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Mortality And Morbidity of Severe Traumatic Brain Injuries; A Pediatric Intensive Care Unit Experience over 15 Years

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ABSTRACT

Objective: To determine the mortality, morbidity, types of intracranial hemorrhages, and factors associated with length of stay (LOS) associated with accidental traumatic brain injury (TBI) at a pediatric intensive care unit (PICU) of a regional trauma center in an Asian city.
Methods: This study is a retrospective review of types of head injury, mortality and morbidity demographics of patients admitted to a PICU with TBI. All patients with accidental TBI were included, namely road traffic injury (RTI) and fall, and their demographics compared. Non-accidental injuries (NAI) were excluded.
Results: 95 children (78% males) were admitted to a PICU with RTI or falls from 2002 to 2017. They accounted for 3.7% of PICU admissions. Comparing with falls, victims of RTI were older ($p<0.001$) and more likely to suffer from skull fracture ($p=0.017$). There were 4 deaths with falls (6.8%) but none with RTI. Subarachnoid hemorrhages, extradural hemorrhages, the use of mechanical ventilation, inotropes and neurological supports were associated with longer LOS in PICU in these injuries ($p<0.001$).
Conclusion: A longer PICU LOS is associated with extradural and subarachnoid hemorrhages, usage of inotropes, mechanical ventilation and neurological supports in falls and RTI. Three-quarters of victims are males. Preventive health education should be especially directed to boys to reduce severe TBI in this Asian city.

Keywords: Mortality; Length of Stay; PICU; Traumatic Brain injury; Falls; Road traffic injury.

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Introduction

Accidental traumatic injury is a major cause of childhood morbidity. According to World Health Organization in 2004, about 950 000 children under 18 years old died because of injury every year worldwide [1]. Traumatic Brain Injury (TBI) is the most common regional injury when severe trauma occurs [2-4]. It was reported that TBI will surpass other diseases and become the major cause of death and disability by 2020 [5,6]. Etiology of HI is heterogeneous and varies from city to city. Referring to an Injury Survey by the Hong Kong Department of Health in 2008, fall was the major cause (41.9%) among all injuries in children aged from 0 to 14 years old; and road traffic injury (RTI) was more likely to cause TBI in adolescent [7]. TBI could also be caused by non-accidental injury (NAI) but the incidence was relatively low in Hong Kong. Hence, severe accidental TBI is primarily due to falls and RTI, and many patients necessitated multi-disciplinary team management and PICU support [8-11].

International guidelines for management of severe TBI have been evolving [12-17]. Among clinical parameters at admission to ICU, low Glasgow Coma Scale (GCS), hypotension (mean arterial pressure ≤80 mmHg), hypoxia (pO_2 ≤60 mmHg, spO_2 ≤90 mmHg), and non-reacting pupils were significantly associated with increased mortality ($p<0.05$) [18]. Often, the available evidence is not sufficient to generate guidelines addressing the most critical questions faced by clinicians and patients. Although there have been some major developments in severe TBI management, it was not possible to make many new evidence-based recommendations. Differences in management and clinical presentation of TBI in pediatrics versus adults are few, including (i) ICP monitoring is indicated in patients with severe TBI with a normal CT scan if ≥2 of the following features are noted at admission, namely age >40 years, unilateral or bilateral motor posturing, or SBP <90 mm Hg; and (ii) maintaining SBP at ≥100 mm Hg for patients 50 to 69 years old or at ≥110 mm Hg or above for patients 15 to 49 or >70 years old may be considered to decrease mortality and improve outcomes [12,13]. This study aims to review patterns of mortality, morbidity, length of stay (LOS) and intracranial hemorrhages of severe accidental TBI at a PICU of a regional trauma center.

