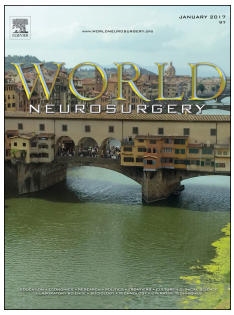
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Epidemiology and Characteristics of Neurosurgical Conditions at Mbarara Regional Referral Hospital

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Keywords:

Africa, Epidemiology, Global surgery, Neurosurgery, Uganda

Abbreviations:

CHI: Closed head injury

CNS: Central nervous system

GCS: Glasgow Coma Scale

HR: Hazard ratio

ICH: Intracranial hemorrhage

ICU: Intensive care unit

IQR: Interquartile range

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LMIC: Low- and middle- income countries

LOS: Length of stay

MHI: Mild head injury

MOI: Mechanism of injury

MRRH: Mbarara Regional Referral Hospital

RTI: Road traffic incident

TBI: Traumatic brain injury

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ABSTRACT

Background: The unmet surgical need, specifically neurosurgical need, in Uganda is significant, yet only two public hospitals currently perform neurosurgery in the country. This study examines the epidemiology and outcomes of neurosurgical conditions presenting to one of 12 regional referral hospitals in Uganda, in an effort to understand the neurosurgical needs of this population.

Methods: The study was conducted at Mbarara Regional Referral Hospital (MRRH), in southwestern Uganda. Demographics, clinical characteristics and outcomes were retrospectively collected for all patients that presented to MRRH with a neurosurgical condition between January 2012 to September 2015.

Results: During the study period, 1854 patients presented to MRRH with a neurosurgical condition. Over 50% of patients were between 19 and 40 years old and the majority of were males (76.1%). The overall median length of stay was 5 days (IQR:2.5-10). The majority of admissions were due to trauma (87%), with almost 60% due to road traffic incidents (RTIs). The overall mortality rate was 12.8%. A multivariable Cox proportional hazards model revealed that age, closed head injury and admission GCS have a strong positive correlation with mortality while getting a diagnostic image and neurosurgical procedure were negatively correlated with mortality.

Conclusion: Traumatic brain injury (TBI) represented the majority of neurosurgical admissions at MRRH, disproportionately affecting young males. Age, closed head injury, admission GCS, getting a diagnostic image and neurosurgical procedure were all independent predictors of mortality. Resource appropriate interventions throughout the health system are needed to meet the demand and improve outcomes.

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INTRODUCTION

The Lancet Commission on Global Surgery estimates that an additional 143 million surgical procedures are needed yearly in order to meet the world's surgical need, with the greatest unmet surgical need in sub-Saharan Africa (SSA) [1]. In these areas, the need for neurosurgery is likely substantial given the high incidence of traumatic brain injuries and congenital disorders [2-4]. Despite the need for neurosurgery, few neurosurgeons are currently trained and practicing in sub-Saharan Africa. Worldwide, there are 0.4 neurosurgeons per 100,000 people in the world, while the ratio in sub-Saharan Africa, other than South Africa, is 0.02 for every 100,000 people [5].

Uganda has a decentralized health system where healthcare is provided through a hierarchy of localized health centers, district hospitals, regional referral hospitals, and national referral hospitals. Of all operations, 73% are performed on an emergency basis, reflective of the high burden of trauma as well as the high proportion of patients that present to a health care provider with advanced pathologies, resulting in a backlog of elective cases [6]. Currently, neurosurgery is only performed at two public hospitals; Mulago National Referral Hospital (MNRH) and Mbarara Regional Referral Hospital (MRRH). Furthermore, there are only 7 neurosurgeons, or 0.02 per 100,000 people in the public hospitals, in Uganda as of 2015.

To overcome the lack of surgical services and build surgical capacity in Uganda, an integrative neurosurgical twinning program was established at MNRH in Kampala Uganda in 2007 through the collaboration between MNRH, Duke University Medical Center, and the Duke Global Health Institute [7]. The Duke-Mulago twinning program aimed to improve neurosurgical capacity in Uganda through three core initiatives: twining, training and technology. In the years since the program's inception, neurosurgical cases performed at MNRH increased by 180% and two neurosurgical residents have successfully completed their residency at MNRH [8]. Based on the success of the twinning program in improving the neurosurgical capacity at MNRH, the Duke-Mulago twinning program will expand to MRRH, the only other public facility in Uganda with a neurosurgery department. Prior to this expansion, it is critical to know the current neurosurgical case mix and patient outcomes at MRRH. The objective of our study was to describe the epidemiology of neurosurgical conditions at MRRH as part of an effort to understand the neurosurgical needs at MRRH for targeted expansion of the Duke-Mulago twinning program.

