those patients who had dilated and non-reacting pupils had the highest mortality of 11(58%).

Associated injuries were injuries that the patient sustained in other parts of the body other than severe TBI; these included limb fractures 58% being the major form of other associated injury.

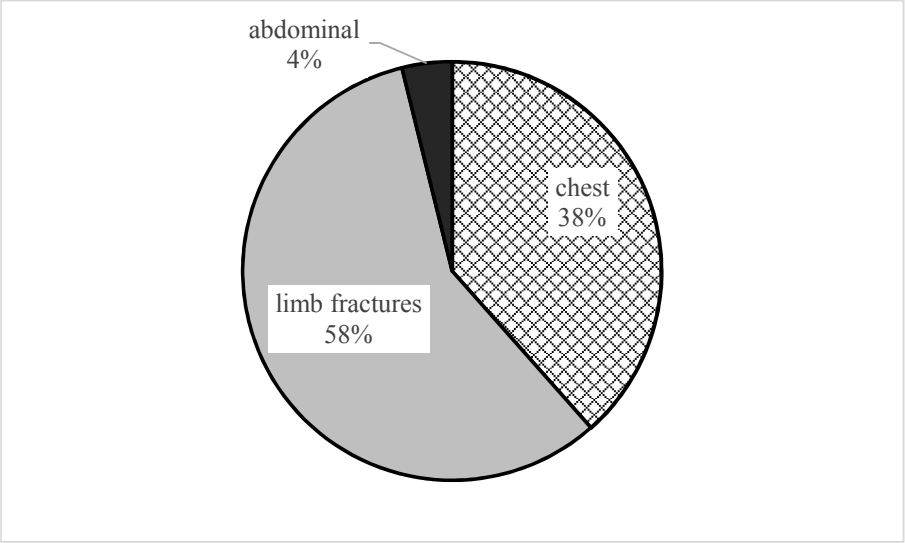


Figure 4: Associated injuries

4.8 Initial management at MTRH

Table 16: Emergency measures instituted at the A / E department of MTRH

Measures	Responses	Percent of Cases
Iv fluids.	84	100.0%
Anticonvulsants.	84	100.0%
Iv mannitol.	82	97.6%
Catheterization.	78	92.9%
Blood for GXM.	76	90.4%
Prophylactic antibiotics.	70	84.5%
Blood transfusion.	8	10.7%

Patients were received at the A/E department of MTRH and resuscitated as per the ATLS guidelines and neuro-protective measures were instituted immediately to

prevent further secondary brain injury. Diagnostic investigations and definitive treatment were initiated upon optimization of the patient.

4.9 Computerized tomography (CT) scan findings

Table 17: Cranial CT scan findings (Multiple findings)

	Responses	Percent of Cases (%)
Cerebral edema.	26	31.7%
Cerebral contusion.	14	17.1%
Intraventricular hemorrhage. (IVH)	2	2.4%
Acute SDH.	24	29.3%
Acute on chronic SDH.	1	1.2%
Fractured skull.	31	37.8%
Extradural hematoma. (EDH)	20	24.4%
Intracerebral hematoma. (ICH)	21	25.6%

The radiology investigations (X-ray examination) involving the skull and other areas (trauma series) were done in 53(60.2%) patients while CT-scan was done all 88 patients. The CT scan findings showed multiple features of the trauma causing severe head injury.

4.10 Treatment of severe head injury

Table 18: Treatment options and the associated outcome

Treatment option	Frequency	Percentage (%)	Fatality n (%)
Operative + ICU	27	32	17 (63%)
Non-operative	16	19	3 (19%)
Non-operative + ICU	21	25	13 (62%)
Operative	20	24	0 (0)
Total	84	100.0	

4.11 Intensive care unit utilization

Table 19: ICU utilization and the associated outcome

	Frequency	Percentage (%)	Fatality n (%)
NO ICU BEDS	42	87.5	26 (61.9%)
Admitted to ICU	6	12.5	4 (66.7%)
Total	48	100.0	30

Most of the patients with severe head injury required ICU care 42(87.5%), but did not receive this care.

4.12 Outcome of severe TBI

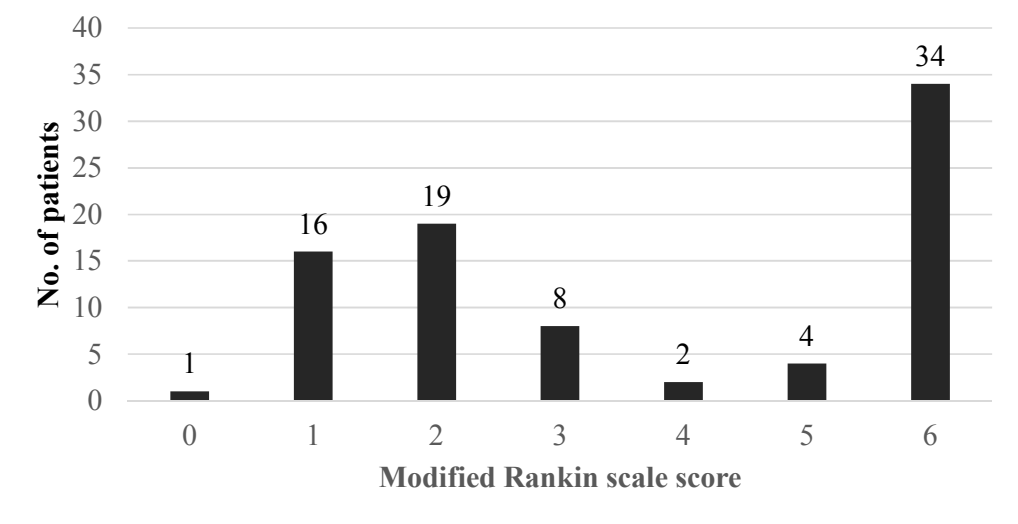


Figure 5: Outcome based on the Modified Rankin scale score

The immediate outcome of severe head injury was based on the modified Rankin scale that was assessed at the time of discharge or death.

The favorable outcomes were no disability, no significant disability, slight disability, moderate disability and moderately severe disability (scores of 0-4)

Unfavorable outcomes were severe disability (score of 5) and death (score of 6). The immediate mortality rate was at 40.5% (n= 34). The patients who had severe disability n = 4 (4.8%). The outcomes were generally favorable (54.7%) with the unfavorable outcomes being 45.3%.

CHAPTER FIVE

5.0 Introduction.

This chapter discusses the 84 recruited patients who had severe head injury. Mortality and morbidity following severe head injury remains very high, this chapter tries to determine and evaluate the factors that are associated with the various outcomes. Head injury places a considerable demand on health providers, community and the country.

5.1 outcome of severe head injury

The outcome of severe head injury at MTRH was generally favorable. The unfavorable outcome was 45.3% with case mortality rate being 40.5% and severe disability being 4.8%. The access and utilization of ICU services would have further improved the outcomes. A total of 50 patients with severe head injury required this care but only 6 (12%) had access to it with 44 (88%) missing this vital care. As a result, 26 (59.1%) patients died. The reason for failure to access and utilize ICU care was inadequate bed capacity in the unit and a prohibitive high admission cost charged at the private health facilities with Intensive Care Units. This unfavorable outcome are in agreement with the KNH and Bugando studies (Chalya et al., 2011; Mwang'ombe & Kiboi, 2001)

5.2 Social demographics.

In this study a total of 84 patients with severe head injury of all ages and both sexes were studied for a period of one year. They comprised of males 72 (85.7%) and 12 (14.3%) females making a M:F ratio of 6:1. This ratio concurs with the KNH study which established a M:F ratio of 8:1(Mwang'ombe & Kiboi, 2001). This contrasts with Tanzania and Nigeria studies which reported a M:F ratios of 1.5:1 and 2:1 respectively (Chalya et al., 2011; Emejulu & Shokunbi, 2010) which almost equal ratios. This is due to the wide catchment area that MTRH serves, being a level 6 hospital serving several counties and neighboring countries.