Materials and Methods

Study Population

Clinical data of all accidental trauma victims of RTI and falls at the PICU of Prince of Wales hospital (PWH) from October 2002 to December 2017 were reviewed. All patients admitted to PICU with RTI and falls were included. Patients without TBI usually did not required PICU admission, and non-accidental injury (NAI) with TBI were excluded for analysis. In RTI, there are two kinds of victims: pedestrians and passengers (on a vehicle or bicycle). In falls, the accidents and injuries could take place indoor or outdoor. Information about the accidents was from the patients or witnesses. From the clinical records, imaging reports and the clinical management system, information on the types of cerebral hemorrhages and skull fractures were obtained. Brain hemorrhages were classified as: intracerebral hemorrhage, subdural hematoma (SDH), subarachnoid hemorrhage (SAH), and epidural/extradural hemorrhage. Ethical approval to perform this retrospective review/audit was obtained from The Joint Chinese University of Hong Kong (CUHK) Hospital Authority New Territories East Cluster (NTEC) Clinical Research Ethics Committee (CREC).

Study Protocol

Information on gender, age, length of stay and diagnosis was extracted from the PICU database which is updated monthly. The diagnoses were confirmed by the diagnostic codes at hospital discharge. PWH is a university-affiliated regional trauma center located in the New Territories of Hong Kong. Data on management of the accidental trauma including mechanical ventilation, use of inotrope, neurological support including neurosurgery, cerebral spinal fluid drainage, intracerebral pressure monitoring, use of antiepileptic drugs and mannitol were reviewed by the investigators. The patients were jointly managed by the PICU and neurosurgical teams according to standard practice and guidelines, with surgical, neurology, otorhinolaryngology, anesthesiology, radiology and multidisciplinary consultations as indicated [12-15, 19]. Indications and timing for neurosurgery and intracerebral monitoring were negotiated among the emergency physicians, the neurosurgeons, anesthesiologists and the intensivists. This review of PICU mortality and morbidity was approved by the institutional review board of the University and Hospital.

Statistical Analysis

Statistical analysis was conducted using SPSS 22. A two-tailed P values less than 0.05 is considered statistically significant. Categorical data between RTIs and falls were analyzed by Pearson's Chi-Square or Fisher's exact test. Continuous data were analyzed by Mann-Whitney test or Kruskal-Wallis test. Predictors of prolonged LOS at PICU due to falls and RTI were determined using a Poisson regression model. The dependent variable is LOS in PICU. Age, admission type, intracerebral hemorrhages, subdural hemorrhages, extradural/epidural hemorrhages, subarachnoid hemorrhages, intubation and mechanical ventilation, inotropes, anticonvulsant and neurosurgical support are taken as independent variables using a backward procedure. Variables with more than 20% of data missing were not included in the regression model.

Results

95 children (78% males) were admitted to a PICU with RTI and falls from 2002 to 2017 (Tables 1 and 2). The percentage of annual PICU admission due to RTI and falls varied from year to year (Table 2: 1.8 to 5.8% of annual PICU admissions), and was especially high in the years 2004 and 2009. The leading cause of childhood accidental injuries requiring PICU supports in this study population is falls. Most of these accidents were witnessed. RTI (n=36, 23

pedestrians, 10 bicycle riders, and 3 passengers.) and falls (n=59, majority occurred indoor) accounted for 3.6% of all the PICU admissions in the same period. In terms of types of HI, 24 patients had skull fractures, 23 patients were diagnosed with epidural hemorrhages, and 20 patients with subdural hemorrhage. Comparing with falls, victims of RTIs were older (median age was 8.9 versus 4.7 years in falls, $p<0.001$), and more likely to suffer from a skull fracture ($p=0.017$). There were 4 deaths with falls but none with RTI. Intracerebral hemorrhages, subarachnoid hemorrhages, extradural hemorrhage, the use of mechanical ventilation, inotropes and neurological supports were associated with a longer LOS in PICU. There was one outlier in the PICU LOS for more than 30 days, who was a RTI patient with a subarachnoid hemorrhage, a closed depressed fracture of skull vault and a low Glasgow coma scale of 5. There were 2 cases of TBI associated with non-accidental injuries (NAI) during the study period. They were not analyzed in this report due to their small number.

