

Burden, Predictors and Short-Term Outcomes of Traumatic Brain Injury Among Patients Admitted to Ugandan Intensive Care Units

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Abstract: Severe Traumatic brain injury (STBI) is a leading cause of morbidity and mortality among young individuals worldwide with worse outcomes being registered in low-income countries. Brain trauma foundation recommends the management of patients with TBI in the intensive care unit (ICU) to prevent secondary brain injury for improved outcome. However, Uganda being a low-income country, still grapples with the availability of ICU resources and space. Information regarding burden, predictors and short-term outcomes of ICU patients with TBI in Uganda has never been reconnoitered. A multicenter prospective observational cohort was conducted between 2013 to 2015 at four Ugandan ICUs. During the study period, we consecutively enrolled 387 critically ill, adult patients with TBI to determine the burden, predictors and short term outcomes in these patients. Baseline demographics, clinical and treatment parameters were recorded and followed till discharge from ICU or death. Of 387 patients enrolled in the study, 277 (71.6%) had moderate TBI, while 113 (29.2%) patients had STBI. The highest burden of TBI was recorded among patients assaulted through mob violence, recorded at 17/21 (81.0%), as shown in table 5. The overall mortality was at 34.4% (95/277) among patients with moderate or severe TBI, and 46.9% (53/113) among patients with STBI alone. Mortality was relatively higher among patients brought by the police, and those brought in at night. Multivariate analysis showed patient intubation, lack of antibiotic use, failure to transfuse, tracheostomy tube not inserted, and being involved in RTA or sustaining a fall were significantly associated with mortality among patients with TBI. We found a high burden of TBI and mortality among ICU patients. Despite limited resources in the local setting, inexpensive and locally available measures can reduce on the length of patient's stay in the ICU and eventually decrease on the mortality. Improvement in prehospital as well as early trauma and airway care, antibiotic use, blood transfusion plus public health safety measures may reduce on the burden of TBI as well as improve outcomes.

Keywords: TBI, Burden, Predictors, Critically Ill, ICU

1. Introduction

Traumatic brain injury (TBI) is a global public health concern infringing on socio-economic development. In high-

income countries like the United States of America and the United Kingdom, there are approximately 275,000

admissions per year in each country [1]. Such numbers are higher in low-income countries such as Uganda, South Africa, Nigeria, and Kenya [2, 3].

While the causes of TBI have fluctuated over the years with falls among young children and elderly surpassing road traffic accidents (RTAs) in the high-income countries [4], RTAs remain among the leading cause of TBI and death worldwide, with males being predominantly affected [5]. RTAs involving pedestrians and motorcycle riders are still the leading cause of TBI in low-income countries such as Uganda [6].

Despite the advancement in treatment options, TBI still causes significant mortality around the world [4, 7-11] and the World Health Organization (WHO) estimates that injury-related incidents will be the fifth most prevalent cause of death worldwide by the year 2030 [5]. Mortality in some high income-countries ranges from 10.8 to 44.2%, while in Uganda and Kenya, it ranges between 25.8% and 54% [3, 12, 13].

Just like most low-income countries, there is a paucity of high-quality epidemiological data on the burden, predictors, and outcomes of TBI in Uganda. The burden of RTAs has significantly risen in Uganda in the last decade, which parallels the surge in the number of commuter motorbikes in the city and increased population growth [8, 14]. Unfortunately, the health system in the country is not sufficiently equipped to manage significant numbers of patients with severe traumatic brain injury (STBI). It is recommended that such patients be treated in Intensive Care Units (ICUs) since protocolized care in the ICU has been shown to improve outcome in patients with STBI [15-17]. Ugandan ICUs are resource-constrained with few functional beds, low human resource and high mortality rates [18-20]. It is also unknown how patients with TBI admitted to Ugandan ICUs compare with others in either a similar or higher income setting.

We sought to determine the burden, predictors, and short-term outcomes among patients with TBI admitted to Ugandan ICUs.

2. Methods

2.1. Study Background

We conducted a prospective observational multicenter cohort study among adult patients between January 2013 to June 2015 at Mulago National Referral ICU, Uganda Heart Institute ICU, International Hospital Kampala ICU and Nakasero Hospital Limited ICU in Kampala city, Uganda.