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MATERIALS AND METHODS

Setting

The study was focused in MRRH, a regional 300 bed referral hospital, located in Mbarara, Western Uganda. MRRH is located approximately 260 kilometers from Kampala, the capital of Uganda, and serves as the teaching hospital for Mbarara University of Science and Technology. In 2015, MRRH had 3,785 total hospital admissions and 1,640 surgeries. In 2012, a neurosurgery department was established and the hospital currently employs one neurosurgeon and several nurses and medical interns who are shared with other surgical specialties in the hospital. The neurosurgery department manages approximately 600 to700 patients and 200 to 250 operations per year.

Study design and Data Collection

A retrospective chart review was performed on all patients suspected to have a neurosurgical conditions admitted to MRRH from January 2012 to September 2015. Patients admitted to MRRH with a neurosurgical disease or injury and collaboratively or primarily managed by the neurosurgery department were eligible for this study. Neurosurgical disease or injury was defined as traumatic and non-traumatic brain injury, spinal cord injury, intracranial and central nervous system (CNS) tumors, intracranial and CNS infections, hydrocephalus, spina bifida, disc disorders and other spinal cord malformations.

Research assistants were trained to extract specific variables from medical charts and surgical logbooks of neurosurgical patients. The variables included: inpatient number, age, sex, date of admission, admission Glasgow coma scale (GCS), primary diagnosis, mechanism of injury (MOI), co-diagnosis, other diagnoses, diagnostic image findings, Intensive care unit (ICU) admission, date of surgery if any, and date of discharge or date of death. The research assistants recorded all the required variables on an excel spreadsheet data collection tool. After cross-checking for errors and completion, the data was de-identified, coded, and cleaned.

Primary diagnosis was coded into 11 categories: mild head injury (unconsciousness, or soft tissue injury [MHI]), closed head injury (brain edema or contusion [CHI]), intracranial hematoma (epidural, subdural, subarachnoid, or intracerebral hemorrhage [ICH]), skull fracture,

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spinal injury or fracture, hydrocephalus, spina bifida, CNS tumor (intracranial or spinal cord tumor), spine (spondylopathy, disc disorders or malformations of the spine), intracranial abscess and others (meningitis, encephalitis, stroke, scalp abscess or lipoma). Co-diagnosis was coded into none, skull fracture or CHI. Comorbidities, other diagnosis, ICU admission, and diagnostic imaging were all dichotomized into 0 or 1 (0 indicating none/no and 1 indicating present/yes). Mechanism of injury was coded into road traffic incident (RTI), fall, assault or other. Admission GCS was coded into mild (GCS of 13-15), moderate (GCS of 9-12) and severe (GCS of 3-8).

Ethical Considerations

Makerere University School of Medicine Research and Ethics Committee, Mbarara University of Science and Technology Research Ethics Committee, and Duke University Health System Institutional Review Board approved this study prior to implementation.

Statistical Analysis

The main outcome of interest was mortality during the hospital stay, including upon admission.

Patient demographic and clinical variables were evaluated with counts and percentages in contingency tables or with medians and interquartile ranges (IQRs) stratified by mortality outcomes.

Bivariate Cox proportional hazards regression was used to determine whether age, sex, LOS (length of stay), primary diagnosis, co-diagnosis (secondary neurosurgical condition), other diagnosis (non-neurosurgical condition), ICU admission, diagnostic imaging, mechanism of injury, admissions GCS and surgical intervention were associated with mortality. Due to small samples in non-trauma related patients, the regression analysis was restricted to trauma patients and to subjects with complete data (complete case analysis). 232 non-trauma patients were excluded and an additional 232 were excluded because of incomplete data, resulting in 1,390 patients in the final Cox proportional hazards model. The proportional hazards assumption was tested using Schoenfeld residuals. In order to create a multivariable model, all variables significant at p-value of 0.20 derived from the bivariate analyses were fit into a multivariable cox proportional hazards regression model. Using backward elimination, variables significant at p-

value of 0.05 were kept in the model, with mortality as the dependent variable. The data was analyzed using Stata software version 12[9].

