The Epidemiology and Predictors of Worse Outcome for Traumatic Brain Injury Patients at Kilimanjaro Christian Medical Center, Moshi Tanzania

by

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Thesis submitted in partial fulfillment of
the requirements for the degree of Master of Science
in the Duke Global Health Institute
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ABSTRACT

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Abstract

Traumatic brain injury (TBI) is a leading cause of death and disability worldwide and this burden is increasing exponentially and will surpass many other diseases by 2020. The burden of TBI rests primarily in low and middle-income countries where they are woefully under-resourced. Kilimanjaro Christian Medical Center (KCMC) in Moshi, Tanzania, a neurosurgical referral center for 11 million people in the northwest of the country, represents many other under-resourced settings as they have limited diagnostic capacity (no computed tomography) and no trained neurosurgeon. In order to address understand how to address the burden of TBI at KCMC this project aims to describe the epidemiology and clinical presentation of TBI patients and determine predictors of worse outcome. This information will inform the next step of creating a KCMC specific clinical practice guideline or management plan for TBI patients in order to standardize and improve clinical care. This project utilized a retrospective review of de-identified data from a newly established Acute TBI Care Registry at KCMC that was developed for quality improvement. Three months of data was extracted yielding 190 patients who suffered TBI most of which were men (4:1 ratio) between 15 and 44 years of age and were motorcycle drivers. Alcohol use at the time of injury occurred for 28% of the patients almost exclusively among men. The mortality rates were high at 12% for all patients, 13% for admitted patients, and over 70% for those admitted to the Intensive

Care Unit. Predictors of mortality were low Glasgow Coma scale on admission and hypotension. Further analysis with a large sample size is necessary to understand the impact of hypoxemia on mortality. Predictors of morbidity were low Glasgow Coma scale only. Further analysis should be planned with a larger sample size in order to improve the accuracy of these findings.

Dedication

This is dedicated to all those patients who have motivated me to try to make their care better. To my all colleagues and collaborators, and especially our research team at Kilimanjaro Christian Medical Center, for your dedication to improving the lives of others and changing the world even if one patient at a time.

And most importantly, this is dedicated to my family and friends who without their support, encouragement, doggie-care skills and understanding, none of this would be possible.

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Acknowledgements

I would like to acknowledge the hard work, dedication, patience and resiliency of my Tanzanian research team and collaborators. You all amaze me every day with your persistence, dedication and perseverance.

I would like to thank my mentors: John Bartlett, Nathan Thielman, Truls Ostbye, Chuck Gerardo, Scott Sasser, David Wright, Deb Houry and Monica Swahn who all have both contributed to my growth, development, education and also the success I have had in global health thus far. Your support, guidance, mentorship, advice and friendships are truly cherished and appreciated.

1 Introduction

1.1 Violence and Injuries

Violence and injuries are a global health crisis causing over 5 million deaths annually or about 10% of the annual mortality.[1] Between 1990 and 2010, injury deaths have increase 24% mainly driven by a profound increase in transport injuries 46%.[1] Of those who survive their injury, there are approximately 650 million people worldwide who are living with disabilities due to injury which account for about 138 million disability-adjusted life-years (DALYs) lost in 2004 alone.[2,3] Over 90% of these unintentional injuries and 90% of DALYs occur in low- and middle-income countries (LMIC).[2,3] Between 1990 and 2010, the DALYs lost due to injuries increased over 13%; concurrently, all transport injuries (34%) and interpersonal injury and self-harm (26%) have increased precipitously.[4] Increasing rates of transport injuries has been predicted due to increased urbanization, motorization and limited access to care prehospital and otherwise in most locations of the world.

Injuries have a particular impact on young people between 5 and 44 years of age.[2] Similarly, injuries have a particular impact on males, as can be seen in Table 1. This difference in overall death amongst men compared to women likely represents the continued gender roles and their impact on risk behavior and exposure to injury risk. By impacting more men, injuries can have a tremendous effect on the patient and their

family since they are most likely to be the most economically productive member of the family. Ultimately, injuries not only the patients but also their families and the commu nities in which they live.[2,3]

Table 1: Global Deaths for 2010 for Individuals aged 15-49, adopted from Lozano, 2013[1]

Global Deaths for 2010 for Individuals aged 15-49			
	Road Traffic Injury	**Self-Harm**	**Other Injuries**
Male Deaths	10.7%	5.7%	6.2%
Female Deaths	0.5%	4.8%	7.5%

1.2 Traumatic Brain Injury

Traumatic brain injuries (TBI) are a leading cause of death and disability world wide.[5] It has been estimated that TBI affects over 10 million people annually leading to either mortality or hospitalization.[6] TBI is the leading cause of disability in people less than 40 years of age causing severe disability in 150-200 people per million annually.[7,8] Over 57 million people worldwide have been hospitalized with one or more TBIs, while the proportion of TBI-related disability is, as of yet, not described.[9] According to the World Health Organization, TBI will surpass many diseases as a major cause of death and disability by the year 2020.[10]

1.3 Traumatic Brain Injury in Low and Middle Income Countries

The burden of TBI is the greatest in low and middle-income countries (LMIC) where 85% of the world's population lives and 90% of deaths due to injury occur.[2] Sub Saharan Africa has a significantly higher rate of TBI (150-170 per 100,000) than the global rate (106 per 100,000).[11] Unfortunately, the true rates, epidemiology, treatment and

outcomes of TBI in LMIC are still relatively unknown due to difficulties in access to care, data collection management and limited research in these settings.

