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Clinical commentary

Pediatric traumatic brain injury at Mbarara Regional Referral Hospital, Uganda

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ABSTRACT

Background: In Uganda, TBI constitute the majority of neurosurgical admissions and deaths specially in the pediatric population. This study aims to determine the factors associated with poor outcome among pediatric TBI cases at a major referral hospital in western Uganda.
Methods: This study was conducted at Mbarara Regional Referral Hospital (MRRH) in western Uganda. All pediatric neurosurgical cases between 2012 and 2015 were reviewed. In-hospital mortality and discharge GCS were the main outcomes of interest. Multivariable logistic regression with backward elimination was used to determine the factors significantly associated with outcome.
Results: A total of 381 pediatric TBI patients were admitted to MRRH between 2012 and 2015. The mean age was 8.6 (SD 5.6) with a male predominance (62.0%). The most common mechanism of injury overall was RTI, which was responsible for 71% of all TBI cases. In the multivariable logistic regression model, admission GCS < 13 was a strong predictor of poor outcome and in-hospital mortality compared to admission GCS $\geq$ 13, with patients demonstrating an odds ratio of 30 (95%CI: 7-132) and OR of 18 (95%CI: 4-79), respectively.
Conclusion: Given the lack of published literature on pediatric TBI in LMICs, this study was the first to describe and evaluate risk factors associated with TBI severity among pediatric patients at a major referral hospital in western Uganda. Injury severity on admission was the only variable found to be significantly associated with discharge outcome. This study ultimately highlights the need for more effective preventative measures to decrease admission severity.

1. Introduction

The Global Burden of Disease study estimated traumatic brain injuries (TBI) to be responsible for 11.2% of total global disability adjusted life years [1]. Road traffic incidents (RTIs) are responsible for the majority of head and spinal injuries especially in LMICs where they cause up to 80% of TBIs [2]. In studies from Uganda, TBI was the predominant cause of neurosurgical admissions and deaths, accounting for 87% of all neurosurgical admissions and resulting in an overall mortality rate of 13% [3,4]. This statistic is expected to increase further over the next decade due to injuries arising from increased use of motor vehicles, especially in low and middle income countries, where 85% of all RTIs are expected to occur [5,6].

There is a dearth of literature of etiology and incidence of pediatric head injuries in LMICs, especially in sub-Saharan Africa, where most studies have focused on adult population [7]. Younger children have a higher risk of head injury due to their larger heads, weak neck musculature and relative thin calvarium [8]. In children, causes of head injuries differ slightly. Previous studies from high income countries (HICs) have concluded that RTIs and falls constitute the two main causes of pediatric TBI [7–15]. For instance, in the US falls constitute the most frequent mechanism for children

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aged under 12 years, while adolescents are more prone to assaults, motor vehicle crashes and sports injuries [15]. However, in Nigeria, where Udoh et al. carried out the only currently published study focusing specifically on etiology of pediatric head trauma in a sub-Saharan African country, the etiology was different with motor vehicle injuries being the major cause (67.7%), followed by falls (14%) and then violence (7%) [15]. The World Health Organization has further substantiated these findings as it has concluded that RTIs are the leading cause of death among young people between 10 and 24 years, while falls constitute the most common cause in infants and toddlers [16].

Aside from the single descriptive study from Nigeria on etiology of pediatric head trauma, little is known regarding injury severity and mortality of pediatric neurotrauma patients. In HICs, the pre-resuscitation Glasgow Coma Scale (P-GCS), rated on scale of 3–15, is commonly used to describe injury severity, with GCS 13–15 representing minor head injuries, 9–12 representing moderate and 3–8 representing severe head injuries. It is useful measure of patient current neurologic status and a predictor of eventual mortality and outcome. However, in LMICs, only a handful of studies have stratified TBIs by GCS severity and studied patient outcomes and only one study which has done this exclusively in the pediatric population [3,15]. One study has suggested that the adult TBI patient population in LMICs, those presenting with severe head injuries have worse outcomes compared to their HIC counterparts [17]. In Uganda and Tanzania, mortality rate for severe TBI patients has been reported to be between 47 and 50% [3,18].

Overall, there is a lack of published literature that exists on pediatric head trauma in LMICs as well as factors associated with more severe presentation. Knowledge on what factors are associated with TBI severity and both poor morbidity and mortality would be beneficial in the development and implementation of effective preventative measures to decrease the number of childhood deaths resulting from TBI. The objective of this study was to evaluate the etiologies of and determine the factors associated with poor outcome, defined as GCS score < 13 and mortality, among pediatric patients at a major referral hospital in western Uganda.