2.2. Sample Size and Eligibility Criteria

We calculated the sample size for the prevalence of TBI post hoc using Kish Leslie method of 1965, where $n = Z^2 pq / d^2$ with $Z = 1.96$, where p is the hypothesized population with TBI. This was estimated from a study by Mehmood A *et al.* which, was 62.9% [30]. Finally, d is a measure of the study's power, the probability of committing a type 2 error, and this was set at 0.05. The calculated sample size was 359

participants.

All patients requiring mechanical ventilation were recruited into the study with informed consent from the next of kin. Eligible patients who were less than 18 years, brain dead and those whose next of kin refused to give consent to participate in the study were excluded.

2.3. Patient Assessment

At study enrolment, we collected socio-demographic data, medical history, social history (smoking, alcohol use, education level), comorbidities and clinical scores. Clinical characteristics included organ function status, surgical status, comorbidities, biochemical and hematological values. Treatment characteristics included sedation drugs, use of restraints, mode of airway control, mode of ventilation, chest X-ray findings, and route of administration of feeds. Severe TBI and Moderate TBI were defined as having an admission GCS of equal to or less than 8 and above 8 respectively. Patients' characteristics, investigations and Organ support parameters were all recorded in study record forms. The primary outcome was death while Secondary outcome was the length of ICU stay.

2.4. Ethical Approval

Both Research and Ethics Committee of Makerere University and Uganda National Council for Science and Technology approved this study. All study participants were treated for TBI as directed by the attending anesthesiologist or Intensivists.

2.5. Data Management and Statistical Analysis

All data were entered in a data entry sheet in excel and analyzed using STATA (StataCorp. 2014. *Stata Statistical Software: Release 14.1*. College Station, TX: StataCorp LP).

We determined the burden of TBI and STBI with the numerator being the number of patients with TBI and STBI respectively and denominator the total number of patients enrolled in the study. We reported the overall prevalence of TBI as well as prevalence among special groups and their corresponding 95% confidence intervals. To compute mortality among TBI patients, the total number of participants who died was divided by the total number of participants with TBI. Data were summarized using proportions/percentages for categorical variables and means with standard deviations for continuous data. To compare characteristics between categorical variables; Chi-square and Fisher's exact test were used. Significance was set at a p-value of less than 0.05.

To assess the predictors of mortality among patients with TBI, we used logistic regression. Bivariate analysis was done for each independent predictor and if it had a P-values of 0.2 or less it was entered into a multivariate logistic model. We assessed for interaction then confounding at 10% difference between adjusted and unadjusted models. Significance was set at a p-value of 0.05 and less.

3. Results

During the study period, we recruited 387 patients admitted in four ICUs majority of whom, 211 (54.5%) were below 35 years of age and were predominantly males 327 (84.5%) (Table 1).

Table 1. Demographic and pre-admission information among patients admitted to Ugandan ICUs.

Variable	n (387)	Percentage
Age		
Less than 35	211	54.52
At least 35	61	15.76
Unknown	115	29.72
Sex of the patient		
Male	327	84.5
Female	60	15.5
Referral		
The patient was referred into the hospital	80	20.67
The patient was not referred	307	79.33
Time when the patient was brought to the hospital		
Day	200	51.68
Evening	77	19.9
Night	110	28.42
Patient was brought by:		
Family or relatives	126	32.6
Police	99	25.6
Not known	162	41.9

Road traffic accidents accounted for almost half of the mechanisms of injuries, at 188 (48.6%), as shown in table 2. Brain CT scan was the commonest investigation done, in 149 patients (38.7%), while 237 (61.2%) received antibiotics (table 3). All patients were mechanically ventilated through endotracheal or tracheostomy tubes with various modes. Mean age of patients was 32 years with males constituting 76% of study subjects. All patients were fed enterally, and 56% had had some form of surgical intervention during their ICU admission.

Table 2. Mechanism, pattern, and severity of injuries among patients admitted to Ugandan ICUs.