The most inclusive international comparison of TBI outcomes has been established the CRASH trial that is a longitudinal study of 10,008 patients from 46 different countries. The CRASH trial is a large double-blind randomized placebo-controlled multinational trial of the effect of a 48 hour infusion of a corticosteroid on the risk of death and disability after TBI. Inclusion into this study obviously biases against the most resource-limited settings where these types of rigorous randomized controlled studies are not able to be performed due to quality of standard of care issues and resource issues. Even still, patients in this study from LMIC had over twice the odds (OR 2.23 95% CI 1.15,3.30) of dying following severe TBI compared to high-income countries.[12] Similarly, LMIC TBI patients have reduced severe disability but increased levels of mild to moderate disability compared to their high income country counterparts. This is likely explained by death of the most severely injured patients in LMIC while they survive elsewhere and limited access to appropriate rehabilitation and reintegration capacity.[12]

In high-income countries, there has been a marked improvement in care and outcomes for patients with severe TBI [Glasgow Coma Score (GCS) 3-8] where mortality rates have decreased to about 28% in the United States. Unfortunately, this change in

mortality has not been seen in LMIC where severe TBI has a mortality rate of 40%.[13] Reasons for this disparity in LMIC are numerous including: limited access to prehospital or hospital-based care, limited treatment resources and diagnostics, limited knowledge or personnel capacity and other quality of care evaluations. Worldwide, access to specialist neurosurgical capacity is limited, and in most LMIC TBI care is performed by generalists who are notoriously undertrained and overworked.[11]

TBI is comprised of two insults; first the initial injury, then any continued tissue damage that occurs in the brain when post injury sequelae including brain swelling, limited blood and oxygen delivery to this injured and peri-injured region. The leading causes of this secondary injury include hypoxemia, hypotension, hypoglycemia and raised intracranial pressure. The first three of these: hypoxemia, hypotension and hypoglycemia can be easily tested controlled in most clinical settings during the post injury time period. Unfortunately, quality evaluations across Africa have shown that preventing secondary brain injury is poorly understood, the care administered is non-standardized, and delays in care are common.[11]

Ultimately, the highest burden of injury, particularly TBI, mortality and morbidity occurs where there are the greatest challenges in providing care, the weakest evidence base to guide interventions, and the fewest resources, policies, or infrastructure to institute effective change.

1.4 Kilimanjaro Christian Medical Center, Moshi Tanzania

Moshi, a city in the Kilimanjaro region of Northern Tanzania covering 59 sq km at the base of Mount Kilimanjaro. Moshi has a nighttime population of 143,799, but given the influx of people for business, the day population is estimated to be at least three times the night population or 497,469 people.[14] Moshi is home to Kilimanjaro Christian Medical Center (KCMC), the third largest hospital in the country and the referral hospital for northwestern Tanzania. KCMC is a regional training center for all types of healthcare workers. KCMC, like most LMIC hospitals, is hampered by limited resources, and limited healthcare personnel and specialists. While KCMC is the regional referral center for a population of 11 million people, and is the most common location for all injured patients to be attended, currently there is no capacity for computed tomography at KCMC. While KCMC is a referral center for neurosurgical patients, all neurosurgical operations performed at KCMC are by general surgeons.

In Tanzania, and specifically at KCMC, while there is likely a significant morbidity and mortality, there are is a paucity of data describing the current burden of mortality or morbidity due to traumatic brain injury. Regional data suggests that upwards of a third of patients in the intensive care units suffer from TBI and TBI is the most common neurosurgical process presenting to hospitals.[15,16] These findings do not even begin to describe the burden across the spectrum of head injury. From what we know about current statistics, at KCMC the burden of TBI is staggering: 6% of all

casualty department visits or about 1000 patients annually present with TBI. About 500 patients are admitted to the intensive care unit annually, of which 68% are traumatic brain injured patients and their overall mortality rate is about 30%.[16]

In order to plan to create a resource appropriate clinical practice guideline for the acute management of TBI, specifically addressing causes of secondary injury, understanding the epidemiology, clinical presentation and predictors of TBI mortality is necessary.

1.5 Objectives

1.5.1 General Objective

The objective of this project is to describe the epidemiology, clinical presentation and predictors of worse outcome of TBI patients who present to Kilimanjaro Christian Medical Center Casualty Department in Moshi, Tanzania.

1.5.2 Specific Objectives

- Describe the epidemiology and clinical presentation of TBI patients who present to KCMC.
- Describe predictors of a worse outcome including death or disability of TBI patients presenting KCMC

2 Methods

2.1 Setting

Kilimanjaro Christian Medical Center (KCMC) is located in Moshi, Tanzania, is the third largest hospital in the country, with 500 inpatient beds, and serves as the referral hospital for northwestern Tanzania. In the KCMC CD, with 6 beds and one resuscitation room containing 2 additional beds, over 15,000 patients are evaluated annually. Approximately 12% of all patient evaluations or about 2000 patients annually present with traumatic complaints. About 500 patients are admitted to the intensive care unit annually, of which 68% are traumatic brain injured patients. The overall mortality of TBI patients treated in the KCMC ICU was about 30%.[16]

2.2 Research Design

This was a retrospective secondary analysis of the newly established Acute Traumatic Brain Injury Registry at KCMC. This registry was established at KCMC to analyze the mortality and morbidity of TBI who present for acute care. This TBI registry started on May 5, 2013 and will continue for at least one year in order to evaluate any improvement in outcomes based on quality improvement changes at KCMC.

2.3 Ethics Approvals

Ethical approval was obtained from Duke University Medical Center and from Kilimanjaro Christian Medical Center for this retrospective analysis of de-identified data.

2.4 TBI Registry Inclusion and Exclusion Criteria

The Acute TBI Care Registry includes all patients who present to KCMC for acute care of their TBI. Patients not included in the registry were those presenting for follow-up care or second visits for their injury. This retrospective analysis extracted all available data from this registry.

2.5 Variables

2.5.1 Outcome Variables

Two main outcome variables will be described: mortality and morbidity. Mortality will be dichotomous variable for death at any time from arrival to the Casualty Department and during the hospital stay. Morbidity will be described using the Glasgow Outcome Score (GOS) collected through structured interview at the time of discharge from the hospital that has been a commonly used and validated scale.[17] The GOS is shown below in Table 2. For this study, GOS will also be dichotomized into full recovery versus other outcome (contingent on survival).

Table 2. Glasgow Outcome Scale

Glasgow Outcome Scale		
5	Good Recovery	Resumption of normal life despite minor deficits
4	Moderate Disability	Disabled but independent. Can work in a sheltered setting.
3	Severe Disability	Conscious but disabled. Dependent for daily support.
2	Persistent Vegetative State	Minimal responsiveness.
1	Death	Non survival.