2. Methods

This was a study at Mbarara Regional Referral Hospital (MRRH), Uganda, which serves as a referral hospital for Western region of Uganda, serving a population of over four million people [19]. The hospital has a capacity of 600 beds, 8 ICU beds and 8 operating theaters and has a surgical volume of 8515 operations per year [20]. The staff consists of 410 persons, of whom only one is a neurosurgeon [19].

We performed a retrospective chart review of all pediatric patients admitted to MRRH for a neurosurgical condition between 2012 and 2015. Patients with a TBI who are 18 years or younger were included in this study. Patient demographics, mechanism of injury (MOI) (categorized into RTI, fall, intentional injury and other), date of admission, date of discharge or date of death, admission and discharge Glasgow Coma Scale (GCS) categorized into mild (GCS of 13 or more), moderate (GCS of 12–13), and severe (GCS of 8 or less), primary diagnosis, categorized into unspecified head injury, brain edema and/or contusion, intracranial hemorrhage and skull fracture, neuroimaging done, and whether the patient had a neurosurgical intervention were recorded.

Our main outcomes of interest were in-hospital mortality (died or discharged), discharge GCS (dichotomized into poor outcome (less than 13) and positive outcome (more than 13). Frequencies and percentages stratified by discharge GCS and in-hospital mortality were reported MOI, length of stay (LOS), admission GCS, neuroimaging, primary diagnosis and neurosurgical intervention. A multivariable logistic regression analysis, using backward elimination, was used to identify variables that are predictive of the outcomes at a 0.05 significance level. The data was analyzed using Stata software version 14.

Ethical approval was obtained from Makarere University School of Medicine Research Ethics Committee, Mbarara University of Science and Technology Research Ethics Committee, and Duke University Health System Institutional Review Board.

3. Results

3.1. Demographics

A total of 381 pediatric TBI patients were admitted to MRRH between 2012 and 2015. The average age was 8.6 (SD 5.6, range 2 months to 18 years) with a male predominance (62.0%). The median length of stay was 5.5 days (IQR 3–10). Severe TBIs, defined as GCS $\leq$ 8, constituted 16.0% were all cases (GCS less than 8), while 13.0% had poor outcome (GCS $\leq$ 12) and 10.0% died. Of 4 age groups (<2, 2–5, 6–11, 12–18 years), patients under 2 years of age had the highest rate of poor outcome and in-hospital mortality (40.0% and 23.0%, respectively). There was no statistically significant difference between gender and GCS outcome ($p = .590$) or in-hospital mortality ($p = .301$). Further details on demographics are found in Table 1.

3.2. Mechanism of TBI

The most common mechanism of injury overall was RTI, which was responsible for 71% of all TBI cases. Falls contributed to 11.5% of injuries, while intentional injuries made up 9.9% and 7.6% of cases were due to other modalities. When stratified by age and sex, RTI remained the most common RTI in all groups (Fig. 1). In patient <2 years, fall was the second most common reported mechanism of injury, contributing to 12.5% of the TBI cases in females and 28.6% in males. Similarly, in patients aged 6–11 years falls remained the second most common TBI etiology, contributing to 18.4% and 30.9% of all TBI cases in females and males, respectively. Intentional injuries were highest in the age group 12–18 years, more common in females than males (20.0% vs 17.0%, respectively).

3.3. Diagnoses

Approximately 40.0% of admitted patients were able to obtain diagnostic neuroimaging (CT scan or Skull X-ray). The mortality rate was higher for those who did not have any neuroimaging done (13.0% vs 4.0%) ($p = .002$), but the GCS outcome was similar for those who did or did not have neuroimaging done (17.0% vs 16.0%) ($p = .410$). The most common documented diagnosis was unspecified head injury, representing 56% of the cases, while others were brain edema and/or contusion (13%), intracranial hemorrhage (13%) or skull fractures (18%).

3.4. Outcomes

Of all TBI cases, 13.0% had a neurosurgical procedure performed and had slightly better GCS outcomes and mortality in comparison to the group who did not have surgery (14.0% vs 17.0% and 9.0% vs 10.0%, respectively). Among patients admitted with a mild TBI, only 2.5 % had a poor outcome and 1% died. Meanwhile among those admitted with a moderate head injury, poor outcome was seen in 22.2% of patients and mortality rate was 7.7%. The greatest proportion of poor outcome and deaths was observed in those

Table 1
Characteristics of pediatric TBI patients presenting to MRRH between 2012 and 2015.