Males are likely to sustain severe head injury due to their greater exposure to the streets, personal and behavioral characteristics. Few females sustained severe head injury

Few females were recruited to the study 12 (13.6%). This hospital being a referral center, some patients may have been attended to in other hospitals.

The common age affected was found to be between 26 – 45 years which compares with what is found in existing literature(J F Kraus, 1990; JESS F Kraus & McArthur, 1996). This is the most active phase of life both physically and socially. This age group is also the most economically active and most of them own cars or motorcycles hence out number other road users and therefore experience more accidents and deaths. Children below the age of 13 years and adults above 65years least sustained severe head injury as they spend most of their time indoors. When they sustain severe head injury the outcomes are mostly unfavorable. This compares with what Kraus et al noted that head injury was lowest in the extreme of ages i.e. < 5 years old and those above 60 years (JESS F Kraus & McArthur, 1996).

The outcome of severe head injury as one advances in age is a function of not only the ability of the aged brain to heal but also the type of injury that is associated with each age group. A general decline in health also predisposes the older patient to systemic complications after severe head injury leading to unfavorable outcomes. The unfavorable outcomes in the aged can be attributed to the following: -

i. Brain atrophy as one advances in age.
ii. They have an increased frequency to develop mass lesions after primary head injury
iii. The elderly patient has an increased frequency of developing systemic complications after injury

iv. The aged often have pre-existing illness e.g. cardiovascular disease, respiratory disease, renal diseases, diabetes mellitus and even an old cerebral vascular accident (stroke)(Jiang, Gao, Li, Yu, & Zhu, 2002).

Kenya is undergoing major urbanization and motorization. The motorized two-wheeler being more economical and fast means of transport has become a very common form of transport. Most people including students use this form of transport resulting in their susceptibility to accidents with the resultant severe head injury. Most of the motorcycle operators and their clients did not wear protective gear such as crash helmets, they easily sustained severe head injury during an accident this is in agreement with studies done in Uganda (Galukande, Jombwe, Fualal, & Gakwaya, 2009; Kitara, 2011; Naddumba, 2004) which established commercial motorcycles also known as" boda-boda" in East Africa to be very popular both in urban and rural areas as a quick means of transport but were associated with a very low use of crash helmets at 30% for the riders and 1% for their passengers. Other factors associated with a high incidence of road crashes were attributed to poor state of the roads, inadequate training and knowledge on safety road measures and alcohol use.

Most head injury patients were students and peasants this was due to injuries sustained as a result of assault and their mode of transport. The mode of transportation was mainly the two-wheel type (boda-boda). As a result, 23(27.3%) sustained severe head injury due to motor cycles crashes. Injuries were sustained as they were either crashed as pedestrians or involved in a road crash between the motorcycle and a motor vehicle or between motorcycles. Most were involved in crashes between motorcycle and motor vehicle 14 (60,9%) with a mortality of 8 (57%) this can be attributed to lack of protective gear, failure to adhere to traffic rules, bad roads and use of alcohol. This

compares with studies extensively done in Uganda (Galukande et al., 2009; Kitara, 2011; Naddumba, 2004; Tran et al., 2015) and Kenya (Odero & Kibosia, 1995)

The boda-boda riders who sustained severe head injuries were 8(9.5%). This people sustained severe head injuries as a result of not having put on protective wear. This is the only group in these study that can relate occupation directly to outcome. Those who were involved in collusion with motor vehicles having unfavorable outcome.

The socioeconomic status of the patient and his family had a significant influence on the outcome as the study established that these patients could afford ICU care in private facilities when the could not be admitted to MTRH, these significantly improved the outcome. This concurs with the Kitagawa and Hauser study that demonstrated evidence of an increase in the differential mortality rates according to socioeconomic levels in the USA between 1930 and 1960, mortality rate being higher in the lower socioeconomic status or class(Kitagawa & Hauser, 1973)

MTRH is the second National Referral Hospital in Kenya, it has a fully functional neurosurgical unit with 5 neurosurgeons and a 6 bed ICU. Almost all patients treated at MTRH are referred from other facilities. In the County Hospitals patients with severe head injury are first managed by medical officers or general surgeons. These hospitals lack the necessary equipment required to diagnose these injuries. This explains why the high number of severe head injury patients are attended to at MTRH. The reasons for referral are varied such as 60 (93.8%) for CT scan and further management, deteriorating GCS hence need for specialized neurosurgical care 2 (3.1%) and 2 (3.1%) for ICU care. The various county referral hospitals lack both human resource and facilities to handle such patients.

Patients who were brought to the emergency room with severe head injury had faced numerous challenges in their management. Some patients were found lying at the road side while unconscious and brought to the hospital directly by police officers or by some good Samaritans. Their transportation to the hospital in police cars and sometimes private vehicles that were not suitable for transporting such patients endangered their lives although the main intention of both the police officers and the good Samaritans was to help out. During this period, it is unknown if the they had an episode of hypotension or hypoxia. While in the hospital, absence of relatives complicated the whole situation as the hospital was seriously understaffed to offer personalized care.

Length of hospital stay ranged between 30 min and 150 days with a median of 6 days. The patients who had a longer hospital stay of more than 30 days are those who had associated injuries for example limb fractures and abdominal injuries and systematic management was instituted. One patient died 30 minutes after recruitment into the study. This patient had sustained other associated injuries, he was admitted with both hypotension and hypoxia the duration of exposure was unknown and this was thought to contribute to the unfavorable outcome which is in agreement with the BTF guidelines((US) & Surgeons, 2000). Axotomy has been found to be a common cause of death among severe head injury patients especially within 12 -24 hours after the primary insult(Reilly, 2001)

5.3 Factors influencing outcome of severe head injury.

Mechanism of injury leading to severe head injury is known to influence the outcome. Penetrating head injuries are associated with an unfavorable outcome, the patients usually present with a very low GCS and often die early (Demetriades et al., 2004; Peek-Asa, McArthur, Hovda, & Kraus, 2001). All the patients recruited in this study sustained blunt head trauma.

Assault to the head was the commonest mechanism of severe head injury (32.1%). This was due to being hit on the head with a blunt object such as a wooden or metallic rod, fist fights and even sharp objects with associated closed skull fracture (closed head injury). Assault to the head can also be due to a blow on the head, punch, fall to the ground and even falling weights from a height Some patients sustained severe head injury after being attacked by a group of people unknown to them who used crude weapons that were either blunt or sharp. This does not compare with the KNH, Bugando and Mulago studies which found Motor vehicle crashes to be the leading cause of severe head injury (Chalya et al., 2011; Mwang'ombe & Kiboi, 2001; Tran et al., 2015)

Post injury factors were varied; beginning the moment an accident occurred. This was aimed at preventing secondary brain insults.

Pre-hospital care was not documented on both the referred patients and those who were transported directly to MTRH from the accident scene. This led to the conclusion that pre-hospital care was not given. Hypoxemia and hypotension occur commonly before the patient reaches the hospital significantly increasing the risk of secondary brain injury and the possibility of unfavorable outcome. This made it difficult to evaluate both hypoxemia and hypotension since the most crucial period of their care these two

parameters had not been documented. Inadequate number of pulse oximeters and inconsistent monitoring of oxygen saturation also made it difficult. An Australian study confirmed that a single episode of hypotension is associated with increased morbidity and doubling of mortality (Fearnside, Cook, McDougall, & McNeil, 1993), with a missed prehospital care it became impossible to associate hypotension with unfavorable outcome.

Though County Referral hospitals have acquired ambulances, the pre-hospital management of the patients from the accident site was not done on any of the patients who were transported from the accident scene to the nearest County health facility. The ambulances had only one member of staff, the driver. For effective handling of the accident victims the ambulance requires two or more paramedical staff who should be well trained in first aid and both BTLS and ATLS. The patients who were referred to MTRH and transported by the County ambulances were accompanied by only one nurse whose training and handling of the severe head injury patients could not be assessed. The equipment's available in the ambulances also could not be verified.