RESULTS

Patient Demographics

During the study time frame, a total of 1,876 charts of patients who were suspected to have a neurosurgical condition were reviewed. Of these, 22 did not have a neurosurgical diagnosis or were not managed by the neurosurgery department and were excluded, resulting in 1,854 included in the final analyses. The overall mortality rate among neurosurgery patients admitted into MRRH was 12.8% (230 patients). The median age of all hospitalized neurosurgery patients was 27 years (IQR: 18-39 years). Over 50% of patients were between 19 and 40 years old and the majority of patients were male (76.1%). The overall median LOS was 5 days (IQR:2.5-10) (Table 1).

Clinical Characteristics

Of all neurosurgical admissions, 87% (1,622) were trauma patients, (defined as MHI, CHI, ICH, skull fracture, spine fracture, or injury. The highest mortality rate (24%) was observed among those with CHI. Diagnostic imaging was obtained for 44.1% of the patients, among whom the mortality rate was lower, 10.8% as compared to 13.3% for those who did not get a diagnostic image. Those with a GCS of 3-8 had a mortality rate of 51.2%, as compared to 13.1% for those with GCS of 12-9 and 3.7% for 13-15. The mortality rates among all patients who underwent a neurosurgical procedure was 9.7%, and was 13.7% among those who did not undergo a neurosurgical procedure (Table 1).

Predictors of Mortality

The median follow-up time was 6 person-days (IQR: 1-1,1112 person-days). The total time at risk was 16,374 days and the total number of deaths was 181. In the bivariate analysis, only age, sex, primary diagnosis, imaging, ICU admission, admission GCS and surgery were all significant at P value of 0.20 and therefore included in the multivariable model. (Table 2).

After multivariable adjustment, neurosurgical procedure and diagnostic imaging were independently negative predictors of mortality (P <0.05) and age, primary diagnosis of CHI, admission GCS were positive predictors of mortality (P <0.05) while sex and ICU admission were not significant after the multivariable adjustment (Table 3). In comparison to trauma patients who did not undergo a neurosurgical procedure, those who underwent a neurosurgical procedure were 38% less likely to die (HR: 0.62 [95% CI: 0.40, 0.96]). Those who had any type of diagnostic imaging done were 39% less likely to die (HR: 0.61, [95% CI: 0.45, 0.83]) as compared to those who did not have any diagnostic imagine done. In comparison to the 0-18 age group, the 19-40 and 41-65 were twice as likely to die (HR: 1.75 and 1.97, [95% CI: 1.25, 3.11 and 1.03, 3.55], respectively). While those who were 65 and above were three times more likely to die (HR: 3.25, [95% CI: 1.64, 6.43]). Those who had a closed head injury were one and half times more likely to die as compared to those with mild head injury (HR: 1.5, [95% CI: 1.09, 2.06]). In comparison to those with a GCS of 13-15, those with a GCS of 9-12 and 3-8 were three times (HR: 3.35, 95% [CI: 2.04, 5.51]) and fifteen times (HR: 15.19, [95% CI: 9.77, 23.61]) more likely to die, respectively.

DISCUSSION

Knowledge regarding the distribution of neurosurgical conditions in low- and middle-income countries (LMICs) and their associated mortality rates is limited. This study was the first to describe the spectrum of neurosurgical conditions and mortality rates of patients presenting to a referral hospital in Mbarara, Uganda. A majority of the neurosurgical admissions were males, the median length of stay was 5 days, and 13 out of every 100 admissions had an adverse outcome. Age, closed head injury, admission GCS, diagnostic imaging and neurosurgical procedure were independent predictors of mortality.