Characteristic	All patients (% of Subgroup Total)	Mild (GCS 13–15) N (%)	Moderate & Severe (GCS 9–12) N (%)	P value	Alive N (%)	Dead N (%)	P Value
Age, years							
<2 years	15 (3.9)	6 (60)	4 (40)	0.129	10 (76.9)	3 (23.1)	0.305
2–5 years	149 (39.3)	91 (80.5)	22 (19.5)		131 (89.7)	15 (10.3)	
6–11 years	93 (24.2)	63 (85.1)	11 (14.9)		83 (91.2)	8 (8.8)	
12–18 years	125 (32.6)	84 (87.5)	12 (12.5)		112 (91.8)	10 (8.2)	
Sex							
Female	148 (38.5)	97 (82.9)	20 (17.1)	0.590	132 (91.7)	12 (8.3)	0.301
Male	236 (61.5)	149 (83.7)	29 (16.3)		206 (89.6)	24 (10.4)	
Mechanism of Injury							
Road-traffic accident (RTI)	273 (71.1)	172 (81.5)	39 (18.5)	0.646	239 (90.2)	26 (9.8)	0.799
Fall	44 (11.5)	30 (90.9)	3 (9.1)		40 (93)	3 (7)	
Intentional Injury	38 (9.9)	23 (85.2)	4 (14.8)		35 (92.1)	3 (7.9)	
Other	29 (7.6)	21 (87.5)	3 (12.5)		24 (85.7)	4 (14.3)	
Mechanism (RTI Binary)							
RTI	273 (71.1)	172 (81.5)	39 (18.5)	0.119	239 (90.2)	26 (9.8)	0.527
Non-RTI	111 (28.9)	74 (88.1)	10 (11.9)		99 (90.8)	10 (9.2)	
Admission GCS							
Mild	193 (53.8)	156 (97.5)	4 (2.5)	<0.001	190 (99)	2 (1)	<0.001
Moderate	107 (29.8)	66 (77.7)	19 (22.4)		96 (92.3)	8 (7.7)	
Severe	59 (16.4)	20 (44.4)	25 (55.6)		35 (60.3)	23 (39.7)	
Length of Stay							
Median (IQR)	5.5 (3 –1 0)	5 (3 –9)	6.5 (2 –1 3)	0.824	6 (3 –1 0)	1 (0 –2)	<0.001
Neuroimaging							
Yes	148 (38.5)	103 (84.4)	30 (17.3)	0.410	139 (95.9)	6 (4.1)	0.002
No	236 (61.5)	143 (82.7)	19 (15.6)		199 (86.9)	30 (13.1)	
Primary Diagnosis							
Head injury, unspecified	202 (56.2)	134 (83.2)	9 (21.4)	0.625	187 (88.6)	24 (11.4)	0.553
Brain edema and/or Contusion	48 (13.3)	33 (78.6)	7 (17.5)		46 (93.8)	3 (6.1)	
Intracranial hemorrhage	47 (13.1)	33 (82.5)	27 (16.8)		44 (89.8)	5 (10.2)	
Skull fracture	63 (17.5)	46 (88.5)	6 (11.5)		61 (93.9)	4 (6.2)	
Neurosurgical Intervention							
Yes	48 (12.53)	32 (86.5)	5 (13.5)	0.527	43 (91.5)	4 (8.5)	0.414
No	335 (87.5)	213 (82.9)	44 (17.1)		294 (90.2)	32 (9.8)	

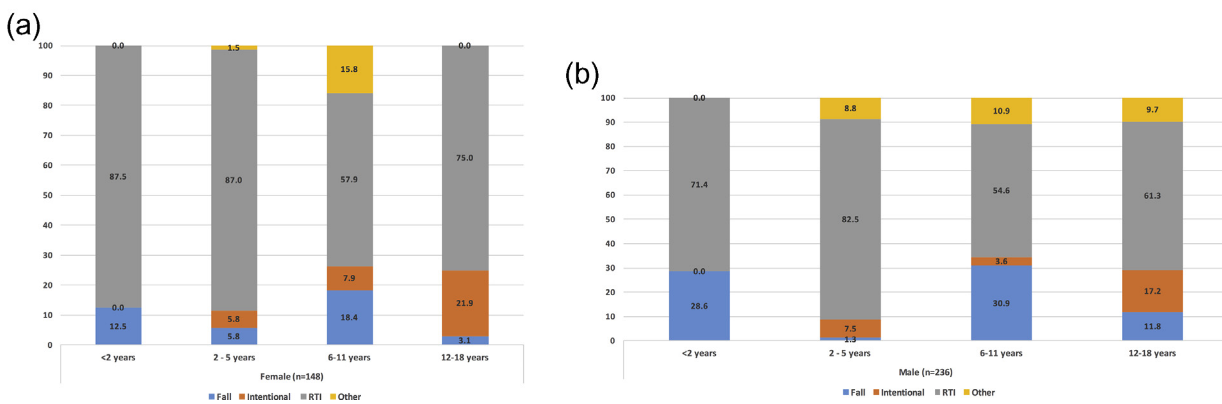

Fig. 1. TBI mechanism of injury by age group and sex.