2.5.2 Predictor Variables

Predictor variables included in this data set include injury severity data. Injury severity for TBI can be determined by physiologic scoring, anatomic scoring or by mentation scoring.

Physiologic scoring utilized physiologic indications of illness or injury, which include patient vital signs and mentation. This dataset includes the Revised Trauma Score (RTS) that is a physiologic score that combines a categorized Glasgow Coma Score, systolic blood pressure and respiratory rate with a coefficient for penetrating versus blunt injury as is seen in Figure 1. RTS is commonly used for research purposes in both high and LMIC.[18]

Glasgow Coma Scale

GCS	Points
15-13	4
12-9	3
8-6	2
5-4	1
3	0

Systolic Pressure

SBP	Points
>89	4
76-89	3
50-75	2
1-49	1
0	0

Respiratory Rate

RR	Points
10-29	4
>29	3
6-9	2
1-5	1
0	0

Figure 1: Revised Trauma Score Categorical Points

Anatomic scoring is not commonly used in the limited resource settings found in LMIC. An example of anatomic scoring is the Injury Severity Score (ISS), which is an

anatomical scoring system based on diagnosis of injury per region of the body that is based upon the Abbreviated Injury Score (AIS). The most widely accepted injury-severity scale, but mostly commonly used in high-income countries, the AIS which ranks each injury in every body region with a numerical score according to an ordinal scale (range: 1 [minor injury]–6 [probably lethal/maximum injury]) The ISS was developed as a way to summarize and take account of the effect of multiple injuries. The ISS was derived from AIS scores and uses an ordinal scale (range: 1–75), which is calculated by assigning AIS scores to injuries in each of six body regions (head/neck, face, thorax, abdomen/visceral pelvis, bony pelvis/extremities, and external structures) and then adding the squares of the highest AIS scores in each of the three most severely injured body regions (i.e., the three body regions with the highest AIS scores). Only the most severe injury in each body region is used in the score. If an AIS score of 6 is assigned to any body region, the maximal ISS of 75 is assigned. Ultimately, the Probability of Survival (Ps, based on Trauma Score-Injury Severity Score (TRISS) methodology[19]) is calculated in order to categorize deaths according to American College of Surgeons (ACS) classifications of non-preventable, potentially preventable and preventable based on the ISS and Ps.[20] Similarly, other studies have utilized AIS describing head injuries as a scale to describe the extent of TBI severity.

This method of injury severity assessment is very well utilized in high-income countries but was not utilized in KCMC due to the limitations of being able to accurately describe the extent of injuries without computed tomography capacity.

The third method of scoring is mentation scoring. The Glasgow Coma Score is a 3-15 point scale as shown in Table 3.[21] The Glasgow Coma Score is standardly categorized into mild TBI (GCS 14-15), moderate TBI (GCS 9-13) and severe (TBI GCS 3-8).

Table 3: Glasgow Coma Score

Eye Opening (choose one)	*Spontaneously*	*4*
	To Speech	*3*
	To Pain	*2*
	None	***1***
Verbal Response (choose one)	*Oriented*	*5*
	Confused	*4*
	Inappropriate	*3*
	Incomprehensible	*2*
	None	***1***
Motor Response (choose one)	*Obeys Commands*	*6*
	Localizes to pain	*5*
	Withdraws from pain	*4*
	Flexion to pain	*3*
	Extension to pain	*2*
	None	***1***

2.5.3 Other Variables

Expected confounding variables collected will be age (continuous and categorical based on international categorical norms), sex (dichotomous), alcohol involvement and mechanism of injury. Alcohol involvement was determined by either patient self-report, the treatment team smelling alcohol, or by a clinical exam that was consistent with intoxication. Initial treatment steps including management of potential secondary injury

including hypoxemia and hypotension will also be associated with outcomes. All variables evaluated in this study are included in Table 4.

Table 4. All variables included in the outcome evaluation of TBI

Outcome Variables	Death Disability
Other Variables	Glasgow Coma Score (GCS continuous, dichotomous (</>9) Alcohol Involvement Revised Trauma Score Systolic Blood Pressure Respiratory Rate Categorized Glasgow Coma Score Age Sex Mechanism of Injury Type of Road Traffic Injury Hypotension (Systolic Blood Pressure <90 mmHg) Hypoxia (Pulse Oxygenation <90%)

2.6 Data Collection

2.6.1 TBI Registry Data Collection

TBI care logs were completed by trained research nurse personnel. The TBI Care Log is attached in Appendix A for review. Research personnel were present in the Casualty Department over 80 hours a week and 7 days a week scheduled at the high patient volume time periods. For patients who came to KCMC when research staff were not present, retrospective review of Casualty Department, Surgical 1 Ward and Intensive Care Unit records to identify any potentially missed patients and to allow their information to be entered into the registry.

2.6.2 TBI Registry Computerized Dataset

Data was written onto these data collection sheets and then were entered manually into REDCap by trained data entry personnel. REDCap software is a tool that

does not require client local software and can be accessed from anywhere on the Internet secured on a Duke Health Technology Services (DHTS) server. The PI reviewed each record in REDCap in order to ensure the data was complete and valid.

2.6.3 Retrospective data analysis data collection

Upon reaching 190 patients the TBI Registry dataset, data extraction was performed by the project PI of the de-identified data from the REDCaps server.

2.7 Monitoring and Evaluation

Monitoring and evaluation of the TBI registry was performed by the project PI as part of a larger project. Oversight of data collection and irregular intervals and oversight of data entry for completeness and validity was performed. Double data entry was not possible given logistical challenges.

2.8 Data Analysis

2.8.1 Univariate Analysis

2.8.1.1 Descriptive Data

Continuous data was reported in means with standard deviations (SD), 95% Confidence Intervals (95% CI) and interquartile ranges (IQR). Categorical data was reported with proportions of total [%, (n)] and utilized Student's T test, Fisher's Exact and Pearson's Chi-squared statistical testing as appropriate. Univariate analysis utilized a standard significance of 0.2 for inclusion into the multivariate models.

2.8.2 Multivariate Analysis

After performing univariate analysis, variables that were significantly associated ($P<0.20$) with the outcome in question were included in a multivariate model. The RTS includes systolic blood pressure, Glasgow Coma Scale and respiratory rate so including RTS as well as hypotension in the model we would be including the same variable twice in the same model. Thus RTS was not included in the models. During the multivariate analysis for disability, there were no patients who suffered disability who were hypotensive.