The patients, who were referred from other facilities to MTRH, required all measures to prevent secondary brain injury to be instituted however this was not fully accomplished. Among the 62 patients referred 41(64%) did not have any neuro-protective measures instituted while 23(36 %) either had one or two measures instituted and this was not monitored at all. Those who had some neuro-protective measures 21 (91.3%) had intravenous fluids running, 13 (56.5%) had an indwelling Foley's catheter inserted, 1 (4.3%) had a rigid cervical collar to stabilize the cervical spine and 1 (4.3%) had an endotracheal tube inserted and the referring nurse manually ventilated the patient until arrival to MTRH. This may have contributed to the unfavorable outcomes. The neuroprotective measures once instituted in full are known to improve the outcome of

severe head injury((US) & Surgeons, 2000), patients in this study had an incomplete institution of this measures during the referral process making it almost impossible to establish its influence on the outcome of severe head injury.

Several factors were noted to be associated with unfavorable outcomes of severe head injury. These were independent factors. Other factors though associated with outcome were not independent and required other factors (confounders) to have a statistical significance on outcome.

Prompt and appropriate resuscitation with early specialist medical and surgical management of severe head injury is associated with favorable outcome(R M Chesnut et al., 1993; Härtl et al., 2006; Lu et al., 2005). The severe head injury patients arrived at the definitive point of care (MTRH) within a time interval between 30 minutes and 6 days with a median of 12 hours. Time is a critical factor in determining outcome of an injured patient, patients who receive definitive care within the first hour (golden hour) have favorable outcomes (Dinh et al., 2013).

Late presentation to hospital after sustaining severe head injury is known to result in unfavorable outcomes. Late referral from county hospitals was the main reason. Time interval from the time of accident to the time of arrival at MTRH had a p – value 0.011 which is statistically significant. This study noted that most patients 54(64%) arrived at the definitive trauma center (MTRH) within 24 hours with most of them 28 (52%) arriving more than 6 hours later. This Patients had an equal chance (50%) of either sustaining a favorable or unfavorable outcome. Those who arrived 24 hours after were 30(36%) patients, 23(77%) had a favorable outcome while 7(23%) had an unfavorable outcome this was likely to be due to the emergency multidisciplinary approach to the trauma patients as specialist medical personnel in all departments readily responded to these patients upon arrival to MTRH. This findings are in agreement with studies

previously done that established that early and prompt management of this patients was associated with favorable outcome (Adams et al., 1989; Baker & O'neill, 1976; Cohen, Montero, & Israel, 1996; Jones et al., 1994; Mamelak, Pitts, & Damron, 1996).

The Glasgow Coma Scale was found to be an important factor that can also be used to predict outcome of severe head injury. In these study unfavorable outcomes significantly increased with a decreasing GCS, an admitting GCS of 3-4 was associated with more unfavorable outcomes 71%, these outcomes improved as the admitting GCS increased, GCS 5 -6 at 58% and 7 – 8 at 29% this findings are in agreement with those found in studies done at KNH and Tanzania respectively (Chalya et al., 2011; Mwang'ombe & Kiboi, 2001). These studies have showed that a lower admitting GCS is often associated with a high morbidity and mortality rate(Colohan et al., 1989; Fearnside et al., 1993; Jiang et al., 2002; Marshall et al., 1991).

Evaluation of the pupil size and its reaction to light is an important step in the management of severe TBI patients. According to the BTF guidelines, it is recommended that severe TBI patients be routinely evaluated for pupil asymmetry in size and their reaction to light (RCRM Bullock et al., 1996). Most patients with severe head injury who had normal sized pupils that reacted normally to light 28(77.8%) had favorable outcome as compared to those with dilated pupils that were unresponsive to light 65% had unfavorable outcome. This is in agreement past studies which established that unreactive pupils in severe head injury patients are often associated with the presence of hypotension, lower GCS and closed basal cisterns indicating an extremely high ICP (Jennett, Teasdale, Braakman, Minderhoud, & Knill-Jones, 1976) The onset of descending trans tentorial herniation and brain stem compression with raising ICP is easily picked up with the examination of the pupil. Pupil asymmetry is associated with an operable mass lesion in approximately 30% of patients with severe head

injury(Randall M Chesnut, Gautille, Blunt, Klauber, & Marshall, 1994). Therefore, early presentation or detection is of utmost importance as appropriate surgical intervention often leads to favorable outcomes.

Past literature has shown that uncontrolled high ICP (> 20mmHg) in a brain injured patient leads to unfavorable outcomes. Monitoring of ICP in a TBI patient is therefore very important, however in this study we relied on features associated with increased ICP such as onset of projectile vomiting, changes in pupil size and its response to light, CT scan intracranial features to detect raised ICP. Pupil dilation and subsequent Herniation as the intracranial pressure rises are late features that are irreversible.

This study established that the pupil size and its reaction to light was an important and independent factor associated with outcome. This findings are in agreement with those found in studies conducted at KNH, Bugando medical center, Tanzania and shanghai, China (Chalya et al., 2011; Jiang et al., 2002; Mwang'ombe & Kiboi, 2001).

Hypotension was associated with unfavorable outcomes, 4 (67%) patients died. When hypotension occurs concurrently with other factors such as a high pulse rate and hypoxemia then the risk of unfavorable outcomes tends to increase. Hypotension is not an independent factor to be associated with unfavorable outcomes. The Brain Trauma Foundation (BTF) guidelines give a level 11 recommendation that SBP of < 90mmHg should be avoided at all times of management ((US) & Surgeons, 2000). When other factors such as high pulse rate and hypoxia are present, the risk of unfavorable outcomes increase (Butcher et al., 2007). Manley et al further concluded that hypoxia in the early stages of severe TBI is the one that should be avoided as compared to the hypotensive episodes later on (Manley et al., 2001). A high SBP of more than 120mmHg was associated with 18 (32%) deaths as compared to those who survived 38 (68%). This

raising SBP is aimed at overcoming the raising ICP hence maintaining cerebral perfusion. A rise in the SBP with a concomitant reduction in the pulse rate was seen as a warning sign that ICP was raising and hence interventions were sought urgently either medically by infusing mannitol or surgically by performing evacuation of an intracranial mass lesion (hematoma) or by performing decompressive craniectomy to prevent cerebral Herniation. Hypertonic saline infusion was not used during the study. This findings are in agreement with what Butcher et al confirmed in their study (Butcher et al., 2007).

Previous studies have shown that Hypoxia (oxygen saturation of less than 90%) and hypotension are significantly associated with increased morbidity and mortality of patients with severe TBI (Manley et al., 2001; Pigula, Wald, Shackford, & Vane, 1993). This study did not confirm hypoxia and hypotension as being independent predictors of outcome though they are important. Hypoxia was to be confirmed by arterial blood gases which were not done in this study due to the financial implications. Hypoxia causes cerebral anaerobic glycolysis with a resultant accumulation of lactic acid. Cerebral lactate accumulation causes cerebral edema with a resultant increase of the intracranial pressure. Hypoxia also causes massive production of endogenous toxic factors that cause further neuronal damage worsening the primary injury sustained. This is the main reason why patients with severe TBI should be ventilated either spontaneously or assisted through an endotracheal intubation or tracheostomy.

The presence of other associated injuries is associated with an unfavorable outcome. Abdominal and thoracic injuries tend to complicate the prevention of secondary brain insult. Thoracic injuries are associated with hypoventilation causing hypercapnia which causes secondary brain insult. Similarly, abdominal injuries are associated with solid

organ injuries which cause massive intra-abdominal bleeding leading to hypotension and hemorrhagic shock. Hypotension causes secondary brain insult due to the resultant hypo-perfusion of the injured brain. This study showed that patients with a low pulse rate of, 60 bpm have an equal risk of either outcome and similarly those with a pulse rate > 120 bpm. Majority of the patients with pulse rate of between 60 and 120 had a favorable outcome 44 (64%) as compared to 25 (36%) who had an unfavorable outcome. This study illustrated that other associated injuries did not independently affect the outcome of severe TBI in patients admitted at MTRH; this was likely due to the rapid and timely interventions with the multidisciplinary approach to the severe TBI patients.