Overall, the most common management modalities in the PICU were mechanical ventilation (over one third of patients), inotrope usage (over 10% of patients) and neurological support (over one third of patients). Using a Poisson regression model, 6 variables were significantly associated with a longer PICU LOS, namely intracerebral hemorrhages, subarachnoid hemorrhages, extradural hemorrhage, mechanical ventilation, inotrope usage and neurological supports (Table 3). In particular, inotrope usage and extradural hemorrhages were the two leading factors associated with long LOS, when controlled for other parameters.

Discussion

This retrospective study over 15-years provides

Table 1. Clinical characteristic and outcomes of the two kinds of childhood accidents requiring PICU support

	RTI (36)	Fall (59)	*p* value
Age, mean (SD)	8.5 (2.91)	4.9 (3.46)	<0.001
Males	28 (77.8)	46 (78.0)	0.983
Hemorrhages			
Intracerebral hemorrhages	1 (2.8)	5 (8.5)	0.403
Subdural hemorrhages	4 (11.1)	16 (27.1)	0.063
Extradural hemorrhages	7 (19.4)	17 (28.8)	0.073
Subarachnoid hemorrhages	7 (19.4)	4 (6.8)	0.061
Skull fracture	14 (38.9)	10 (16.9)	0.017
Management			
Mechanical ventilation	16 (44.4)	23 (39.0)	0.600
Inotropes	5 (13.9)	7 (11.9)	0.761
Anticonvulsant(s)	12 (33.3)	17 (28.8)	0.653
Neurological supports	15 (41.7)	22 (37.3)	0.671
Death	0 (0)	4 (6.8)	0.294
PICU stay, mean(SD)	5.0 (6.24)	3.0 (3.52)	0.081

Values are number (%), unless stated and *p*-value was calculated using chi-square test except Mann-Whitney test for age and PICU stay; SD: standard deviation

Table 2. Annual PICU admissions due to RTI and falls from 2003 to 2017

Year	RTI & FALL	Total PICU Admission	Percentage
2003	7	122	5.74%
2004	9	155	5.81%
2005	5	112	4.46%
2006	6	127	4.72%
2007	6	144	4.17%
2008	5	138	3.62%
2009	8	140	5.71%
2010	5	149	3.36%
2011	9	198	4.55%
2012	5	187	2.67%
2013	4	226	1.77%
2014	7	190	3.68%
2015	5	216	2.31%
2016	4	212	1.89%
2017	10	234	4.27%
Total	95	2550	3.70%

RTI: Road Traffic Injuries

important information on morbidity of severe childhood HI due to falls and RTI. Over three-quarters of our patients were male. Several studies have documented a male preponderance in trauma and accidents which appears to be a worldwide phenomenon [20-23]. Male preponderance is observed in both RTI and fall. RTI victims can be a passenger or pedestrian. Many of the victims are not accompanied by an adult when the accident occurred. The male preponderance may be due to the cognitive-based factors of gender socialization regarding injury beliefs and risk taking behaviors, which contribute to a high-risk behavior in boys [7, 24, 25]. A previous Hong Kong study suggested that there is a higher male to female ratio comparing to other developed countries in childhood injury [7].

Mortality

Our analyses showed that the mortality of fall injury was 6.8% but none in RTI. The difference is not statistically significant. Worldwide, RTI ranks higher than falls in the top 15 leading causes of mortality and DALYs (disability-adjusted life years) among children under 15 years old [1, 26]. Although bicycle riding is a unique phenomenon in this part of the city, most children still travel by public transport system such as trains and buses. As such, injury as passengers in cars and small vehicles occurs less frequently. We speculated that a small number of children would have died before they were admitted to the PICU, and hence not represented in this sample. However, all RTI patients admitted to PICU survived. Hence rigorous management of RTI in PICU ensures survival. Overall falls account for the higher number of injury admissions in PICU in this hospital. There is evidence of increasing rates of fall-related attendance in accident and emergency department in Hong Kong and the rate remains high [4]. Many falls occurred indoors in Hong Kong. Death is usually due to delay in seeking medical attention [8, 27]. In a city full of high rises, falls from height is invariably fatal. Public education should focus on awareness of these avoidable factors, namely early medical attention and home window safety.