3 Results

3.1 Univariate Analysis

Overall, data from a total of 190 patients were extracted retrospectively from the TBI Acute Care Registry.

3.1.1 Demographics

3.1.1.1 Patient Demographics

The mean age of these patients was 32.1 (SD 17.32, range 1-99, IQR 22-41). An age histogram is listed in Figure 2.

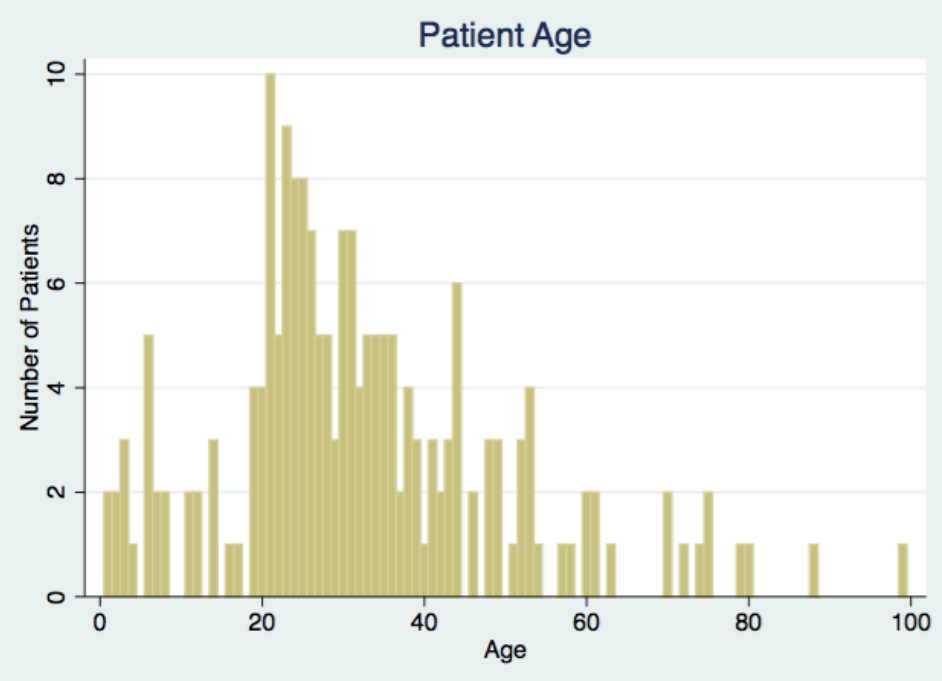


Figure 2: TBI Patient Age

While patient age seems shifted to the left, we categorized age into standard guidelines for age categories for injury registries in order to be able to make

international comparisons. Listed in Table 5 are the age categories and distribution by sex that showed significantly more males.

Overall, there are significantly more males (82.6%) compared to females who suffer TTBI. For each age category, there remains a persistent male predominance as seen in Table 5. Overall there is approximately 4:1 ratio of male to female TBI patients.

Table 5: Age Category and Sex of TBI Patients

Age Category	% of Total Patients (#)	% Male (n)*
<5 years	4.2%(8)	62.5% (5)
5-14 years	8.4% (16)	68.8% (11)
15-29 years	36.8% (70)	87.1% (61)
30-44 years	32.6% (62)	88.7% (55)
45-64 years	12.6% (24)	66.7% (16)
>64 years	5.3% (10)	90.0% (9)
Total	100% (190)	82.6% (157)
*Fisher's Exact p=0.034		

3.1.1.2 Mechanism of Injury

Overall the leading mechanism for all TBI was road traffic injuries followed by assaults and fall. The leading cause of road traffic injury was motorcycle crashes followed by car occupants. The proportion of males was significantly different across types of road traffic injuries. Table 6 shows the mechanisms of injury and types of road traffic injury frequencies amongst TBI patients.

Table 6: Total and Male proportion of patients by Mechanism of Injury

Mechanism of Injury	Total % (n)	%Male* (n)
Road Traffic Injury (RTI)	74.2% (141)	81.6% (115)
Car*	30.5% (43)	69.8% (30)
Motorcycle*	51.8% (73)	91.8% (67)
Pedestrian*	17.7% (25)	72.0% (18)
Fall	8.4% (16)	75.0% (12)
Assault	13.2% (25)	92.0% (23)
Drowning	0.5% (1)	100% (1)
Other	3.7% (7)	85.7% (6)
TOTAL:	100% (190)	82.6% (157)
***Pearson's Chi2 p= 0.005**		

3.1.1.3 Alcohol Involvement

More than 28% of patients had alcohol involved TBI, and there were significantly more males with an alcohol-related injury. The total and male proportion of alcohol involvement in TBI patients is listed in Table 7. Alcohol involvement was associated with type of road traffic injury (Fisher's Exact, $p=0.173$) and sex (Fisher's Exact, $p<0.001$) but not mechanism of injury, RTS, Severity of TBI (GCS Categories), death or GOS.

Table 7: Alcohol involvement and Sex

Alcohol Involvement**	Total	Proportion, % being Male, (n)
No	63.8% (120)	74.2% (89)
Unknown	7.5% (14)	100% (14)
Yes	28.7% (54)	98.2% (53)
Fisher's exact, $p<0.001$		

3.1.2 Patient Clinical Characteristics on Presentation

3.1.2.1 Glasgow Coma Scale on Presentation

The mean Glasgow Coma Scale (GCS) on presentation was 12.7 (SD 3.95, range 3-15, IQR 13-15). The histogram for GCS on presentation is in Figure 3.