The Patients were promptly resuscitated as per the ATLS guidelines and definitive treatment commenced upon optimization of the patients. The operative intervention conducted on the patients included elevation of the depressed skull fractures, craniotomy to evacuate the intracranial mass (hematoma), decompressive craniectomy and burr holes. Some patients required both a surgical intervention and ICU care 27 (32%) majority of these patients had an unfavorable outcome as 17 (63%) of them died. The patients who required surgical intervention alone 20 (24%) all had a favorable outcome and were later admitted to the general surgical wards. Some patients required non-operative management only in the general surgical wards 16 (19%) and only 3 (19%) died. Those who required non-operative management in ICU were 21 (25%) with 13 (62%) of them having an unfavorable outcome (death). These highlights the importance of ICU care in improving outcome of severe head injury patients. This is in agreement with the study conducted in Sweden to assess the effect of neurointensive care on outcome of severe head injury patients(Elf, Nilsson, & Enblad, 2002)

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

This study established that the outcome of severe head injury among patients treated at MTRH was generally favorable (54.7%). The case mortality rate for severe head injury was (40.5%) with the unfavorable outcomes being (45.3%). The factors associated with unfavorable outcome of severe head injury were advanced age of 60 years and above, a low admitting GCS of 6 or less, unequal pupils that were dilated and were unresponsive to light and delayed presentation to the hospital beyond 24hours. These factors when present can be used to accurately predict the outcome of severe head injury patients

6.2 Recommendations

1. Formulate a standard of care protocol for severe head injury patients so as to admit to ICU,
    a) All elderly patients who are 60 years and above who sustain severe head injury,
    b) All patients with GCS of 6 or less following trauma.
    c) Patients with unequal pupils that are unresponsive to light following severe head injury.
2. Emphasis on adherence to the BTF guidelines on severe head injury management both at the referring facility (County referral hospital) and MTRH.
3. Referring facilities should be given feedback on the outcome of severe head injury and the importance of commencing neuroprotective measures early emphasized on all patients with head injury.

REFERENCES

Abbott, D., Brauer, K., Hutton, K., & Rosen, P. (1998). Aggressive out-of-hospital treatment regimen for severe closed head injury in patients undergoing air medical transport. *Air Medical Journal*, *17*(3), 94–100.

Adams, J. H., Doyle, D., Ford, I., Gennarelli, T. A., Graham, D. I., & McLellan, D. R. (1989). Diffuse axonal injury in head injury: definition, diagnosis and grading. *Histopathology*, *15*(1), 49–59.

Alberico, A. M., Ward, J. D., Choi, S. C., Marmarou, A., & Young, H. F. (1987). Outcome after severe head injury: relationship to mass lesions, diffuse injury, and ICP course in pediatric and adult patients. *Journal of Neurosurgery*, *67*(5), 648–656.

Assum, T. (1998). Road safety in Africa: appraisal of road safety initiatives in five African countries. In *The World Bank and United Nations Economic Commission for Africa, 1998 (Working Paper No. 33). 2. THE GLOBAL IMPACT 67*: Citeseer.

Badjatia, N., Carney, N., Crocco, T. J., Fallat, M. E., Hennes, H. M. A., Jagoda, A. S., … Moriarty, T. M. (2008). Guidelines for prehospital management of traumatic brain injury 2nd ed. *Prehospital Emergency Care*, *12*(SUPPL. 1).

Bailey, H., Bulstrode, C. J. K., & Love, R. J. M. (2008). *Bailey & Love's short practice of surgery*: Crc Press.

Baker, S. P., & O'neill, B. (1976). The injury severity score: an update. *Journal of Trauma and Acute Care Surgery*, *16*(11), 882–885.

Barr, R. M., Gean, A. D., & Le, T. H. (2007). Craniofacial trauma. *Fundamentals of Diagnostic Radiology*, 69.

Bayır, H., Kagan, V. E., Borisenko, G. G., Tyurina, Y. Y., Janesko, K. L., Vagni, V. A., … Kochanek, P. M. (2005). Enhanced oxidative stress in iNOS-deficient mice after traumatic brain injury: support for a neuroprotective role of iNOS. *Journal of Cerebral Blood Flow & Metabolism*, *25*(6), 673–684.

Bouma, G. J., Muizelaar, J. P., Stringer, W. A., Choi, S. C., Fatouros, P., & Young, H. F. (1992). Ultra-early evaluation of regional cerebral blood flow in severely head-injured patients using xenon-enhanced computerized tomography. *Journal of Neurosurgery*, *77*(3), 360–368.

Bowers, S. A., & Marshall, L. F. (1980). Outcome in 200 consecutive cases of severe head injury treated in San Diego County. *Neurosurgery*, *6*(3), 237–242.

Brooks, D. N., Hosie, J., Bond, M. R., Jennett, B., & Aughton, M. (1986). Cognitive sequelae of severe head injury in relation to the Glasgow Outcome Scale. *Journal of Neurology, Neurosurgery & Psychiatry*, *49*(5), 549–553.

Bullock, R., Chesnut, R. M., Clifton, G., Ghajar, J., Marion, D. W., Narayan, R. K., … Wilberger, J. W. (1996). Guidelines for the management of severe head injury. *European Journal of Emergency Medicine*, *3*, 109–127.

Bullock, R., Zauner, A., Woodward, J. J., Myseros, J., Choi, S. C., Ward, J. D., … Young, H. F. (1998). Factors affecting excitatory amino acid release following severe human head injury. *Journal of Neurosurgery*, *89*(4), 507–518.

Butcher, I., Maas, A. I. R., Lu, J., Marmarou, A., Murray, G. D., Mushkudiani, N. A., … Steyerberg, E. W. (2007). Prognostic value of admission blood pressure in traumatic brain injury: results from the IMPACT study. *Journal of Neurotrauma*, *24*(2), 294–302.

Celli, P., Fruin, A., & Cervoni, L. (1997). Severe head trauma. Review of the factors influencing the prognosis. *Minerva Chirurgica*, *52*(12), 1467–1480.

Chalya, P. L., Kanumba, E. S., Mabula, J. B., Giiti, G., & Gilyoma, J. M. (2011). Aetiological spectrum, injury characteristics and treatment outcome of head injury patients at Bugando Medical Centre in north-western Tanzania. *Tanzania Journal of Health Research*, *13*(1), 74–81.

Chesnut, R. M., Gautille, T., Blunt, B. A., Klauber, M. R., & Marshall, L. E. (1994). The localizing value of asymmetry in pupillary size in severe head injury: relation to lesion type and location. *Neurosurgery*, *34*(5), 840–846.

Chesnut, R. M., Marshall, L. F., Klauber, M. R., Blunt, B. A., Baldwin, N., Eisenberg, H. M., … Foulkes, M. A. (1993). The role of secondary brain injury in determining outcome from severe head injury. *The Journal of Trauma*, *34*(2), 216–222.

Chesnut, R. M., Marshall, S. B., Piek, J., Blunt, B. A., Klauber, M. R., & Marshall, L. F. (1993). Early and late systemic hypotension as a frequent and fundamental source of cerebral ischemia following severe brain injury in the Traumatic Coma Data Bank. In *Monitoring of Cerebral Blood Flow and Metabolism in Intensive Care* (pp. 121–125). Springer.

Chong, Z. Z., Li, F., & Maiese, K. (2005). Oxidative stress in the brain: novel cellular targets that govern survival during neurodegenerative disease. *Progress in Neurobiology*, *75*(3), 207–246.

Cohen, J. E., Montero, A., & Israel, Z. H. (1996). Prognosis and clinical relevance of anisocoria-craniotomy latency for epidural hematoma in comatose patients. *Journal of Trauma and Acute Care Surgery*, *41*(1), 120–122.

Colohan, A. R. T., Alves, W. M., Gross, C. R., Torner, J. C., Mehta, V. S., Tandon, P. N., & Jane, J. A. (1989). Head injury mortality in two centers with different emergency medical services and intensive care. *Journal of Neurosurgery*, *71*(2),

202–207.