Length of PICU Stay

LOS in the PICU can be used as a measure of resource utilization. Our study shows that the presence of skull fracture does not significantly lengthen LOS which is consistent with a cohort analysis in the United States [28]. However, another United States study suggested that the presence of intracranial hemorrhage with skull fracture was associated with a longer LOS in general [29]. Nevertheless, the researcher did not further subdivide the CT findings [29]. This inconsistency may be due to many factors, including the heterogeneity of the study populations, model building as well as the difference in research design. A large-scale prospective study may provide more consistent results.

Patient suffering from subarachnoid or extradural hemorrhages had significantly longer LOS in PICU than those without these hemorrhage, which accounts to about 1.5 and 4.56 more days, respectively. A previous study found the presence of subarachnoid hemorrhage was associated with increased mortality among TBI patients [30]. Also subarachnoid or extradural hemorrhages are poor prognosis factor for TBI patients [31]. Interestingly, the presence of intracerebral hemorrhages is associated with increased odds of a better outcome in term of shorter LOS in PICU.

The use of mechanical ventilation is significantly associated with longer LOS in PICU. The use of mechanical ventilation may lead to ventilator-associated pneumonia which could prolong the LOS in ICU [32, 33]. Therefore, effective nursing caring should be applied to prevent ventilator-associated pneumonia in the PICU. Besides, the use of inotropes and neurological also indicates a longer LOS in the PICU. These factors may simply reflect the severity of the injury.

Limitations

Our study has several advantages. First, severe accidental injuries due to RTI or falls are relatively rare. Data about these injuries are generally not normally distributed. LOS is often treated as a continuous variable and the linear regression model is applied; but this can result in biased estimates. Therefore, a Poisson regression model is used in this study. We have collected relatively detailed information on the TBI condition. While doing the Poisson regression model we perform a selection of significant variable on the 13 variables and obtain the final model. We use backward selection in this study. A limitation of our study is that the sample size is relatively small. The result based on a region hospital may not representative. Also, since this is a retrospective study. Some of the variables which are not originally collected for research are less detailed. The potential risk factors studied were limited to those

Table 3. The Poisson regression model for length of stay in PICU among the patient admitted

Independent variable	Rate ratio	Estimate marginal means*	*p* value
Intracerebral hemorrhages	0.619	-3.54	0.024
Subarachnoid hemorrhages hemorrhageshemorrhages	1.501	1.50	0.001
Extradural hemorrhages	1.846	4.56	0.007
Mechanical ventilation	1.579	3.37	<0.001
Inotropes	2.234	6.05	<0.001
Neurological supports	1.537	3.18	<0.001

Table 4. Selected studies on outcomes of pediatric severe TBI in PICU

Countries	Mortality	PICU LOS	Long term outcomes	Year/References
Hong Kong (3/4 of victims are males)	6.8% in falls, none in RTI	A longer PICU LOS is associated with extradural and subarachnoid hemorrhages, usage of inotropes, mechanical ventilation and neurological supports in falls and RTI.	Not evaluated	2019
Canada	23% A lower PICU mortality for survivors beyond 24 hours who developed paroxysmal sympathetic hyperactivity,	A greater PICU LOS in survivors beyond 24 hours who developed paroxysmal sympathetic hyperactivity,	A lower likelihood of home discharge in survivors beyond 24 hours who developed paroxysmal sympathetic hyperactivity	2019 [44]
Singapore	Early hyperglycemia predicts for in-hospital mortality	Early hyperglycemia predicts for reduced ventilation-free, PICU-free and hospital-free days	Not evaluated	2017 [45]
Tennessee, USA	29% Mortality rates improved after implementation of a standardized protocol	7 days (mean)	Discharge disposition improved after implementation of a standardized protocol	2016 [46]
Singapore	20% Early hyperglycemia is associated with increased mortality	Early hyperglycemia is associated with prolonged duration of mechanical ventilation, and PICU stay	Not evaluated	2015 [47]
USA (70% male)	14%	Both fever and infection were associated with longer LOS.	Patients with higher fever burden had poor hospital discharge GCS score.	2006 [48]
Washington DC, USA	24% Patients with higher 6-hr GCS were more likely to survive Supranormal blood pressures are associated with improved outcome	2 days (median) Mannitol administration was associated with prolonged LOS, yet conferred no survival advantage.	Mannitol administration conferred no survival advantage.	2001 [49]