Among our patient population, traumatic brain injuries (TBI) were the predominant cause of neurosurgical admissions and deaths at MRRH. In fact, 87% of neurosurgical admissions were TBI patients. The mortality rate from TBI overall was 13%, while mortality from severe TBI was around 50%. A study by Staton et al. in Moshi, Tanzania reported similar results, with a 9% mortality rate for all TBI patients and 47% mortality rate for severe TBI patients [10]. Moreover, a four-month prospective study at Jimma University Hospital, Ethiopia, reported a mortality rate of 21% for all TBI patients [11]. Additionally, Tran et al. reported a 26% mortality rate for severe TBI

patients treated at Mulago National Referral Hospital in Kampala, Uganda [2]. In high-income countries, the mortality rate for severe TBI patients is estimated to be 30%, markedly lower than our findings, primarily due to the availability of pre-hospital care, quicker access to advanced imaging modalities, and better developed trauma systems [12,13]. Additionally, it is important to note that at MRRH, ICU level of care is severely lacking. In fact, there is only 1 ICU nurse to take care of 8 ICU beds. Moreover, there are no nurses trained in the provision of neuro-intensive care. Finally, there are only 3 ventilators for the 8 ICU beds.

Our findings demonstrate that young adults are disproportionately affected by TBI, with 60% of all TBI patients in our sample population falling between the ages of 19 and 40 years of age. Other studies in LMICs have reported that young working males are most vulnerable to TBI [14 15 10 2]. In comparison, there is a shift in the population affected by TBI in high-income countries towards older age groups [16]. Based on our anecdotal experience at MRRH, these individuals are more likely to operate boda-bodas (motorcycles), which significantly increases their risk of trauma. In fact, road traffic incidents (RTIs) were most common mechanism of injury in our study. Data from around the world show that 85% of RTIs occur in developing countries [17]. Although only 4% of motor vehicles in the world are in Africa, one tenth of deaths are in Africa secondary to RTIs and a higher burden of TBI is anticipated in the future [15,18].

Imaging was found to be negatively associated with mortality. Severity of injury could affect the ability to get a diagnostic image; if the patient has suffered a severe injury, they might not be stable enough to have imaging done and thus succumb to their severe head injury.

Surgical intervention was shown to be negatively correlated with mortality, even after adjusting for other important factors such as the patient's age, diagnosis, and GCS score. Timely and effective neurosurgical intervention can save a patient from a rapidly expanding brain hemorrhage, which would otherwise lead to GCS deterioration, herniation and death. However, there may be an element of confounding since patients with an extremely low GCS and a low chance of recovery may not be suitable neurosurgical candidates. Neurosurgeons, especially those in LMICs working with limited resources, have to be selective in whom they choose to intervene on. Still, despite the negative association between surgery and mortality, the mortality rate is high. This may be due to lack of prehospital care, trained and available neurosurgical workforce and severity of neurosurgical conditions at presentation.

There is an urgent need to expand the surgical workforce, improve the surgical infrastructure, and strengthen other supporting services [19]. Opportunities exist to improve neurosurgical care at MRRH. It is necessary to encourage more detailed documentation and tracking of patient data. Admission characteristics such as initial GCS, neurological examinations and vital signs are essential to triage head injury patients and develop prognostic models, especially in limited-resource settings[20,21]. Additionally, there is no pre-hospital care and this is one area that has been shown to improve outcomes. Jayaraman et al. demonstrated that implementing a first-responder program in Kampala aimed at addressing the lack of prehospital care is cost-effective, it would cost $25 per life-year saved and $598 per death averted [22]. A study by Mock and colleagues estimated that, in LMICs, up to 34–38% of all injury deaths could be averted by improving both prehospital care and in-hospital acute care [23]. Given limited resources, expanding the neurosurgical workforce and improving training of neurosurgical residents through creative solutions is vital. For instance, using electronic video conferences at neurosurgical training institutions can allow students from LMICs to discuss and seek advice on complex neurosurgical cases with collaborators worldwide[24]. Eventually, telemedicine and robotics will enable expert neurosurgeons to teach surgical procedures to neurosurgical residents remotely, in real time [24].

Strengthening neurosurgical support services, including rehabilitation, by training nurses and physical therapists in the care of neurosurgical patients and equipping the ICU with the necessary equipment and infrastructure will allow for better post-operative management and improve long-term cognitive outcomes and quality of life. Finally, it is necessary to note that technology and training have many advantages to building neurosurgical capacity within LMICs, real progress cannot be fully embraced without government support[25]. Although diseases of the central nervous system have not been viewed as a priority in LMICs, neurosurgeons worldwide must exert enough pressure on health care planners to prove the value of neurosurgery in their country [25].