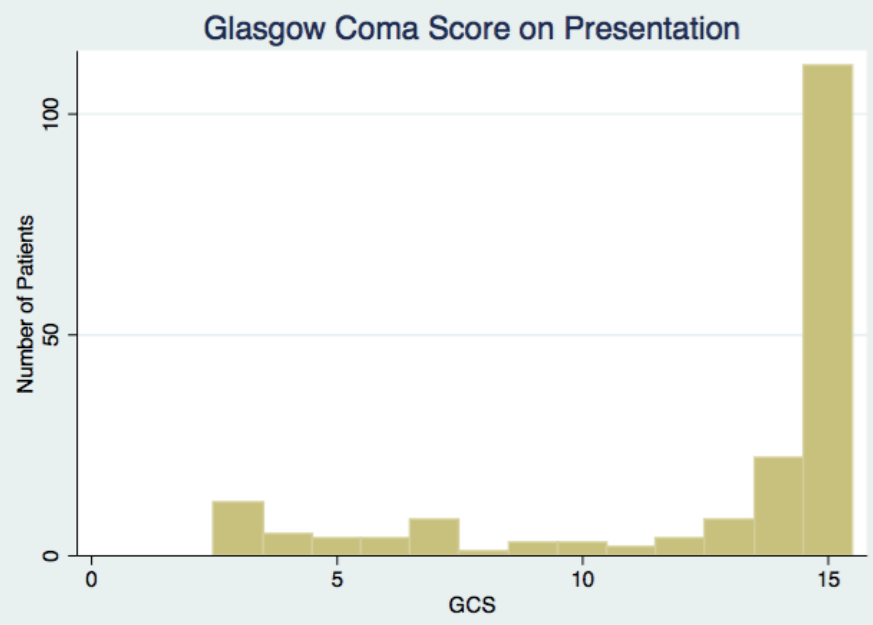


Figure 3: Histogram of TBI patient's Glasgow Coma Scale on Presentation

Standard categorization of GCS, as described in the methods, was performed yielding 71.6% (136) of patients had mild TBI, 10.5% (20) of patients had moderate and 17.9% (34) of patients had severe TBI. Patient age category, sex, alcohol involvement, mechanism of injury or road traffic injury were not significantly different among these different TBI severity categories.

3.1.2.2 Vital Signs, Revised Trauma Score on Presentation

Patient vital signs on presentation are listed in Table 8. Overall, 10.5% (20) were hypoxic with a oxygen saturation less than 90% on arrival while only 3.2% (6) of patients were hypotensive with a systolic blood pressure less than 90 mm Hg.

Table 8: Vital Signs and Revised Trauma Score on Presentation to the Casualty Department

Vital Sign (N)	Mean ± SD	Range (Min-Max)	InterQuartile Range (p25-p75)
Respiratory Rate (183)	23.0 ± 4.63	16-48	20-22
Pulse (187)	87.7 ± 19.66	47-166	77-84
SBP (181)	125.2 ± 21.84	57-249	112-122
Pulse Oxygen (182)	95.1 ± 11.90	20-100	97-99
Revised Trauma Score (174)	7.27 ± 1.11	3.56-7.48	7.11-7.84

3.1.3 Outcome Variables

3.1.3.1 Mortality

The overall mortality of all Casualty Department TBI patients in the registry is 12.6% (24 of 190). The mortality of patients who were admitted to the hospital was 13.5% (21 of 156). The mortality of patients who were admitted to the Intensive Care Unit was 72.7% (8 of 11).

Initial univariate analysis found death to be associated with RTS, severity of TBI based on GCS categorization, hypoxia and hypotension but not sex, age, mechanism of injury as seen in Table 10.

3.1.3.2 Morbidity

The Glasgow Outcome Scale (GOS) of the TBI patients is shown in Table 9.

Table 9: Glasgow Outcome Score for TBI patients

	GOS total (n=177)	Disability (n=153)
Good Recovery	77.4% (137)	89.5% (137)
Moderate Disability	4.5% (8)	10.5% (16)
Persistent Vegetative	1.6% (3)	
Severe Disability	2.8% (5)	
Death	13.5% (24)	N/A

GOS was further categorized into full recovery versus disability contingent on survival. Disability variable was found to be associated with TBI severity based on categorical GCS, categorical age and RTS but not gender, hypotension, mechanism of injury or type of road traffic user as seen in Table 10.

Table 10: Characteristics and comparison of all patients and those with poor outcomes

	All patients	**Patients who died**		**Patients with disability**	
Age*	32.1 (17.32)	37.0(20.0)	P=0.145	28.4(19.2)	P=0.360
Male**	82.6%	79.2%	P=0.575	87.5%	P=0.464
Mechanisms of Injury**					
RTI	74.2%	58.3%	P=0.132	87.5%	P=0.940
Assault	13.2%	16.7%		6.3%	
Fall	8.4%	20.8%		6.3%	
Drowning	0.7%	0.0%		0.0%	
Other Injuries	3.3%	4.2%		0.0%	
Type of RTI**					
Car	30.5%	35.7%	P=0.931	28.6%	P=0.910
Motorcycle	51.8%	50.0%		57.1%	
Pedestrian	17.7%	14.3%		14.3%	
Injury Characteristics					
Alcohol Involvement **	28.7%	14.8%	P=0.411	7.0%	P=0.449
GCS on arrival*	12.7 (4.0)	**6.5 (4.3)**	**P<0.001**	**8.4 (4.0)**	**P<0.001**
GCS <9	17.9%	**75.0%**	**P<0.001**	**56.3%**	**P<0.001**
Hypoxia**	10.5%	**45.8%**	**P<0.001**	**18.8%**	**P=0.054**
Hypotension **	3.2%	**12.5%**	**P=0.028**	0%	P=0.716
Revised Trauma Score*	7.27(1.11)	**5.45(1.34)**	**P<0.001**	**6.13(1.31)**	**P<0.001**
Mean (sd), or %; *TTest, ** Fisher's Exact; Comparisons made between all patients and outcome subgroup					

3.1 Multivariate Analysis

3.1.1 Mortality

The variables found in univariate analysis to be associated with mortality included RTS, TBI severity based on GCS categorization, continuous age, hypoxia and hypotension. Given that RTS is composed of systolic blood pressure, categorical Glasgow coma score and respiratory rate, there is likely significant co-linearity between the Categorical GCS and RTS and RTS and hypotension. Given this, RTS was not included in the multivariate analysis.