Cunningham, A. S., Salvador, R., Coles, J. P., Chatfield, D. A., Bradley, P. G., Johnston, A. J., … Smielewski, P. (2005). Physiological thresholds for irreversible tissue damage in contusional regions following traumatic brain injury. *Brain*, *128*(8), 1931–1942.

Davis, D. P., Dunford, J. V, Poste, J. C., Ochs, M., Holbrook, T., Fortlage, D., … Hoyt, D. B. (2004). The impact of hypoxia and hyperventilation on outcome after paramedic rapid sequence intubation of severely head-injured patients. *Journal of Trauma and Acute Care Surgery*, *57*(1), 1–10.

Davis, P. C. (2007). Head trauma. *American Journal of Neuroradiology*, *28*(8), 1619–1621.

Demetriades, D., Kuncir, E., Velmahos, G. C., Rhee, P., Alo, K., & Chan, L. S. (2004). Outcome and prognostic factors in head injuries with an admission Glasgow Coma Scale score of 3. *Archives of Surgery*, *139*(10), 1066–1068.

DeWitt, D. S., & Prough, D. S. (2003). Traumatic cerebral vascular injury: the effects of concussive brain injury on the cerebral vasculature. *Journal of Neurotrauma*, *20*(9), 795–825.

Dinh, M. M., Bein, K., Roncal, S., Byrne, C. M., Petchell, J., & Brennan, J. (2013). Redefining the golden hour for severe head injury in an urban setting: the effect of prehospital arrival times on patient outcomes. *Injury*, *44*(5), 606–610.

Elf, K., Nilsson, P., & Enblad, P. (2002). Outcome after traumatic brain injury improved by an organized secondary insult program and standardized neurointensive care. *Critical Care Medicine*, *30*(9), 2129–2134.

Emejulu, J. K. C., & Shokunbi, M. T. (2010). Aetiological patterns and management outcome of paediatric head trauma: One-year prospective study. *Nigerian*

Journal of Clinical Practice, *13*(3).

Enevoldsen, E. M., & Jensen, F. T. (1978). Autoregulation and CO2 responses of cerebral blood flow in patients with acute severe head injury. *Journal of Neurosurgery*, *48*(5), 689–703.

Fearnside, M. R., Cook, R. J., McDougall, P., & McNeil, R. J. (1993). The Westmead Head Injury Project outcome in severe head injury. A comparative analysis of pre-hospital, clinical and CT variables. *British Journal of Neurosurgery*, *7*(3), 267–279.

Floyd, C. L., Gorin, F. A., & Lyeth, B. G. (2005). Mechanical strain injury increases intracellular sodium and reverses Na+/Ca2+ exchange in cortical astrocytes. *Glia*, *51*(1), 35–46.

Galukande, M., Jombwe, J., Fualal, J., & Gakwaya, A. (2009). Boda-boda injuries a health problem and a burden of disease in Uganda: a tertiary hospital survey. *East and Central African Journal of Surgery*, *14*(2), 33–37.

Garner, A., Crooks, J., Lee, A., & Bishop, R. (2001). Efficacy of prehospital critical care teams for severe blunt head injury in the Australian setting. *Injury*, *32*(6), 455–460.

Gurdjian, E. S., Lissner, H. R., Hodgson, V. R., & Patrick, L. M. (1966). Mechanism of head injury. *Neurosurgery*, *12*(CN_suppl_1), 112–128.

Härtl, R., Gerber, L. M., Iacono, L., Ni, Q., Lyons, K., & Ghajar, J. (2006). Direct transport within an organized state trauma system reduces mortality in patients with severe traumatic brain injury. *Journal of Trauma and Acute Care Surgery*, *60*(6), 1250–1256.

Hasar, T. B., & Bir, T. (2009). Traumatic brain injury due to gunshot wounds: a single institution's experience with 442 consecutive patients. *Turkish Neurosurgery*,

19(3), 216–223.

Hauerberg, J., Xiaodong, M., Willumsen, L., Pedersen, D. B., & Juhler, M. (1998). The upper limit of cerebral blood flow autoregulation in acute intracranial hypertension. *Journal of Neurosurgical Anesthesiology*, *10*(2), 106–112.

Hukkelhoven, C. W. P. M., Steyerberg, E. W., Rampen, A. J. J., Farace, E., Habbema, J. D. F., Marshall, L. F., … Maas, A. I. R. (2003). Patient age and outcome following severe traumatic brain injury: an analysis of 5600 patients. *Journal of Neurosurgery*, *99*(4), 666–673.

Hyder, A. A., Wunderlich, C. A., Puvanachandra, P., Gururaj, G., & Kobusingye, O. C. (2007). The impact of traumatic brain injuries: a global perspective. *NeuroRehabilitation*, *22*(5), 341–353.

Inoue, Y., Shiozaki, T., Tasaki, O., Hayakata, T., Ikegawa, H., Yoshiya, K., … Sugimoto, H. (2005). Changes in cerebral blood flow from the acute to the chronic phase of severe head injury. *Journal of Neurotrauma*, *22*(12), 1411–1418.

Jennett, B., Teasdale, G., Braakman, R., Minderhoud, J., & Knill-Jones, R. (1976). Predicting outcome in individual patients after severe head injury. *The Lancet*, *307*(7968), 1031–1034.

Jeremitsky, E., Omert, L., Dunham, C. M., Protetch, J., & Rodriguez, A. (2003). Harbingers of poor outcome the day after severe brain injury: hypothermia, hypoxia, and hypoperfusion. *Journal of Trauma and Acute Care Surgery*, *54*(2), 312–319.

Jiang, J.-Y., Gao, G.-Y., Li, W.-P., Yu, M.-K., & Zhu, C. (2002). Early indicators of prognosis in 846 cases of severe traumatic brain injury. *Journal of Neurotrauma*, *19*(7), 869–874.

Jones, P. A., Andrews, P. J. D., Midgley, S., Anderson, S. I., Piper, I. R., Tocher, J. L., … Dearden, N. M. (1994). Measuring the burden of secondary insults in head-injured patients during intensive care. *Journal of Neurosurgical Anesthesiology*, *6*(1), 4–14.

Kelly, D. F., Kordestani, R. K., Martin, N. A., Nguyen, T., Hovda, D. A., Bergsneider, M., … Becker, D. P. (1996). Hyperemia following traumatic brain injury: relationship to intracranial hypertension and outcome. *Journal of Neurosurgery*, *85*(5), 762–771.

Kelly, D. F., Martin, N. A., Kordestani, R., Counelis, G., Hovda, D. A., Bergsneider, M., … Becker, D. P. (1997). Cerebral blood flow as a predictor of outcome following traumatic brain injury. *Journal of Neurosurgery*, *86*(4), 633–641.

Kim, J. J., & Gean, A. D. (2011). Imaging for the diagnosis and management of traumatic brain injury. *Neurotherapeutics*, *8*(1), 39–53.

Kitagawa, E. M., & Hauser, P. M. (1973). Differential mortality in the United States: A study in socioeconomic epidemiology.

Kitara, D. L. (2011). Boda Boda Injuries in Gulu Regional Hospital, Northern Uganda. *East and Central African Journal of Surgery*, *16*(2), 97–101.

Kraus, J. F. (1990). Epidemiology: In: Elizabeth Frost (eds) Head Injury Management and Research AIREN-Geneva. Switzerland.

Kraus, J. F., & McArthur, D. L. (1996). Epidemiology of brain injury. *Neurology and Trauma*, 1.

Larner, A. J. (2003). False localising signs. *Journal of Neurology, Neurosurgery & Psychiatry*, *74*(4), 415–418.

Lee, J. H., Martin, N. A., Alsina, G., McArthur, D. L., Zaucha, K., Hovda, D. A., & Becker, D. P. (1997). Hemodynamically significant cerebral vasospasm and

outcome after head injury: a prospective study. *Journal of Neurosurgery*, *87*(2), 221–233.

Lewelt, W., Jenkins, L. W., & Miller, J. D. (1980). Autoregulation of cerebral blood flow after experimental fluid percussion injury of the brain. *Journal of Neurosurgery*, *53*(4), 500–511.