admitted with severe injury (GCS of 8 or less), where more than half of these patients had a poor outcome (55.6%) and 39.7% died. There was an observed association between injury severity and poor outcome ($p \leq .001$) as well as injury severity and mortality ($p \leq .001$). A poor outcome rate of 17.5% and mortality rate of 6.1% was observed in those with brain edema and/or contusion. Those with a documented intracranial hemorrhage had second highest proportion of poor outcomes rate of 16.8% and a mortality of 10.2%, while those with a skull fracture had the lowest rate of poor outcome (11.5%) and a mortality rate similar to those with brain edema and/or contusion (6.2%). However, there was no statistically significant association between diagnosis and poor outcome ($p = .625$) or mortality ($p = .553$).

3.5. Multivariable analysis

In the multivariable logistic regression model, admission GCS < 13 was a strong predictor of poor outcome and in-hospital mortality compared to admission GCS ≥ 13, with patients demonstrating an odds ratio of 30 (95% CI: 7–132, $p < .001$) and OR of 18 (95% CI: 4–79, $p < .001$), respectively (Table 2). The odds of poor outcome in RTI related TBI cases was 1.3 compared to non-RTI related TBI cases

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Table 2
Multivariable logistic regression of predictors of mortality and poor outcome.

Predictor	Mild vs Moderate/Severe				Alive vs Dead			
	Odds Ratio	95% CI		P > z	Odds Ratio	95% CI		P > z
Age								
2–5 vs < 2 years	0.4	0.1	2.5	0.3	0.4	0.1	1.9	0.2
6–11 vs < 2 years	0.4	0.1	2.6	0.3	0.3	0.1	1.7	0.2
12–18 vs < 2 years	0.3	0.0	1.8	0.2	0.3	0.0	1.6	0.1
Sex								
Male vs Female	0.8	0.4	1.7	0.6	1.2	0.5	2.7	0.7
Mechanism of Injury								
RTI vs Non-RTI	1.3	0.6	3.1	0.5	0.6	0.2	1.6	0.3
Admission GCS								
<13 vs ≥ 13	30.9	7.2	132.3	<0.001	18.1	4.2	78.6	<0.001
Neuroimaging								
Yes vs No	0.7	0.3	1.6	0.4	0.2	0.1	0.7	<0.001
Primary Diagnosis								
Brain edema and/or Contusion vs Unspecified head injury	1.3	0.4	3.8	0.7	0.6	0.1	3.1	0.5
Intracranial hemorrhage vs Unspecified head injury	1.3	0.4	4.2	0.7	1.7	0.4	6.7	0.5
Skull fracture vs Unspecified head injury	0.9	0.3	2.7	0.8	0.9	0.3	3.0	0.9
Neurosurgical Procedure								
Yes vs No	1.3	0.4	4.3	0.7	0.5	0.1	2.5	0.4

(95% CI: 0.6–3.1, p = .5). Meanwhile the odds of mortality for a RTI patient compared to one who did not have an RTI related head trauma was 0.6 (95% CI: 0.2–1.6, p = .3). Patients who had a neurosurgical procedure demonstrated 0.5 odds of dying compared to those who did not (95% CI: 0.1–2.5, p = .4) but 1.3 times the odds of a poor outcome (95% CI: 0.4–4.3, p = .7) (Table 2).

4. Discussion

Head trauma constitutes one of the most common causes of death among children LMICs [21]. An understanding of factors associated with positive patient outcomes among pediatric TBI cases is sparse, particularly in Sub-Saharan Africa. These factors are important to understand given the particular vulnerability of children and the limited resources present in LMICs and Uganda. Only one such study exists, and it examined pediatric TBI epidemiological patterns in Nigeria [14,15]. Our study sought to demonstrate similar epidemiological patterns, but also to examine factors that may be particularly associated with positive outcomes following a TBI. The results show that admission GCS was the only factor significantly associated with discharge GCS. Additionally, while neuroimaging was not associated with improved discharge GCS, it was associated with improved mortality. Further studies should focus on corroborating these data and seeking to explain the lack of association of other factors.