Table 11: Multivariate Model 2 and 3 for Mortality

	Model 1		**Model 2**		**Model 3**	
	OR	**P (95% CI)**	**OR**	**P (95% CI)**	**OR**	**P (95% CI)**
Age	1.02	0.14 (0.99-1.05)	1.02	0.17 (0.99-1.04)	--	--
Gender	0.4	0.21 (0.09-1.68)	--	--	--	--
Hypoxia	2.58	0.15 (0.70-9.50)	2.63	0.14 (0.73-9.45)	2.5	0.15 (0.71-8.47)
Hypotension	**13.38**	**0.04 (1.15-155.71)**	10.5	0.05 (0.97-113.86)	**11.41**	**0.04 (1.12-115.85)**
Moderate vs mild TBI	4.92	0.10 (0.73-33.16)	4.66	0.11(0.70-31.01)	4.51	0.12 (0.69-29.38)
Severe vs mild TBI	**36.53**	**0.00 (8.35-159.93)**	**32.45**	**<0.01(7.74-136.01)**	**31.56**	**<0.01(7.68-129.67)**
AIC		**0.52203**		**0.51956**		**0.51945**

Based on the Akaike information criteria (AIC) which is a measure of the relative quality of the statistical model weighing the goodness of fit of the model and the complexity of the model excluding age and gender (Model 3, Table 11) has the best quality. Based on model 3 those with hypoxia are 11 times more likely to die; and those with a GCS <9 are over 31 times more likely to die.

3.1.2 Morbidity

Based on the univariate analysis of morbidity, a dichotomous outcome of full recovery versus any disability was associated with severity of TBI based on categorical GCS, hypoxia, hypotension, categorical age were found to be significant. These variables were entered into a model again excluding RTS given its components were included in the model already. Outcomes of these multivariate models are listed in Table 12. These results suggest a significant relationship between presenting GCS and odds of disability yet no association with hypoxia or hypotension.

Table 12: Multivariate models for Morbidity

	Model 1		**Model 2**		**Model 3**	
	OR	p (95% CI)	OR	p (95% CI)	OR	p (95% CL)
Age	0.99	0.66 (0.95-1.03)	0.99	0.68 (0.96-1.03)	--	--
Gender	1.26	0.83 (0.15-10.31)	--	--	--	--
Hypoxia	0.36	0.35 (0.042-3.07)	0.36	0.35 (0.042-3.04)	0.35	0.34 (0.04-2.97)
Mod v mild TBI	**12.4**	**<0.01 (2.40-64.12)**	**12.77**	**<0.01 (2.52-64.81)**	**13.37**	**<0.01 (2.67-67.01)**
Severe v mild TBI	**136.42**	**<0.01 (19.50-954.58)**	**137.49**	**<0.01 (19.65-962.10)**	**139.34**	**<0.01 (19.99-971.32)**
AIC	0.4809		0.4682		0.4563	

4 Discussion

4.1 Summary

This study evaluated the injury and patient demographics and clinical presentation as well as searched for predictors for poor outcome based on a retrospective analysis of a TBI Clinical Registry. This study found most TBI patients at KCMC are males between ages 15 and 44 years of age and are predominantly injured by transport injuries most commonly motorcycle crashes. While the overall mortality for all comers is relatively low at 13%, the mortality rate for patients admitted to the ICU is exorbitant at 73%. While hypoxemia and hypotension were relatively uncommon amongst the whole population, hypotension increased the odds of death 11-fold while statistical significance was not reached for hypoxia ($p=0.15$) a larger sample size could bear out this association. Similarly, a low initial GCS (GCS <9) is significantly associated with death and with increased rates of morbidity. Hypotension and hypoxia were not significantly associated with disability.

4.2 TBI Epidemiology

Our data found that about 70% of TBI patients were between 15 and 44 years of age and most were male. About 74% of our TBI were caused by transport injuries of which over half were motorcycle riders. International statistics have found similar statistics with 60% of patients being injured in transport injuries and have found tri-modal age specific TBI incidences with peaks in the early childhood, late

adolescence/early adulthood and in the elderly.[10] While our data didn't support this tri-modal distribution according to the histogram, our limited numbers and preponderance of transport related injuries likely is causing and increased peak during the early adulthood time period. Alternatively, other data from Africa has supported a bimodal distribution in age specifically in children below 10 years and the other adolescents and young adults.[23,24] While our numbers might be too small to support either of these modal distributions, it is obvious that there is a significant preponderance in the young economically active ages.

Our data supports a 4:1 male preponderance which has been seen in multiple other African studies ranging anywhere from 5.69:1 to 1.7:1 in younger children.[24] This male preponderance is not only common for TBI, it is a common finding amongst all injuries globally. The large proportion of males is likely due to increased risk due to exposure and risk-taking behaviors. One significant caveat would be that since our data is limited to those who have been able to seek care and arrange transport to the hospital, there might be a very large selection bias based on persistent cultural gender inequalities.

Globally and in Africa, road traffic injuries are the leading cause of TBI that corresponds to our data. Since the introduction of inexpensive motorcycles to Africa over the last decade, motorcycles have become a larger proportion of transport injuries

but vulnerable road users (motorcyclist and pedestrians) bear a large burden TBI.[10,25] Interestingly, the rates of pedestrian injury at KCMC are markedly lower than that of car occupants but this is also likely due to a large selection bias introduced by the difficulties with access to care and delays in care that likely would have caused prehospital deaths for these pedestrians struck. In many other African countries, interpersonal violence accounts for 30-40% of TBI patients[10,26] yet our data showed that only 13% of total TBI patients were assaulted with an impressive but common male preponderance.

Our data found the proportion of alcohol-related injuries amongst our TBI registry to be 28%, which could be a gross underestimate given our lack of testing capacity. Data from neighboring countries have shown rates from 45% in South Africa to 18-22% in Mozambique.[27,26] Similar to our data, most countries have found that alcohol related-injuries are markedly more common among men.[27]

4.3 Hypoxemia and Hypotension

As hypoxemia and hypotension can cause secondary injury recognizing and intervening on them is imperative. While hypoxemia and hypotension were rare in our patients, hypotension was significantly associated with death. New data are suggesting hyper-oxygenating patients to a PaO2 of between 250 mmHg to 486 mmHg for the first 72 hours may provide benefit.[28] Hypotension is a significant predictor of death for TBI patients as hypotension worsens secondary injury.[29] While our data didn't show

hypoxemia as a predictor of death, our sample size and limited numbers of patients with hypoxemia or hypotension could have impacted our results. Similarly, difficulty with access to care given a lack of prehospital care and long transport times might prove fatal for a large proportion of patients who might have been hypotensive.