Lu, J., Marmarou, A., Choi, S., Maas, A., Murray, G., Steyerberg, E. W., & Group, I. and A. S. (2005). Mortality from traumatic brain injury. In *Intracranial Pressure and Brain Monitoring XII* (pp. 281–285): Springer science and business media

Lucas, S., Rothwell, N. J., & Gibson, R. M. (2006). The role of inflammation in CNS injury and disease. *British Journal of Pharmacology*, *147*(S1), S232–S240.

Maas, A. I. R., Braakman, R., Schouten, H. J. A., Minderhoud, J. M., & van Zomeren, A. H. (1983). Agreement between physicians on assessment of outcome following severe head injury. *Journal of Neurosurgery*, *58*(3), 321–325.

Maas, A. I. R., Stocchetti, N., & Bullock, R. (2008). Moderate and severe traumatic brain injury in adults. *The Lancet Neurology*, *7*(8), 728–741.

Mamelak, A. N., Pitts, L. H., & Damron, S. (1996). Predicting survival from head trauma 24 hours after injury: a practical method with therapeutic implications. *Journal of Trauma and Acute Care Surgery*, *41*(1), 91–99.

Manley, G., Knudson, M. M., Morabito, D., Damron, S., Erickson, V., & Pitts, L. (2001). Hypotension, hypoxia, and head injury: frequency, duration, and consequences. *Archives of Surgery*, *136*(10), 1118–1123.

Marshall, L. F., Gautille, T., Klauber, M. R., Eisenberg, H. M., Jane, J. A., Luerssen, T. G., … Foulkes, M. A. (1991). The outcome of severe closed head injury. *Special Supplements*, *75*(1S), S28–S36.

McIntosh, T. K., Smith, D. H., Meaney, D. F., Kotapka, M. J., Gennarelli, T. A., &

Graham, D. I. (1996). Neuropathological sequelae of traumatic brain injury: relationship to neurochemical and biomechanical mechanisms. *Laboratory Investigation; a Journal of Technical Methods and Pathology*, *74*(2), 315–342.

McLaughlin, M. R., & Marion, D. W. (1996). Cerebral blood flow and vasoresponsivity within and around cerebral contusions. *Journal of Neurosurgery*, *85*(5), 871–876.

Michaud, L. J., Rivara, F. P., Grady, M. S., & Reay, D. T. (1992). Predictors of survival and severity of disability after severe brain injury in children. *Neurosurgery*, *31*(2), 254–264.

Miller, J. D., Butterworth, J. F., Gudeman, S. K., Faulkner, J. E., Choi, S. C., Selhorst, J. B., … Becker, D. P. (1981). Further experience in the management of severe head injury. *Journal of Neurosurgery*, *54*(3), 289–299.

Mousa, H. I., & Abed, A. H. (n.d.). Civilian Craniocerebral gunshot wounds in Basrah .*International* Journal of Medicine and pharmaceaticalSciences,4(6),1-10

Mwang'ombe, N. J. M., & Kiboi, J. (2001). Factors influencing the outcome of severe head injury at Kenyatta National Hospital. *East African Medical Journal*, *78*(5), 238–241.

Naddumba, E. K. (2004). A cross-sectional retrospective study of boda boda injuries at Mulago hospital in Kampala-Uganda. *East and Central African Journal of Surgery*, *9*(1).

Narayan, R. K., Greenberg, R. P., Miller, J. D., Enas, G. G., Choi, S. C., Kishore, P. R. S., … Becker, D. P. (1981). Improved confidence of outcome prediction in severe head injury: a comparative analysis of the clinical examination, multimodality evoked potentials, CT scanning, and intracranial pressure. *Journal of Neurosurgery*, *54*(6), 751–762.

Obrenovitch, T. P., & Urenjak, J. (1997). Is high extracellular glutamate the key to excitotoxicity in traumatic brain injury? *Journal of Neurotrauma*, *14*(10), 677–698.

Odero, W. O., & Kibosia, J. C. (1995). Incidence and characteristics of injuries in Eldoret, Kenya. *East African Medical Journal*, *72*(11), 706–710.

Opondo, E. A., & Mwangombe, N. J. M. (2007). Outcome of severe traumatic brain injury at a critical care unit: a review of 87 patients. *Annals of African Surgery*, *1*(1).

Parikh, S., Koch, M., & Narayan, R. K. (2007). Traumatic brain injury. *International Anesthesiology Clinics*, *45*(3), 119–135.

Peek-Asa, C., McArthur, D., Hovda, D., & Kraus, J. (2001). Early predictors of mortality in penetrating compared with closed brain injury. *Brain Injury*, *15*(9), 801–810.

Piek, J., Chesnut, R. M., Marshall, L. F., Berkum-Clark, M. van, Klauber, M. R., Blunt, B. A., … Foulkes, M. A. (1992). Extracranial complications of severe head injury. *Journal of Neurosurgery*, *77*(6), 901–907.

Pigula, F. A., Wald, S. L., Shackford, S. R., & Vane, D. W. (1993). The effect of hypotension and hypoxia on children with severe head injuries. *Journal of Pediatric Surgery*, *28*(3), 310–316.

Rankin, J. (1957). Cerebral vascular accidents in patients over the age of 60: II. Prognosis. *Scottish Medical Journal*, *2*(5), 200–215.

Reilly, P. L. (2001). Brain injury: the pathophysiology of the first hours.'Talk and Die revisited'. *Journal of Clinical Neuroscience*, *8*(5), 398–403.

Riggio, S., & Jagoda, A. (2004). What You Forgot About the Neurologic Exam, Part 1. *Headache*.

Rodríguez‐Baeza, A., Reina‐de la Torre, F., Poca, A., Martí, M., & Garnacho, A. (2003). Morphological features in human cortical brain microvessels after head injury: a three‐dimensional and immunocytochemical study. *The Anatomical Record Part A: Discoveries in Molecular, Cellular, and Evolutionary Biology: An Official Publication of the American Association of Anatomists*, *273*(1), 583–593.

Stocchetti, N., Furlan, A., & Volta, F. (1996). Hypoxemia and arterial hypotension at the accident scene in head injury. *Journal of Trauma and Acute Care Surgery*, *40*(5), 764–767.

Tavazzi, B., Signoretti, S., Lazzarino, G., Amorini, A. M., Delfini, R., Cimatti, M., … Vagnozzi, R. (2005). Cerebral oxidative stress and depression of energy metabolism correlate with severity of diffuse brain injury in rats. *Neurosurgery*, *56*(3), 582–589.

Teasdale, G., & Jennett, B. (1974). Assessment of coma and impaired consciousness: a practical scale. *The Lancet*, *304*(7872), 81–84.

Thornhill, S., Teasdale, G. M., Murray, G. D., McEwen, J., Roy, C. W., & Penny, K. I. (2000). Disability in young people and adults one year after head injury: prospective cohort study. *Bmj*, *320*(7250), 1631–1635.

Tran, T. M., Fuller, A. T., Kiryabwire, J., Mukasa, J., Muhumuza, M., Ssenyojo, H., & Haglund, M. M. (2015). Distribution and characteristics of severe traumatic brain injury at Mulago National Referral Hospital in Uganda. *World Neurosurgery*, *83*(3), 269–277.

(US), Brain Trauma Foundation., & Surgeons, American Association of Neurosurgery. (2000). *Management and prognosis of severe traumatic brain injury* (Vol. 17). American Association of Neurological Surgery.

van Dijk, G. W. (2011). Head injury. *Practical Neurology*, *11*(1), 50–55.

Verweij, B. H., Muizelaar, J. P., Vinas, F. C., Peterson, P. L., Xiong, Y., & Lee, C. P. (2000). Impaired cerebral mitochondrial function after traumatic brain injury in humans. *Journal of Neurosurgery*, *93*(5), 815–820.

Werner, C., & Engelhard, K. (2007). Pathophysiology of traumatic brain injury. *BJA: British Journal of Anaesthesia*, *99*(1), 4–9.