Variable	N (387)	Percentage
Mechanism		
RTA	188	48.58
Thermal burns	17	4.39
Falls	11	2.84
Mob violence	21	5.43
Assault	34	8.79
Others	116	29.9
Number of injuries		
Not multiply injured	357	92.5
Multiply injured	29	7.5
Glasgow Coma Scale		
Above 12	111	28.7
Between 8 and 12	163	42.1
Below 8	113	29.2
Blood pressure measurements		
Normotensive	164	42.38
Hypertensive	85	21.96
Hypotensive	82	21.19
Unrecorded	56	14.47
Pulse rate		
Normal	144	37.21

Variable	N (387)	Percentage
High	104	26.87
Low	29	7.49
Unrecorded	110	28.42

Table 3. Investigations and interventions.

Variable	N	Percentage
Investigations done		
X-ray	80	20.73
Ct scan	149	38.7
Ultrasound	51	13.18
Other investigations	54	13.95
Interventions		
Cardio Pulmonary Resuscitation	40	10.34
Intubation	123	31.78
Chest drain	12	3.1
Airway management	180	46.51
Others**	118	30.65
Treatment		
Antibiotics	237	61.24
Analgesia	227	58.66
Anesthesia	56	14.47
Anticonvulsants	106	27.39
Transfusion	43	11.11
Tracheostomy tube	76	19.64
Diuretics	81	20.93
Others	52	13.44

Data shows that 48.8% of TBI patients had undergone some form of surgery compared to those who didn't have TBI (33.8%). Comorbidities, seizures and cardiac arrests were more prevalent among patients without STBI (table 4).

Table 4. Comparing characteristics between patients with STBI and those without STBI.

Characteristics	No STBI (274) N (percentage)	STBI (113) N (percentage)	P value
Comorbidities			
HIV	61 (22.08)	24 (20.73)	0.001
Diabetes mellitus	29 (10.39)	3 (2.44)	0.003
Hypertension	18 (6.49)	4 (3.66)	0.002
Acute kidney injury	7 (2.60)	6 (4.88)	0.874
Acute respiratory distress syndrome	46 (16.88)	21 (18.29)	0.042
Sepsis	36 (12.99)	32 (28.05)	0.894
PH			
Normal	68 (24.68)	23 (20.73)	0.49
Acidosis	142 (51.95)	70 (62.20)	
Alkalosis	25 (9.09)	7 (6.10)	
Hemoglobin			
Normal	75 (27.27)	26 (23.17)	0.551
Anemia	199 (72.72)	87 (76.83)	
Surgery done	93 (33.77)	55 (48.78)	0.055
Seizure	39 (14.29)	18 (15.85)	0.758
Cardiac arrest	57 (20.78)	10 (8.54)	0.028
Self-extubation	28 (10.39)	26 (23.17)	0.016

Overall, 277 (71.6%) patients had TBI, of whom 113 (29.2%) had severe TBI. The highest burden of TBI was recorded among patients assaulted through mob violence, recorded at 81.0% (17/21) (Table 5). The overall mortality was at 34.4% (95/276) among patients with TBI, and 46.9% (53/113) among patients with STBI. Mortality was relatively higher among patients brought by the police, and those brought in the night (table 6).

Table 5. Prevalence of traumatic brain injury among patients admitted to Ugandan ICUs.

Category	n/N	Prevalence (95% CI)	P-value
Overall prevalence of TBI	277/387	71.6 (66.9 – 75.9)	
Severe TBI	113/387	29.2 (24.9 – 33.9)	
Sex			
Male	242/327	74.0 (69.0 – 78.5)	0.013
Female	35/60	58.3 (45.2 – 70.4)	
Age			
Less than 35	155/211	73.5 (67.0 – 79.0)	0.04
At least 35	40/61	65.6 (52.5 – 76.6)	
Number of injuries			
Not multiply injured	273/357	76.5 (71.7 – 80.6)	0.001
Multiply injured	4/29	13.8 (4.9 – 33.0)	
Mechanism of injury			
No mob violence	260/366	71.0 (66.2 – 75.5)	0.327
Mob violence	17/21	81.0 (56.4 – 93.3)	

At multivariate analysis, intubation, failure to transfuse, or administer antibiotics (table 6), tracheostomy tube not inserted and being involved in RTA (table 7) or sustaining a fall were significantly associated with mortality among patients with TBI.