Our data shows that the majority of TBIs affect children aging 2–5 years and 12–18 years and that older children were less likely to have a moderate/severe discharge GCS compared to children <2. Previously published studies have showcased a possible explanation for this age distribution. Older adolescents appear to be more likely to suffer TBIs secondary to traffic crashes while infants and toddlers common suffer TBI from falls due to larger head size, thinner skulls and an inability to protect themselves during a fall [9,15,22]. While RTIs were most common across all age groups, our results also demonstrate that infants were more affected by falls than other age groups.

In our study, males were more commonly affected by TBI across the age spectrum. Several other studies found similar results that TBI was more common among male children [8,22,23]. Satapathy and Chabok suggest that male gender predisposition to injury may due to differences in their physical activity preferences and risk-taking activities [8,23], though no associated was found between age and severity of outcome.

RTI was the most common mechanism of injury, followed by falls. Transport injuries are responsible for the majority of head and spinal injuries, particularly in developing countries [24]. Although RTI is most common overall falls continue to make up a significant proportion of head injuries in pediatric patients, especially those <2 years [8,12]. It is likely that contributors to this distribution include increased urbanization and traffic volume within Uganda in conjunction with lack of imposed traffic laws [25]. In our study, there was no association between mechanism of injury, including when we compared RTI vs non-RTI injuries, and severity of outcome. It is important to note that, most pediatric RTIs are actually pedestrian accidents and pedestrian RTIs tend to be severe in nature [22]. It is likely that outcome severity is associated with the specific role of the patient in the RTI, i.e. pedestrian, motorcycle passenger, etc, although the patient's role in an RTI was not specified in our study. We are currently conducting a detailed prospective study of pediatric patients presenting with head injuries to capture this detailed level of data.

We found that the most common primary diagnosis among pediatrics TBI presenting to MRRH was unspecified head injury, accounting for over half of all diagnosis in this patient population. Unfortunately, having an undiagnosed head injury means more limited treatment options and likely poorer outcomes. A study from the US noted that the presence of a subdural hematoma had a much higher sensitivity for poor outcome than the presence of other TBI subtypes [26]. It is possible that the same is true for the patient population in Uganda. A currently ongoing study as part of Duke Global Neurosurgery and Neurology (DGNN)'s partnership with MRRH, attempts to prospectively capture patient clinical presentation, radiographic findings, diagnosis, and management of all trauma patients presenting to MRRH in order to better guide treatment and improve outcomes.

There was no significant difference in outcome GCS of patients receiving neuroimaging investigations upon presentation compared to those who did not. However, patients were less likely to die if they underwent neuroimaging studies as part of their workup. Thus, it is possible that while neuroimaging findings can necessitate the need for a life-saving surgery in the most severe TBI patients, these investigation modalities are overused in patients presenting with mild head injuries. Similarly, Udoh et al.

has previously found that more than 90% of CT scans performed on alert children with mild TBIs are negative, suggesting CTs may be overused [15].

Over the four year course of this study, only a small number of patients had a moderate/severe GCS score at discharge, demonstrating a predilection for mild injury upon admission at all ages. Researchers have previously noted that between 48% and 65% of TBI patients present for hospital admission with mild TBIs [22,27]. This is likely why most children within our study did not undergo neuroimaging investigations or subsequent surgery following admission. Admission GCS was the only variable found to be significantly associated with discharge GCS. Being admitted with a GCS < 13 conferred a much greater chance of being discharged with a moderate or severe GCS. Fujii et al. also found that a lower GCS upon admission was associated with less favorable outcomes among adult TBI patients in the US [28]. Our study confirms the same association persistent among pediatric TBI patients in Uganda. This highlights the importance of increasing preventative measures to limit the occurrence and severity of pediatric TBIs on admission.

Data analyzed were retrospectively collected via a review of patient files and registers. Study limitations include an inability to track down information from patients during data collection. Moreover, other risk factors associated with outcome GCS may be present that we did not account for due the unavailability of this data in the patient charts. Furthermore, the documentation of the data depended on the individual healthcare provider, and thus was likely not consistent across all patient files. Finally, measuring GCS in younger children is often challenging and inconsistent, particularly the eye and verbal components [29]. This may mean that GCS is not an accurate and reliable outcome measure in pediatric TBI studies.

5. Conclusion

Given the lack of published literature on pediatric TBI in LMICs, this study was the first to describe and evaluate risk factors associated with TBI severity among pediatric patients at a major referral hospital in western Uganda. Admission GCS was the only variable found to be significantly associated with discharge outcome, though reception of neuroimaging was found to be associated with mortality. While future prospective studies are needed to further assess factors affecting the incidence and outcomes of pediatric TBI patients, this study ultimately highlights the need for more effective preventative measures to decrease admission severity.

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