Wilson, J. T. L., Hareendran, A., Grant, M., Baird, T., Schulz, U. G. R., Muir, K. W., & Bone, I. (2002). Improving the assessment of outcomes in stroke: use of a structured interview to assign grades on the modified Rankin Scale. *Stroke*, *33*(9), 2243–2246.

Winchell, R. J., & Hoyt, D. B. (1997). Endotracheal intubation in the field improves survival in patients with severe head injury. *Archives of Surgery*, *132*(6), 592–597.

Yi, J.-H., & Hazell, A. S. (2006). Excitotoxic mechanisms and the role of astrocytic glutamate transporters in traumatic brain injury. *Neurochemistry International*, *48*(5), 394–403.

APPENDICES

Appendix 1: Consent Form

INVESTIGATOR – DR KULOBA BURUDI DOUGLAS. P.O.BOX 46628,00100, NAIROBI, KENYA.

I _____of P.O Box_____

Tel_____

Hereby give informed consent to participate in this study in Moi Teaching and Referral Hospital. The study has been explained to me clearly by **Dr. KULOBA BURUDI DOUGLAS**.

I have understood that to participate in this study, I shall volunteer information regarding my medical condition, and undergo medical examination and I am aware that I can withdraw from this study any time without prejudice to my right of treatment at MTRH now or in the future. I have been assured that no injury shall be inflicted on me from my participation in this study. I have also been assured that all information shall be treated and managed in confidence.

Name of participant_____

Signature _____

Date _____

Name of witness_____

Signature _____

Date _____

Appendix 2: Questionnaire

DATE……

GENERAL INFORMATION

Patients initials…… **Patient's No /code…….**

Age …….

Sex…….

Telephone / cellphone No…….

Occupation…….

Site of accident…….

Referring hospital…….

Person referring the patient Dr □ RCO. □ Nurse □ others □

GCS of patient at referring hospital ……/ 15

Reasons for referral…….

Person accompanying the patient. Police □ relatives □ others □

MEDICAL HISTORY

1. Time interval between the time of injury and arrival to hospital ……
2. Is the patient under the influence of alcohol? yes □ No □
3. does the patient have the following (tick where applicable)?

Cervical color □ Endotracheal intubation □ Indwelling urinary catheter □ Iv fluids running □

Trauma series (X-ray of the chest, spine, pelvis, limbs). Complete □ Incomplete □ Not done □

Type of trauma.

1. Motor vehicle accident □

   Was the patient, the Driver □ Passenger □ Pedestrian □

   Type of accident. vehicle rolling □ head on collusion □ knocked down □

   Type of motor vehicle. Personal □ Psv bus □ lorry □ Psv matatu □

   don't know □

   Did the car have airbags? yes □ no □ don't know □

   Was the patient wearing a seat belt? yes □ no □ don't know □

   Were there any fatalities at the accident scene? yes □ no □ don't know □

   Was the driver under the influence of alcohol yes □ no □ don't know □

2. **Motor cycle accident** □

   Was the patient, the rider □ passenger □ pedestrian □

   Type of accident: free fall □ collusion with a car □

   collusion between motorcycles □

   Was the patient wearing a helmet? yes □ no □ don't know □

3. **Bicycle accident** □

   Was the patient, the □ rider □ passenger □ pedestrian

   Type of accident: Free fall □. Collusion with a vehicle □

   collusion with a motorcycle □ collusion with another bicycle □

   knocked down a pedestrian □

4. **Fall from a height** □

   less than 3 meters □ 3 – 10 meters □ more than 10 meters □

5. **Assault on the head** □

   Type of violence: Domestic violence □ Thugs □ brawls among friends □

   Type of object was used? blunt object□ sharp object □ gun shot □

   Don't know □

6. **Sports accidents.** □

   What type of sport? football □ rugby □ boxing □ hockey others □

7. Others □ (explain)……

Other types of injuries

1. Chest injuries. Blunt injuries □ Penetrating □
   others(explain)
   ……
   ……
   ……

   ……

2. Abdominal injuries. Raptured spleen □ Raptured liver □ Transected gut □

   Others(explain)

   ……

   ……

   ……

   ……
   …….
3. Fractures: Right upper limb □

   Left upper limb □

   Right lower limb□

   Left lower limb. □

4. Blood loss approximately……mls

SYMPTOMS OF HEAD INJURY

1. Did the patient Loose consciousness at the accident scene? yes □ No □

   for how long? ……..

   Did the patient later regain consciousness? Yes □ no □

2. Headache before loss of consciousness □

3. confusion before loss of consciousness □

4. vomiting yes □ No □

5. convulsions. Yes □ No □

6. CSF leaking from the nose (csf rhinorrhea)? yes □ No □

7. CSF leaking from the ears (csf otorrhea)? Yes □ No

SIGNS OF HEAD INJURY

Vital signs

1. Bp …../……. mmhg. pulse……. bpm. RR ……Bpm.

2. SPO_2……

Table: Glascow coma scale [GCS] (tick where applicable and add total score)

ADULT	SCORE		INFANT	
EYE OPENING (E)				
Opens spontaneously	**4**		Opens spontaneously	
Opens to verbal command	**3**		Opens to verbal command	
Opens in response to pain	**2**		Opens in response to pain	
No response	**1**		No response	
VERBAL RESPONSE (V)				
Talking / oriented	**5**		Coos, babbles	
Confused speech / disorientated	**4**		Cries but consolable	
Inappropriate words	**3**		Persistently irritable	
Incomprehensible sounds	**2**		Grunts to pain /restless	
No response	**1**		No response	
BEST MOTOR RESPONSE (M)				
Obeys commands	**6**		Normal movement	
Localizes to pain	**5**		Localizes pain	
Flexion /withdrawal	**4**		Withdraws from pain.	
Abnormal flexion	**3**		Abnormal flexion	
Abnormal Extension	**2**		Abnormal Extension.	
No response	**1**		No response	
TOTAL SCORE 3/15 - 15/15				

Pupils

a) are they reacting to direct light? yes □ no □

b) are they reacting to consensual light? yes □ no □

Pupil size. Normal □ constricted □ dilated reacting □ dilated not reacting □

Don't know □

CSF leaking from the ears (CSF otorrhea)? Right □ left □

CSF leaking from the nose (CSF Rhinorrhea)? yes □ no □

Neurological deficits

Lateralizing signs yes □ No □

If yes, to which side? right □ left □

Paralysis.?

a) Upper right limb yes □ no □

b) Upper left limb yes □ no □

c) Right lower limb yes □ no □

d) Left lower limb yes □ no □

INITIAL TREATMENT AT MTRH

1. upon arrival, the patient was attended to within?

   the 1st hr. □ 1 hr. – 3 hours □ 3-6 hrs.□ 6 – 12hrs. □ after 12 hrs. □

2. At the A/E what was done to the patient?

   a) Resuscitation: iv fluids □ catheterization □ iv mannitol □ iv hypertonic saline □ anticonvulsants □ blood for GXM □, blood transfusion □ prophylactic antibiotics □

   b) Stabilization of C- spine, yes □ No □

   c) Endotracheal tube insertion, yes □ No □

What radiological tests were done on the patient? (tick as applicable)

a) Trauma series (CXR, spine, pelvis, limbs x- ray) yes □ No □
if yes what are the findings

……
……
……
……

b) CT scan □

findings (in case of EDH, SDH and intracerebral hematoma. Outline the site, Dural, midline shift, volume)

……

……

……

……

……

What treatment option did the doctor discuss with you?

Surgery □ conservative management □

what treatment option was agreed on?

3. How long were you in the hospital?

4. What was the outcome of the treatment? (tick where applicable)

Alive □ dead □

5. Modified Rankin scale score (outcome of alive patients)

0. □ 1. □ 2. □ 3. □ 4. □ 5 □ 6. □

Modified Rankin Scale. Structured Interview (MRSSI)

0 = No symptoms at all; no limitations and no symptoms.

1 = No significant disability; symptoms present but no other limitations. Question: Does the person have difficulty reading or writing, difficulty speaking or finding the right word,
problems with balance or coordination, visual problems, numbness (face, arms, legs, hands, feet), loss of movement (face, arms, legs, hands, feet), difficulty with swallowing, or
other symptom resulting from the injury?