While hypoxemia and hypotension are associated with mortality in the literature, very often in LMIC they are associated with minor disabilities but not severe morbidity. While this might be counter-intuitive, it is likely that patients who have hypoxemia and hypotension in LMIC are markedly sick and more likely to die, and therefore being less likely to have severe disabilities. Similarly, mild secondary injury is more apparent in LMIC due to poor access and quality of care for acute TBI management.

4.4. Initial Glasgow Coma Score

Our data showed that Severe TBI as defined by Glasgow Coma Score of 8 or less is significantly associated with mortality and morbidity and Moderate TBI as defined by a Glasgow Coma Score of 9-13 is significantly associated with increased morbidity. While these findings are common-place internationally, now that we have found these to correlate with mortality and morbidity here at KCMC we can likely strategize how to utilize resources most appropriately for those most in need.[29] For instance, since ICU beds are at a premium, and the fatality rate of patients going to the ICU is 70%, further in-dept analysis of these ICU patients is warranted to understand the point of futility of

care to ensure that those with the most likely change to survive are given required treatment. More concretely, utilization of GCS as part of a clinical practice guideline we can discuss mortality rates and have set destinations in the hospital where these ill patients will be appropriately monitored.

4.5 Limitations

Limitations of this project include a limited sample size of all TBI patients and of severely ill TBI patients as well as those who have hypoxemia and hypotension. Most large trials on TBI are only can be performed as multi-center projects, like the through the NETT or Neurosciences Emergencies Treatment Trials group or CRASH trials, given the relative rarity of TBI. Given this, our sample size that was obtained over a three-month time period is still robust enough for this pilot study.

Another limitation of this study is the clinical environment and culture of KCMC. Documentation of vital signs and GCS is quite limited so retrospective enrollment of patients can be quite challenging. Tracking the patient and their chart through their hospital stay to determine outcome is also a difficult task in this resource-constrained environment. Similarly, we currently have only one set of vital signs during their whole Casualty Department stay. While this might be a quick snapshot of patients status, knowing continuous monitoring values or having more frequent pulse oxygen

sampling would improve the sensitivity of hypoxemia and hypotension sampling and likely then show more of an association with mortality.

4.6 Next Steps

With the information from this pilot, we are going to add more vital sign data to the TBI registry on arrival to the surgical ward in order to assess the success of Casualty Department treatment of hypotension or hypoxemia. Next we are going to start creating a clinical practice guideline which takes into account how many patients we expect to see that are severe and will take an organized systematic approach to acute TBI management starting with stabilization, diagnostics, referral and admission as seen in Appendix B. This TBI registry will continue uninterrupted for one year at which time will likely have enough data for a very detailed repeat descriptive analysis of TBI at KCMC.

5 Conclusion

Traumatic brain injury at KCMC is a relatively common event that has significant mortality with over 12% for all CD patients and over 70% for ICU patients. Most patients are men between the ages of 15 and 45 and are injured in road traffic injuries especially motorcycle crashes. Alcohol use is prevalent, 28%, and more common among men. Hypotension and initial Glasgow Coma Score are predictors of death and Glasgow Coma Score is a predictor of disability contingent on survival. Further studies with increased numbers are needed to understand the relationship of hypoxemia with mortality and morbidity at KCMC.

Appendix A

K.C.M.C **Traumatic Brain Injury Treatment and Care Log** SID: _____

MRN:_____
Date of Injury: (dd/mm/yy) ___/___/___
Time of Injury: (24hr) ___:____
Date of Arrival: (dd/mm/yy) ___/___/___
Patient arrival time: (24 hr) ___:___
Treatment team arrival: (24 hr)
Casualty MD: ___:___
Anesthesia MD: ___:___
Surgery MD: ___:___

Patient age: _____
Patient sex: Male Female
Mechanism of Injury: (Circle One)
□ Road Traffic: (Pedestrian, Motorcycle, Car)
□ Drowning
□ Assault: (Fist/Foot, Gun, Knife, Domestic)
□ Fall: (from height_____, from ground)
□ Other:_____

Was the injury: (□ unknown)
□ Unintentional □ Self-Inflicted □ Inflicted by other
Alcohol involved?: □No □Yes □Unknown

VS: T ____ RR _____ Pulse _____

BP _____ / _____ Pulse Oxygen _____
□ NP due to lack of BP cuff
□ Done by researcher □ Done by nurse

Repeat VS: T ____ RR _____ Pulse _____

BP _____ / _____ Pulse Oxygen _____

Eye Opening (choose one)	*Spontaneously*	*4*
	To Speech	*3*
	To Pain	*2*
	None	***1***
Verbal Response (choose one)	*Oriented*	*5*
	Confused	*4*
	Inappropriate	*3*
	Incomprehensible	*2*
	None	***1***
Motor Response (choose one)	*Obeys Commands*	*6*
	Localizes to pain	*5*
	Withdraws from pain	*4*
	Flexion to pain	*3*
	Extension to pain	*2*
	None	***1***
GCS Total Score:		*/15*

AVPU: (circle one)
Alert
Responds to Verbal stimuli only
Responds to Painful Stimuli only
Unresponsive

Pupils on arrival: Right: ____mm □R □NR
Left: ____ mm □R □NR
□EQUAL

AIRWAY:
□ intact (no gurgling, snoring, drooling)
□ NOT intact
□ oral/nasal airway time ___:___ □ NP □ PTA
□ intubation time ___:___ □ not performed

BREATHING:
□ chest auscultated
□ NOT auscultated
□ oxygen applied time ___:___ □ NP □ PTA
□ chest radiograph time ___:___ □ NP □ PTA
□ chest tube placed time ___:___ □ NP □ PTA

CIRCULATION:
□ pulses evaluated
□ pulses NOT evaluated
□ Fluids started time ___:___ □ NP □ PTA
□ Labs Sent time ___:___ □ not performed
□ Hgb □ not performed
□ Blood grouping □ not performed