Table 6. Mortality among patients with TBI admitted to Ugandan ICUs.

Category	n/N	Mortality (95% CI)	P-value
Overall mortality among TBI patients	95/276	34.4 (29.0 – 40.3)	
Mortality among patients with STBI	53/113	46.9 (37.8 – 56.2)	
Sex			
Male	82/241	34.0 (28.3 – 40.3)	0.717
Female	13/35	37.1 (22.3 – 54.9)	
Age			
Less than 35	50/155	32.3 (25.3 – 40.1)	0.651
At least 35	14/40	35.0 (21.4 – 51.5)	
Patient was brought by:			
Family or relatives	31/93	33.3 (24.4 – 43.7)	0.05
Police	33/73	45.2 (34.0 – 56.9)	
Not known	31/110	28.2 (20.5 – 37.4)	
Referral			
Patient was referred into the hospital	21/61	34.4 (23.4 – 47.5)	0.999
Patient was not referred	74/215	34.4 (28.3 – 41.1)	
Time when the patient was brought			
Day	39/128	30.5 (23.0 – 39.1)	0.148
Evening	20/64	31.3 (20.9 – 43.9)	
Night	36/84	42.9 (32.5 – 53.8)	
Intubation			
Patient was intubated	57/101	56.4 (46.5 – 65.9)	0.001
Patient was not intubated	38/175	21.7 (16.2 – 28.5)	
Antibiotic use			
No antibiotic given	52/173	30.1 (23.6 – 37.4)	0.048
Antibiotics were given	43/103	41.7 (32.5 – 51.6)	

Table 7. Factors associated with mortality among patients with TBI admitted to Ugandan ICUs.

Characteristics	Bivariate analysis		Multivariate analysis	
	OR (95% CI)	P-Value	OR (95% CI)	P-Value
Sex				
Male	1		1	
Female	1.15 (0.55 – 2.39)	0.717	0.92 (0.69 – 1.24)	0.602
Age				
Less than 35	1			
At least 35	1.14 (0.86 – 1.51)	0.355		
Patient was brought by:				
Not known	1		1	
Family or relatives	1.27 (0.70 – 2.31)	0.428	0.68 (0.38 – 1.23)	0.205
Police	2.10 (1.13 – 3.91)		1.63 (0.86 – 3.08)	
Referral				
Patient referred into the hospital	1			
Patient was not referred	0.99 (0.55 – 1.82)	0.999		
Time when the patient was brought				

Characteristics	Bivariate analysis		Multivariate analysis	
	OR (95% CI)	P-Value	OR (95% CI)	P-Value
Day	1			
Evening	1.04 (0.54 – 1.98)	0.912		
Night	1.71 (0.96 – 3.04)	0.066		
Interventions reference	1			
Patient was intubated	0.21 (0.13 – 0.36)	0.001	0.22 (0.13 – 0.37)	0.001
Antibiotics were not given	1.67 (1.00 – 2.77)	0.049	2.11 (1.23 – 3.60)	0.006
Anti-convulsant given	1.03 (0.61 – 1.73)	0.918		
IV fluids administered	0.73 (0.42 – 1.29)	0.28	0.89 (0.50 – 1.58)	0.683
No transfusion	0.54 (0.23 – 1.22)	0.139	0.48 (0.22 – 0.98)	0.047
Tracheostomy tube not inserted	2.41 (1.15 – 5.07)	0.02	1.82 (1.01 – 3.62)	0.049
Mechanism of injury				
No mob violence	1			
Mob violence	0.78 (0.27 – 2.29)	0.654		
Falls	1.43 (0.70 – 2.92)	0.328	2.39 (1.02 – 5.65)	0.046
Road traffic accidents	1.44 (0.94 – 2.21)	0.098	2.00 (1.16 – 3.46)	0.013
Number of injuries				
Multiply-injured	1		1	
Not multiply-injured	0.63 (0.06 – 6.15)	0.692	1.16 (0.47 – 2.87)	0.746
Blood pressure				
Normotensive	1		1	
Hypertensive	2.34 (1.32 – 4.15)	0.004	2.62 (1.38 – 4.97)	0.003
Hypotensive	2.61 (1.47 – 4.65)	0.001	2.92 (1.51 – 5.66)	0.001