2 = Slight disability; limitations in participation in usual social roles, but independent for
ADL. Questions: Has there been a change in the person's ability to work or look after others if these were roles before stroke? Has there been a change in the person's ability to participate in previous social and leisure activities? Has the person had problems with
relationships or become isolated?

3 = Moderate disability; need for assistance with some instrumental ADL but not basic ADL. Question: Is assistance essential for preparing a simple meal, doing household chores, looking after money, shopping, or traveling locally?

4 = Moderately severe disability; need for assistance with some basic ADL, but not

requiring constant care. Question: Is assistance essential for eating, using the toilet, daily

hygiene, or walking?

5 = Severe disability; someone needs to be available at all times; care may be provided by

either a trained or an untrained caregiver. Question: Does the person require constant care?

6 = Death

Appendix 3: IREC Approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET

Reference: IREC/2013/123
Approval Number: 0001081

3rd October, 2013

Dr. Kuloba Burudi Douglas,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
APPROVED
03 OCT 2013
P.O. Box 4606 ELDORET

Dear Dr. Kuloba,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee have reviewed your research proposal titled:-

"Outcome of Severe Head Injury Patients, Moi Teaching and Referral Hospital (Kenya) Experience".

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 1081*** on 3rd October, 2013. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 2nd October, 2014. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc Director - MTRH Dean - SOM Dean - SON
Principal - CHS Dean - SPH Dean - SOD

Appendix 4: MTRH Approval

MOI TEACHING AND REFERRAL HOSPITAL

Telephone: 2033471/2/3/4
Fax: 61749
Email: director@mtrh.or.ke
Ref: ELD/MTRH/R.6/VOL.II/2008

P. O. Box 3
ELDORET

3rd October, 2013

Dr. Kuloba Burudi Douglas,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

RE: APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:-

"Outcome of Severe Head Injury Patients, Moi Teaching and Referral Hospital (Kenya) Experience".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

DR. J. KIBOSIA
DIRECTOR
MOI TEACHING AND REFERRAL HOSPITAL

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
APPROVED
03 OCT 2013
P.O. Box 4606 ELDORET

CC - Deputy Director (CS)
- Chief Nurse
- HOD, HRISM

Appendix 5. Study Budget

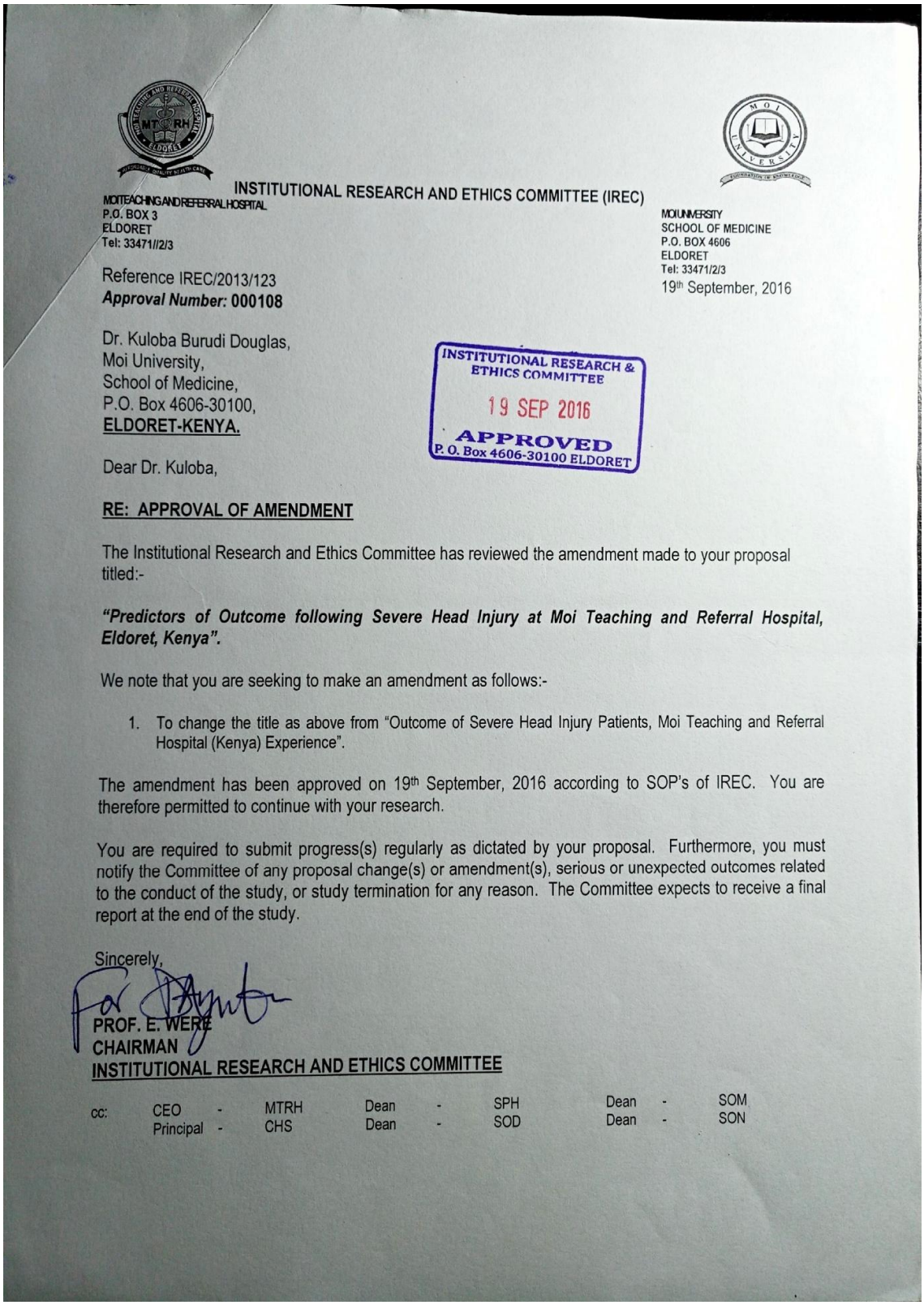
My budget for the 12 MONTHS was as outlined below: -

1. Plain paper reams x 10 @ 600/= .....6000/=
2. Pens, pencils, erasers and folders
    a. Pencils x 10 @ 30 ……....300/=
    b. Pens x 10 @ 15 …….....150/=
    c. Eraser x 4 @ 40 ……160/=
    d. Folders x 10 @ 250 ……. 2500/=

    Total ……. 3100/=
3. Computer flash disk x 2 @ 1200/= ……2400/=
4. Printing research proposals 10 prints @520/=…….5200/=
5. Printing thesis, 6 copies @ 2500/=…….15,000/=
6. Binding thesis copies, 6 copies @1000/=…….....6000/=
7. IREC fees …….2000/=
8. Data handling (one time) ……20,000/=
9. Research assistant 12 months @ 3000/= ……36,000/=

TOTAL ……95,700/=

Appendix 6. IREC Approval Amendments



INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference IREC/2013/123
***Approval Number:* 000108**

19th September, 2016

Dr. Kuloba Burudi Douglas,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
19 SEP 2016
APPROVED
P. O. Box 4606-30100 ELDORET

Dear Dr. Kuloba,

RE: APPROVAL OF AMENDMENT

The Institutional Research and Ethics Committee has reviewed the amendment made to your proposal titled:-

"Predictors of Outcome following Severe Head Injury at Moi Teaching and Referral Hospital, Eldoret, Kenya".

We note that you are seeking to make an amendment as follows:-

1. To change the title as above from "Outcome of Severe Head Injury Patients, Moi Teaching and Referral Hospital (Kenya) Experience".

The amendment has been approved on 19th September, 2016 according to SOP's of IREC. You are therefore permitted to continue with your research.

You are required to submit progress(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change(s) or amendment(s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc: CEO - MTRH; Dean - SPH; Dean - SOM
Principal - CHS; Dean - SOD; Dean - SON