DEFICIT:
□ GCS calculated □ GCS not calculated
□ moved all extrem □ not examined
□ Seizure? □ no sz
□ skull radiograph time ___:___ □ NP □ PTA
□ CT brain _dd_/_mm/_yy_ time ___:___□NP □ PTA
□ Mannitol started time ___:___ □ NP □ PTA
□ cervical collar placed time ___:___ □ NP □ PTA
□ anti-sz med started time ___:___ □ NP □ PTA
Med:_____

EXPEDITE:
□ transported to ICU time ___:___ □ NP
□ to surgery time ___:___ □ NP
□ to OT time ___:___ □ NP
□ death, mortuary time ___:___ □ NP
□ to home time ___:___ □ NP

Traumatic Brain Injury Treatment and Care Log SID: _____

History:

Hospital Course

□ had surgery for TBI injury Date _____ Time_____ □ No TBI surgery
□ had surgery for other injury Date _____ Time_____ □ No surgery
□ went from surgery 1 to ICU Date _____ Time_____ □ No ICU time

Outcome

□ Death Date _____ Time of Death_____ □ Alive at discharge
Location of Death: □ ICU
□ surgery 1
□ OT

□ Discharged from ICU Date _____ □ Not in ICU

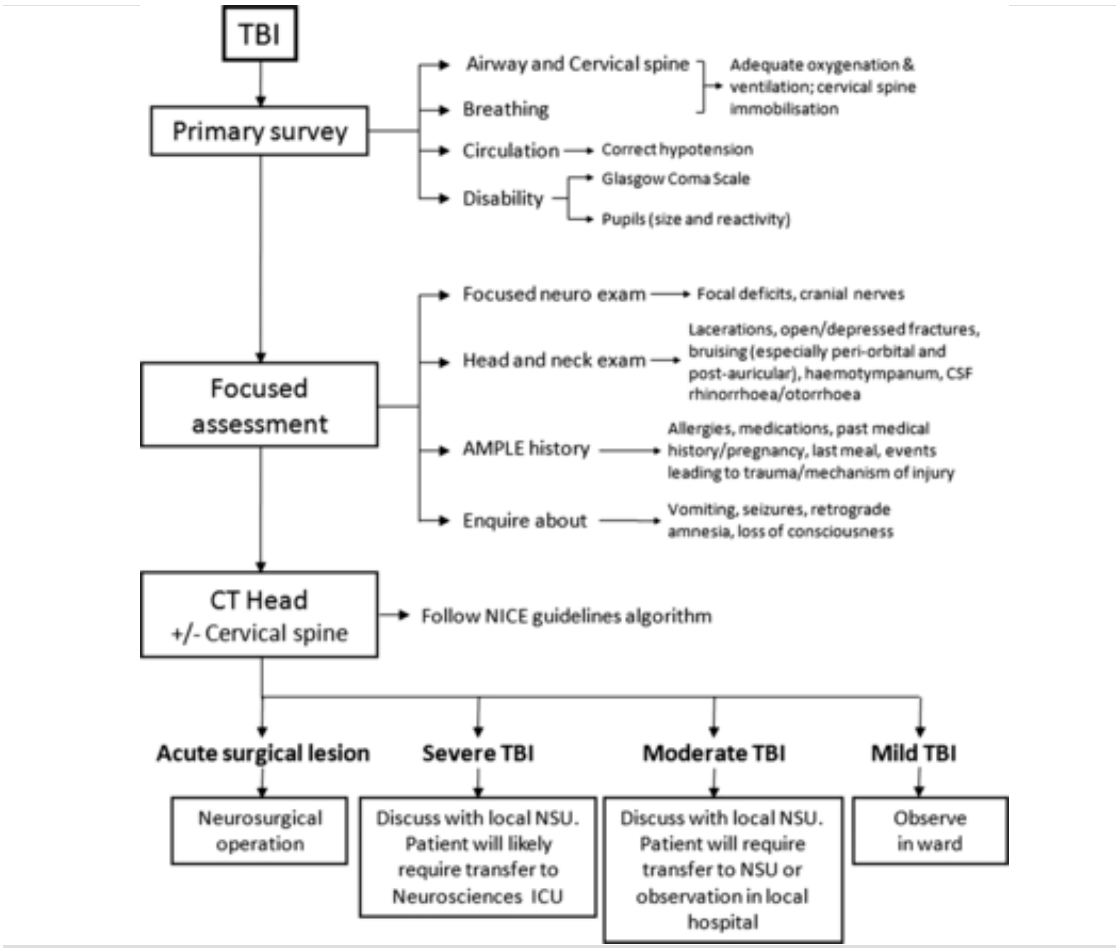
Discharged from hospital Date _____

Presumed cause of death, Reasons for or against surgery:

Glasgow Outcome Score: _____

5	Good Recovery-	Resumption of normal life despite minor deficits
4	Moderate Disability	Disabled but independent. Can work in a sheltered setting
3	Severe Disability	Conscious but disabled. Dependent for daily support
2	Persistent vegetative	Minimal responsiveness
1	Death	Non Survival

Appendix B


TBI
Primary survey
Airway and Cervical spine
Adequate oxygenation & ventilation; cervical spine immobilisation
Breathing
Circulation
Correct hypotension
Disability
Glasgow Coma Scale
Pupils (size and reactivity)
Focused assessment
Focused neuro exam
Focal deficits, cranial nerves
Head and neck exam
Lacerations, open/depressed fractures, bruising (especially peri-orbital and post-auricular), haemotympanum, CSF rhinorrhoea/otorrhoea
AMPLE history
Allergies, medications, past medical history/pregnancy, last meal, events leading to trauma/mechanism of injury
Enquire about
Vomiting, seizures, retrograde amnesia, loss of consciousness
CT Head +/- Cervical spine
Follow NICE guidelines algorithm
Acute surgical lesion
Severe TBI
Moderate TBI
Mild TBI
Neurosurgical operation
Discuss with local NSU. Patient will likely require transfer to Neurosciences ICU
Discuss with local NSU. Patient will require transfer to NSU or observation in local hospital
Observe in ward

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