Limitations

There are several limitations to our study. Our data was retrospectively collected, and was thus likely subject to confounding. Specifically, other risk factors associated with mortality may be present that we did not account for due the unavailability of this data in the patient charts we analyzed. Additionally, given data was abstracted from patient files and registrars, it was not

possible to track down missing information in real time. Furthermore, the documentation of the data depended on the individual healthcare provider, and thus was likely not consistent across all patient files. Finally, it is important to note that patients who survive severe or moderate traumatic brain injury may have residual neurological deficits with significant impairment in quality of life. Due to lack of necessary data, we were not able to address the morbidity of neurosurgical conditions at MRRH in this study.

CONCLUSIONS

Our study provides insights into the distribution and outcomes of neurosurgical conditions in Mbarara. The majority of neurosurgical admissions at MRRH are TBI, primarily due to RTI, with a large proportion being young males. Younger and mild TBI patients had a higher probability of survival, in addition to those who had a diagnostic image or a neurosurgical intervention. Going forward, further exploration of patient characteristics is necessary to fully describe mortality outcomes and implement targeted interventions that ultimately improve morbidity and mortality.

ETHICS COMMITTEE APPROVAL

Ethics committee approval was obtained from Mbarara University for Science and Technology Research Ethics Committee and Duke University Health System Institutional Review Board.

CONFLICTS OF INTEREST

None: The authors have no conflicts of interest.

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Table 1: Characteristics of Neurosurgery Patients at MRRH (n=1854)

Variable			All (n=1854) N (%)	Deaths (n=230) N (%)	Alive (n=1574) N (%)
Age		0-18	482 (27.45)	41 (8.51)	452 (91.49)
		19-40	918 (51.03)	118 (13.17)	778 (86.83)
		41-65	296 (16.17)	34 (11.97)	250 (88.03)
		65+	97 (5.35)	14 (14.89)	80 (85.11)
Sex		Female	431 (23.90)	38 (8.82)	393 (91.18)
		Male	1372 (76.10)	192 (13.99)	1180 (86.01)
LOS *		Median (25^{th},75th)	5 (2.5, 10)	1 (0,4)	6 (3,11)
Diagnosis	Trauma (n=1622)	MHI	511 (27.56)	29 (5.68)	482 (94.32)
		CHI	445 (24.00)	109 (24.49)	336 (75.51)
		ICH	384 (20.71)	50 (13.02)	334 (86.98)
		Skull fracture	209 (11.27)	18 (8.61)	191 (91.39)
		Spine fracture or Injury	73 (3.94)	7 (9.59)	66 (90.41)
	Non-trauma (n=232)	Hydrocephalus	34 (1.83)	2 (5.88)	32 (94.12)
		Spina bifida	23 (1.24)	0 (0.00)	23 (100.00)
		Tumor	48 (2.59)	8 (16.67)	40 (83.33)
		Spine	62 (3.34)	3 (4.84)	59 (95.16)
		Brain Abscess	11 (0.59)	3 (27.27)	8 (72.73)
		Other	54 (2.91)	1 (1.85)	53 (98.15)
Co-diagnosis		None	1653 (90.63)	207 (12.52)	1446 (87.48)
		CHI	120 (6.65)	18 15.00)	102 (85.00)
		Skull fracture	31 (1.72)	5 (16.13)	26 (83.87)
Other Diagnosis		None	1543 (85.53)	185 (11.99)	1358 (88.01)
		One or more	261 (14.47)	43 (17.24)	216 (82.76)
ICU Admission		No	1695 (93.96)	192 (11.33)	1503 (88.67)
		Yes	109 (6.04)	38 (34.86)	71 (65.14)
Diagnostic Imaging		No	1008 (55.88)	144 (13.29)	864 (85.71)
		Yes	796 (44.12)	86 (10.80)	710 (89.20)
MOI †		RTI	1082 (59.98)	153 (14.14)	929 (85.86)
		Fall	114 (6.32)	13 (11.40)	101 (88.60)
		Assault	332 (18.40)	37 (11.14)	295 (88.86)
		Other	276 (15.30)	27 (9.78)	249 (90.22)
Admission GCS ‡		Mild (13-15)	990 (60.66)	37 (3.74)	953 (96.26)
		Moderate (12-9)	390 (23.90)	51 (13.08)	339 (86.92)
		Severe (3-8)	252 (15.44)	129 (51.19)	123 (48.81)
Neurosurgical Procedure		No	1426 (76.96)	189 (13.68)	1193 (86.32)
		Yes	427 (23.04)	41 (9.74)	380 (90.26)