collected in the hospital record. The evaluation is cross-sectional. Since all the information is obtained from the hospital record, so the accuracy is reliable. Future studies in a large-scale population and collect the information prospectively will help address these issues. It is also possible that some variables that were not part of the hospital database could affect extended LOS (i.e., medical complication, GCS score [28, 34]. Other non-clinical factors (i.e., primary payor source, social support, discharge destination) could also be significant predictors of LOS [34-38].

Last, the small size of our study precluded us from studying outcomes with Glasgow outcome scale (GOS) and modified Rankin scale (mRS). In the literature, the most widely used and most studied coma score to date is the Glasgow Coma Scale (GCS), which is used worldwide to assess level of consciousness and predict outcome after traumatic brain injury (TBI). One study aimed to determine whether the Full Outline of Unresponsiveness (FOUR) score is an accurate predictor of outcome in TBI patients and to compare its performance to GCS [39]. The study was performed at a neuro-ICU unit and not a PICU. There was a high degree of internal consistency for both the FOUR score (Cronbach's alpha=0.89) and GCS. The FOUR score is a neurologic assessment score. Its benefit over pre-existing scores is its evaluation of brainstem reflexes and respiratory pattern. Studies including a systematic review of the literature on the application of the FOUR score within pediatric patients suggest the FOUR score is equivalent to GCS in outcome prediction in pediatric patients [40]. The FOUR score is an accurate predictor of outcome in TBI patients. It has some advantages over GCS, such as all components of FOUR score but not GCS can be rated in intubated patients. Neurologic outcome (Glasgow Outcome Scale (GOS) and Modified Rankin Scale (mRS) score 3-6) at 3-6 months were also among some of the scores used for longer term assessment of outcomes. The GOS-E Peds is sensitive to severity of injury and is associated with changes in TBI sequelae over time. This pediatric revision provides a valid outcome measure in infants, toddlers, children, and adolescents through age 16. Findings support using the GOS-E Peds as the primary outcome variable in pediatric clinical trials [41]. mRS is a commonly used scale for measuring the degree of disability or dependence in the daily activities of adult people who have suffered a stroke or other causes of neurological disability. It has become the most widely used clinical outcome measure for stroke clinical trials [41, 42].

Besides these two kinds of injuries, abuse would also cause abusive head trauma (AHT) or non-accidental injury (NAI) which is a unique problem in the field of pediatric TBI and has shown as an increasing contributing factor to the TBI cases in children in the United States [43]. However, there were only 2 cases of child abuse from 2002 to 2017 which is a rather small sample size. Therefore, we did not include them in analyses.

In conclusion, this study shows patients who were admitted as RTI or fall have a longer PICU LOS if they present with subarachnoid hemorrhages, extradural hemorrhage, use of inotropes, mechanical ventilation and neurological supports. An early identification and appreciation of these risk factors can lead to better treatment and resource utilization. This study provides mortality and morbidity information of severe childhood accidental trauma and injuries in Hong Kong. The results concur with those of other studies. Three-quarters of victims are males. Preventive health education should be especially directed to boys to reduce childhood accidents and injuries. The clinical data from the research focused on these children population can be useful in the future policy making or health service allocation.

Conflicts of Interest: None declared.

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