4. Discussion

In this study, we found the burden of TBI to be very high; this is comparable to similar studies in the same setting. Tran *et al.* reported TBI incidence of 89/100,000 patients in Mulago hospital's neurosurgical unit [3]. This was a one-year single centre retrospective chart review that had comparatively fewer patients with STBI. In addition, they did not include ICU patients and this may account for the lower mortality. Min Li *et al.* reported an incidence of 7.2-811/100,000 per year depending on the location [10]. Data from New Zealand shows that rate in rural areas is higher than in urban areas, this could explain why the incidence in our setting is much higher than expected [23], considering the different mechanisms of injury in New Zealand and Uganda.

We found ICU mortality of patients with STBI at 46.9%. This was higher than mortality figures from high-income countries but somewhat similar to low-income country data for example, in Kenya, Opondo *et al.* reported a mortality rate of 54% in STBI patients admitted at a Kenyan ICU [12]. Similarly, in Benin, a low-income country in West Africa and Tanzania in East Africa with STBI related mortality of 47% [12, 21]. In the Tanzanian study, only one patient received mechanical ventilation and highlights resource constraints associated with skills, staffing and equipment. Previous studies at Mulago hospital in Uganda noted most deaths occurred during the evening and overnight shifts where the nursing coverage was significantly reduced [19]. Therefore, it is not surprising that in our study, the highest mortality occurred during the nights. Objective monitoring of ICP was not done in this study, and yet ICP monitoring has been shown to improve outcomes in TBI patients managed in the ICU [31-33]. We speculate that the nature of primary brain injury could have contributed to the high mortality rate among TBI patients as shown in studies where radiological

characteristics on computed tomography scans were associated with midline shift, extensive subarachnoid hemorrhage and diffuse axonal injuries, leading to higher mortality in this patient category. And most factors at bivariate and multivariate analysis were only weakly associated with death. Several studies also found that the need for mechanical ventilation in STBI patients was an independent risk factor for mortality, and all our study patients required mechanical ventilation [21, 34]. This could account for the high mortality demonstrated in this particular study when compared to similar studies in similar settings since all our study patients were mechanically ventilated.

From our study, we found most TBI patients to be young male adults with a mean age of 33. This data agrees with most studies in TBI patients where similar gender and age groups of patients are admitted to ICU due to RTAs [11, 20, 21]. This is because the mechanism of injury resulting in STBI in this age bracket has not significantly changed. Males are predominantly affected because most are motorcyclist business riders which is similar to the Tanzanian situation where 49% of all RTAs involved motorcyclists [6, 20, 22]. Studies in high-income countries noted older group of patients with a mean age of 60 years and children presenting to ICU with TBI [4, 20]. This is because the older patients being more prone to falls as opposed to RTAs; this is part of the changing epidemiology of TBI being observed in the high-income countries [4].

At multivariate logistic regression, significantly, transfusion and intubation reduced the risk of mortality by almost 50% and 80% respectively. While the mortality risk was double if a patient did not receive antibiotics or a tracheostomy. Intubation and tracheostomy both being protective against death further asserts the importance of airway management among patients with trauma [27]. Antibiotic use prophylactically prevents infections but also treats the already present infections which, by themselves,

could cause death. Finally, patients that sustained falls and those involved in RTAs were more likely to die. This could be due to the nature and severity of the injuries these mechanisms cause which, is usually multiple and severe.

5. Conclusion

Our study has demonstrated a high burden of TBI to the already scarce ICU resources associated with a high mortality and prevalence of STBI among patients admitted to Ugandan ICUs. Despite limited resources in the local setting, findings from our work have shown that inexpensive and locally available measures can reduce on the length of patient's stay in the ICU and eventually decrease on the mortality. Measures such as early trauma and airway care, antibiotic use, blood transfusion plus public health safety measures may reduce on the burden of TBI as well as improve outcomes.

Data Availability

Data used to support the findings of this study can be accessed at <https://osf.io/z6s7y/>.

Data are available under the terms of the Creative Commons Zero "No rights reserved" data waiver (CC0 1.0 Public domain dedication). DOI 10.17605/OSF.IO/Z6S7Y.

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