*LOS: Length of stay

†MOI: Mechanism of Injury

‡ GCS: Glasgow Coma Scale

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Table 2: Bivariate Cox Proportional Hazards Modeling of Variables Independently Associated With Mortality in Trauma Patients With Complete Data (n=1390)

Clinical variable		N (%)	HR (95% CI)	P- value
Age	0-18	346 (24.89)	ref	-
	19-40	763 (54.89)	1.43 (0.97, 2.11)	0.068
	41-65	213 (15.32)	1.21 (0.73, 2.02)	0.457
	65+	68 (4.89)	1.82 (0.94, 3.51)	0.076
Sex	Female	286 (20.58)	ref	-
	Male	1104 (79.42)	1.37 (0.92, 2.04)	0.120
Primary Diagnosis	MHI	443 (31.87)	ref	-
	CHI	385 (27.70)	4.14 (2.66, 6.44)	<0.001
	ICH	336 (24.17)	2.82 (1.24, 3.33)	0.005
	Skull fracture	180 (12.95)	1.34 (0.71, 2.54)	0.370
	Spine fracture or Injury	46 (3.31)	1.14 (0.34, 3.77)	0.834
Co-diagnosis	None	1256 (90.36)	ref	-
	CHI	108 (7.77)	0.82 (0.47, 1.41)	0.471
	Skull fracture	26 (1.87)	1.09 (0.40, 2.94)	0.466
Other Diagnosis	None	1192 (85.76)	ref	0.428
	One or more	198 (14.24)	1.17 (0.80, 1.70)	
ICU Admission	No	1320 (94.96)	ref	<0.001
	Yes	70 (5.04)	2.88 (1.94, 4.30)	
Diagnostic Imaging	No	757 (54.46)	ref	0.008
	Yes	633 (45.54)	0.67 (0.49, 0.90)	
MOI*	RTA	943 (67.84)	ref	-
	Fall	85 (6.12)	0.81 (0.41, 1.59)	0.537
	Assault	276 (19.86)	0.63 (0.41, 0.96)	0.032
	Other	86 (6.19)	0.64 (0.33, 1.26)	0.200
Admission GCS†	Mild (13-15)	827 (59.50)	ref	-
	Moderate (12-9)	351 (25.25)	3.76 (2.32, 6.10)	<0.001
	Severe (3-8)	212 (15.25)	16.05 (10.43, 24.69)	<0.001
Neurosurgical Procedure	No	1135 (81.65)	ref	0.054
	Yes	255 (18.35)	0.67 (0.45, 1.01)	

* MOI: Mechanism of Injury

† GCS: Glasgow Coma Scale

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Table 3: Multivariate Cox Proportional Hazards Modeling of Variables Independently Associated With Mortality in Trauma Patients With Complete Data (n=1390)

Predictor		HR (95% CI)	P-value
Age	**0-18**	ref	-
	19-40	1.75 (1.19, 2.58)	0.005
	41-65	1.97(1.17, 3.31)	0.010
	65+	3.25 (1.64, 6.43)	0.001
Primary Diagnosis	**MHI**	ref	0.012
	CHI	1.50 (1.09, 2.06)	
Imaging	**No**	ref	0.002
	Yes	0.61 (0.45, 0.83)	
Admission GCS*	**Mild (13-15)**	ref	-
	Moderate (12-9)	3.35 (2.04, 5.51)	<0.001
	Severe (8-3)	15.19 (9.77, 23.61)	<0.001
Neurosurgical Procedure	**No**	ref	0.031
	Yes	0.62 (0.40, 0.96)	

* GCS: Glasgow Coma Scale

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Highlights:

- The majority of admissions were due to trauma, with almost 60% due to road traffic incidents (RTIs).
- The overall mortality rate was 12.8%.
- Age, closed head injury and admission GCS were positively correlated with mortality.
- Getting a diagnostic image and neurosurgical procedure were negatively correlated with mortality.

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CONFLICTS OF INTEREST

None: The authors have no conflicts of interest.

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